

**ABPI
DATA SHEET
COMPENDIUM
1983-84**

Gift Aid Product



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Data Sheet Compendium

1983–84

**Datapharm Publications Limited
12 Whitehall, London SW1A 2DY**

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The Compendium

Physiological Values

Weights and Heights

Obstetric Table

For the convenience of users of the Compendium, this edition includes physiological values for certain body fluids, tables of 'desirable' weights for men and women and an obstetric table.

This information can be found in the tinted section at the back of the Compendium.

Indexes

An alphabetical index of products, an index of non-proprietary names and a directory of participating companies (together with their telephone numbers) are provided in the tinted section at the back of the Compendium.

A list is also provided of products which are the subject of data sheets in this edition of the Compendium but which were not included in the 1981-82 edition.

Data sheets

Data sheets are supplied to practitioners in order to comply with the requirements of the Medicines Act 1968.

They are prepared by the individual companies concerned and, in consequence, vary somewhat in style. All follow, however, the requirements which are laid down by 'The Medicines (Data Sheet) Regulations 1972'.

Participation in the Compendium is open to all companies manufacturing medicinal products intended for use under medical supervision.

Further information

The regulations which relate to data sheets restrict the scope of the material which may be given under the heading 'Further information' and require insertion of the word 'Nil' in any data sheet where there is no entry under that heading. Manufacturers are, of course, none the less always willing to provide additional information on their products upon request.

Enquiries should be directed to the companies concerned.

Legal category

The following abbreviations are used under the heading 'Legal category' in entries in the Compendium.

GSL A preparation which is included in the General Sale List.

P A pharmacy sale medicine which can be sold only from a retail pharmacy.

POM A prescription only medicine.

MDA A preparation containing a substance included in Schedule 2 to the Misuse of Drugs Regulations 1973 (Misuse of Drugs Act 1971).

Doctors are reminded that the Misuse of Drugs Regulations 1973 lay down special requirements relating to the writing of prescriptions for products coming within Schedule 2.

Date of preparation

The data sheets included in this Compendium were prepared or reviewed during the third quarter of 1982 and the compendium itself was published in January 1983.

Revised data sheets

Individual participating companies may issue loose leaf data sheets which supersede those included in this Compendium.

It is advisable to retain any such revised data sheets which are received and to appropriately mark the corresponding entries in the Compendium.

Trade marks

An asterisk by the name of a product indicates that the name is a trade mark. The company symbols which appear in certain participants' sections are also trade marks.

Code of Practice for the Pharmaceutical Industry

Revised Fifth edition (April 1982)

For many years members of the Association of the British Pharmaceutical Industry have voluntarily agreed to observe the principles set out in a *Code of Practice for the Pharmaceutical Industry*; a Code which regulates the standards of conduct to be followed in the marketing of medicines intended for use under medical supervision.

The Code was first published in 1958 and has been regularly revised to take account of changes in marketing practices. A fifth edition was introduced in 1978 and revised in 1982; publication on each occasion following consultation with the British Medical Association and the Department of Health and Social Security. The Code embodies the basic principles and procedures which the pharmaceutical industry believes to be essential for the conduct of its marketing activities and for the maintenance of standards which are in the interests alike of the public, the medical and allied professions and the industry.

On occasion, the criticism has been made that members of the medical profession were not aware of the provisions of the Code and, consequently, that the Code had been less effective than might otherwise have been the case. To ensure that these provisions become better known, the revised fifth edition of the Code has been reproduced in its entirety below.

Those who feel that the promotion of a medical speciality product has fallen below the standards which are required by the Code may write, if they so wish, to the Secretary, Code of Practice Committee, The Association of the British Pharmaceutical Industry, 12 Whitehall, London SW1A 2DY, and ask that the matter be investigated.

INTRODUCTION

a This Code of Practice for the Pharmaceutical Industry has been drawn up after consultation with the British Medical Association and the Department of Health and Social Security.

b The Code owes its origin to the determination of the Association of the British Pharmaceutical Industry to secure the acceptance and adoption of high standards of conduct in the marketing of medical products designed for use under medical supervision.

c Medical products usually owe their existence to research carried out by their manufacturers or to the development by them of results of academic research. Before a medical product is placed on the market the manufacturer will have accumulated considerable toxicological, pharmacological and clinical evidence and will have met all the statutory requirements for the testing, manufacture and marketing of that product. Comprehensive legislation has been introduced to safeguard the public by ensuring that all products meet standards of quality, efficacy and safety which are acceptable in the state of present knowledge and experience.

d It is necessary, however, for the manufacturer, operating as he does in a keenly competitive industry and serving professions for which freedom of choice is essential, to draw attention to the existence and nature of a particular product; for example, by appropriate promotional measures and the dissemination of further knowledge and experience gained in widespread use.

e While it is possible to legislate satisfactorily for the testing, manufacture and control of medical products, the Association believes that appropriate standards of

marketing conduct cannot be defined by the same means. For this reason, members of the Association have concurred in the promulgation of the Code of Practice and submitted to its restraints.

f The Code emphasises the importance in the public interest of providing the medical and allied professions with accurate, fair and objective information on medical products so that rational prescribing decisions can be made. Moreover, the Code accepts the principle that such information should be presented in a form and by ways and means which conform not only to legal requirements but also to ethical standards and canons of good taste.

The industry recognises its obligations to provide information about medical products to the pharmaceutical profession and the principles set out in this Code, therefore, apply equally to communications addressed to that profession. However, there may be instances where compliance with every provision of the Code would be inappropriate; for example, in connection with promotional material the purpose of which is to convey information of a commercial nature to pharmacists or pharmaceutical distributors.

g The Code, therefore, represents an act of self-discipline. Acceptance and observance of its provisions are a condition of membership of the Association of the British Pharmaceutical Industry. Member companies also acknowledge that the Code itself is to be applied in the spirit, as well as in the letter.

Pharmaceutical companies outside the Association are invited to accept and observe the Code because it is considered that high ethical standards should be followed throughout the whole industry if it is to maintain the confidence of all the interests which it serves.

CODE OF PRACTICE FOR THE PHARMACEUTICAL INDUSTRY

h The Code is administered by a Committee established by the Board of Management of the Association. The Committee, with an independent legally qualified Chairman from outside the industry, consists of two independent members who are medically qualified persons not engaged in the industry, and twelve members who are drawn from the senior management of member companies, including at least four medical directors or medically qualified persons of equivalent status.

The Chairman has general authority to obtain expert assistance in any field, and has an original and a casting vote.

i The Committee meets regularly to deal with complaints, to secure compliance with the Code, and to make such recommendations as it deems fit for the amendment of the provisions of the Code.

j An outstanding feature has been the success of voluntary compliance with the provisions of the Code and acceptance of the rulings of the Committee. It has not been found necessary to apply sanctions to secure compliance because members of the Association are anxious to ensure that their marketing activities conform to the highest standard.

k It is important, therefore, that the Code should accurately reflect that standard and for this reason it is kept under constant review by the Board of Management and amended from time to time where necessary to clarify it and bring it up to date. Notes for the guidance of member companies are issued periodically to keep them informed of the rulings and recommendations of the Committee and of any alterations to the Code.

l This edition of the Code supersedes all previous issues and is the fifth edition since the Code was established in 1958. It embodies the basic principles and provisions which the pharmaceutical industry believes are essential for the conduct of its marketing activities and for the maintenance of standards which are in the interests alike of the public, the medical and allied professions and the industry.

PROVISIONS OF THE CODE

The supplementary text, which appears in italics, is intended to give guidance as to the interpretation of the Code.

1 Definition of certain terms

1.1 The term 'promotion' means those informational and marketing activities, undertaken by the product licence holder or with his authority, the purpose of which is to induce the prescribing, supply or administration of his medical products. It includes, for example, the activities of representatives; various aspects of sales promotion such as journal and direct mail advertising; the use of films and other audio-visual material and exhibitions; and the provision of samples, gifts or hospitality.

The term 'promotion' does not extend to:

(i) Replies made in response to enquiries from particular doctors or to replies in response to a specific communication, whether of enquiry or comment, including letters published in a medical journal.

(ii) Announcements of pack changes, adverse reaction warnings or recall of products provided they contain no product claims.

(iii) 'Trade advertisements' as defined in the Medicines

(Advertising of Medicinal Products) Regulations 1975, i.e. catalogues, price lists or other documents issued with a view to wholesale dealing but not containing any reference to product usage other than a therapeutic classification.

By 'wholesale dealing' is meant the sale of a product to a person who, during the course of his business or professional practice, buys it for the purpose of selling it or administering it or causing it to be administered to one or more human beings.

1.2 The term 'medical product' means any unbranded or branded pharmaceutical product intended for use in humans which is promoted to the medical profession rather than directly to the lay public.

1.3 The term 'medical profession', 'practice of medicine', 'practitioner' and 'doctor' should be interpreted to extend to the dental profession and be construed accordingly.

1.4 The term 'medical representative' means a representative whose duties comprise or include calling upon members of the medical profession.

2 Methods of promotion

Methods of promotion must never be such as to bring discredit upon, or reduce confidence in, the pharmaceutical industry.

The issue of rubber stamps to doctors for use as aids to prescription writing is one of the methods of promotion barred by this clause.

3 Nature and availability of information

3.1 Upon reasonable request, the company concerned shall promptly provide members of the medical profession with accurate and relevant information about the medical products which the company markets.

3.2 Information about medical products should accurately reflect current knowledge or responsible opinion.

3.3 Information about medical products must be accurate, balanced and must not mislead either directly or by implication.

Claims for superior potency per unit weight are meaningless and best avoided unless they can be linked with some practical advantage, e.g. reduction in side-effects or cost of effective dosage.

3.4 Information must be capable of substantiation, such substantiation being provided without delay at the request of members of the medical profession.

4 Claims and comparisons

4.1 Claims for a medical product must be based on an up-to-date evaluation of all the evidence and must reflect this evidence accurately and clearly.

4.2 Exaggerated claims should not be made and all-embracing claims and superlatives avoided. Claims should not imply that a medical product, or an active ingredient, has some special merit, quality or property unless this can be substantiated.

Claims such as 'agent of choice' should be avoided unless they can be clearly substantiated.

4.3 Any statement about side-effects should be specific and based on data submitted with the licence application or notified to the licensing authority, or on published data to which references are given. It should not be stated that a product has no side-effects, toxic

hazards or risks of addiction. The word 'safe' must not be used without qualification.

4.4 The word 'new' should not be used to describe any product or presentation which has been generally available, or any therapeutic indication which has been generally promoted, for more than twelve months in the United Kingdom.

4.5 Comparisons of products must be factual, fair, and capable of substantiation. In presenting a comparison, care must be taken to ensure that it does not mislead by distortion, by undue emphasis, or in any other way.

'Hanging' comparatives, which merely claim that a product is 'better' or 'stronger' etc, should not be used.

4.6 Brand names of products of other companies must not be used unless the prior consent of the proprietors has been obtained.

5 Disparaging references

5.1 The products or services of other companies should not be disparaged either directly or by implication.

Substantiated comparative claims inviting fair comparisons with a group of products or with other products in the same field are permissible, provided that such claims are not presented in a way which is likely to mislead, whether by distortion, undue emphasis or otherwise.

5.2 The clinical and scientific opinions of members of the medical and allied professions should not be disparaged either directly or by implication.

6 Printed promotional material

6.1 The Medicines Act 1968 requires a pharmaceutical company to provide a practitioner with a data sheet before promoting a product directly to him. The content of such data sheets is determined by Regulations made under the Medicines Act.

Data Sheets for many prescription products are published in the ABPI Data Sheet Compendium which is issued at regular intervals. Copies of the Compendium are supplied to members of the medical and pharmaceutical professions.

6.2 All other printed material (including journal advertising) which is issued for promotional purposes by the product licence holder or with his authority must include certain information specified in this Code.

The requirements of Clause 6.3 or 6.4, as appropriate, must be complied with in any advertising directed towards the medical profession even if it is of a general nature, e.g. prestige advertisements listing a company's products.

An advertisement which would not otherwise conform with the Code should not be regarded as doing so by reason only of the fact that the content of the data sheet is reproduced as part of the advertisement or because a data sheet is sent with the advertisement.

6.3(i) Except for 'abbreviated advertisements', as defined in Clause 6.4, the following information must be given clearly and concisely on printed promotional material:

- a** The number of the relevant product licence and the name and address of the holder of the licence, or the business name and address of the part of his business responsible for the sale of the product.
- b** A quantitative list of the active ingredients, using approved names where such exist, or other non-proprie-

tary names; alternatively, the non-proprietary name of the product if it is the subject of an accepted monograph.

Attention is drawn to the fact that the Medicines (Advertising to Medical and Dental Practitioners) Regulations 1978 (SI 1978 No. 1020) impose additional requirements which relate to the position and type size of this information.

c At least one authorised indication for use consistent with the data sheet.

d A succinct statement of the information in the data sheet relating to the dosage and method of use relevant to the indications quoted in the advertisement and, where not otherwise obvious, the route of administration.

e A succinct statement of the side-effects, precautions and contra-indications relevant to the indications in the advertisement, giving, in an abbreviated form, the substance of the relevant information in the data sheet.

f Any warning issued by the Medicines Commission, a committee appointed under Section 4 of the Medicines Act 1968 or the licensing authority, which is required to be included in advertisements.

g The cost of a product, except in the case of advertisements in journals which have an appreciable proportion of their circulation outside the United Kingdom.

The cost of a product is the cost (excluding value added tax) of either a specified package of the product, or a specified quantity or recommended daily dose, calculated by reference to any specified package of the product.

Attention is drawn to the fact that the Medicines (Advertising to Medical and Dental Practitioners) Regulations 1978 (SI 1978 No. 1020) impose a specific requirement to that proportion of the circulation of a journal which has to be outside the United Kingdom in order to qualify for the exception to this requirement.

6.3(ii) The information required by Clause 6.3 (i) (d), (e) and (f) must be printed in such type and in such a position that its relationship to the claims and indications is readily appreciated by the reader.

6.4(i) The requirements of Clause 6.3 do not apply in the case of an 'abbreviated advertisement'. An 'abbreviated advertisement' is one, the text of which contains in relation to the product no more than:

- a** The brand name of the product.
- b** The approved names of the active ingredients, where such names exist, or other non-proprietary names; alternatively, the non-proprietary name of the product if it is the subject of an accepted monograph.

Attention is drawn to the fact that the Medicines (Advertising to Medical and Dental Practitioners) Regulations 1978 (SI 1978 No. 1020), impose additional requirements which relate to the position and type of this information.

c The name and address of the product licence holder, or the business name and address of the part of his business responsible for the sale of the product.

d One indication for use, or more than one indication provided that these are related, consistent with the data sheet.

e A concise statement, consistent with the data sheet, giving the reason why the product is recommended for such indication or indications.

f A form of words which indicates clearly that further

information is available on request to the licence holder or is to be found in the data sheet relating to the product.

6.4(ii) An 'abbreviated advertisement' must always contain the information required by Clause 6.4(i) (a), (b), (c) and (f). The information required by Clause 6.4(i) (d) and (e) is optional. An 'abbreviated advertisement' must not include any illustration which is likely to convey any information about the product or imply claims which are additional to those provided in accordance with Clause 6.4(i) (a) to (e) inclusive.

6.4(iii) An 'abbreviated advertisement' directed towards a doctor is permissible only when it constitutes an advertisement appearing in a publication sent or delivered wholly or mainly to doctors. A loose insert included in such a publication cannot be an 'abbreviated advertisement'.

Attention is drawn to the fact that the Medicines (Advertising to Medical and Dental Practitioners) Regulations 1978 (SI 1978 No. 1020) impose additional requirements which relate to the maximum permitted size of an 'abbreviated advertisement'.

6.4(iv) An 'abbreviated advertisement' is not permissible where the Medicines Commission, a committee appointed under Section 4 of the Medicines Act 1968 or the licensing authority, have required a warning to be included in any advertisement relating to the medical product, and the licensing authority have issued a direction that 'abbreviated advertisements' should not be issued.

6.5 Promotional material, such as mailings and journal advertisements, must not be designed to disguise its real nature.

Doctors rightly resent receiving promotional material in the guise of personal communications, as when advertisements are enclosed in a plain envelope or are addressed in real or facsimile handwriting on letters or postcards.

Envelopes should not be used for the dispatch of promotional material if they bear words implying that the contents are non-promotional, e.g. that the contents provide information relating to safety.

It is advisable to use first class mail only for important communications of a non-promotional nature such as notifications of warnings or cautions or the withdrawal or recall of a product.

Advertisements in journals should not be designed so as to resemble editorial matter.

6.6 Promotional material should conform, both in text and illustration to canons of good taste and should recognise the professional standing of the recipients.

Representations of the nude female form (even in silhouette) or partly clothed figures should not be used in promotional material in such a way as to arouse a visual or emotional response in order to attract attention to the text.

Displays of part of the naked body which are necessary to illustrate pictorially the message of the text are permissible provided that they conform to the dictates of decency and good taste.

6.7 Doctors' names or photographs must not be used in a prominent manner in promotional material or in any other way that is contrary to the ethical code of the medical profession.

6.8 Promotional material should not imitate the devices, copy, slogans or general layout adopted by other companies in a way that is likely to mislead or confuse.

6.9 Where appropriate, for example, in technical and other informative material, the date of printing or the last review should be stated.

6.10 Extremes of format, size or cost of printed material should be avoided.

Large size mailings which cannot be put through letter boxes are a source of irritation to doctors and should be avoided as far as possible.

6.11 Postcards, other exposed mailings, envelopes or wrappers should not carry matter which might be regarded as advertising to the lay public or which could be considered unsuitable for public view.

Postcards and other exposed mailings should not contain copy or illustrations which ought not to be read or seen by lay persons.

6.12 Telegrams must not be used for promotional purposes.

6.13 In a multi-page press advertisement in which the pages follow consecutively, only one page need include the information required by Clause 6.3 of the Code, provided that each of the other pages (except the page on which, or facing which, the information is printed) includes a reference, on an outer edge, in at least 8 point type, indicating on which page that information appears. No initial recto or final verso must be false or misleading if read in isolation.

A loose insert included in a journal is not regarded as a 'multi-page press advertisement' for the purpose of this clause.

6.14 In a multi-page advertisement other than a press advertisement, the information required by Clause 6.3 of the Code must appear on one or more continuous pages and, where such an advertisement consists of more than four pages, the advertisement must include a clear indication as to where this information may be found.

7 References to official bodies

Promotional material should not include any reference to the Medicines Commission, a committee appointed under Section 4 of the Medicines Act 1968 or the licensing authority, unless this is specifically required by the licensing authority.

8 References to the National Health Service

8.1 Where reference is made to the prescribing of a product under the National Health Service, the phrase 'freely prescribable' or similar phrases suggesting a lack of restriction or restraint must not be used.

This clause was inserted in the first edition of the Code in deference to the wishes of the then Ministry of Health. 'Freely' in this context means 'without restriction or restraint'.

Although NHS doctors are free to prescribe whatever medicines they consider necessary for the treatment of a patient, they are nevertheless required to exercise due economy.

8.2 Reproductions of official documents, such as prescription form FP 10, should not be used for promotional purposes unless the agreement of the appropriate Government department has been received.

The term 'reproduction' includes any depiction which simulates or might be taken to simulate the document in question.

9 Artwork, graphs, illustrations, etc.

9.1 Illustrations must not mislead as to the nature of the claims or comparisons being made, nor as to the purposes for which the product is used; nor should illustrations detract from warnings or contra-indications.

9.2 Artwork and graphs must conform to the letter and the spirit of the Code. Graphs and tables should be presented in such way as to give a clear, fair, balanced view of the matters with which they deal, and should only be included if they are strictly relevant to the claims or comparisons being made.

9.3 Graphs and tables must not be used in any way which might mislead; for example, by their incompleteness or by the use of suppressed zeros or unusual scales.

10 Reprints, abstracts and quotations

This clause is included to accord with the views of the Ethical Committee of the British Medical Association; its object is to avoid the risk of contravention of the BMA Code of Ethics.

10.1 Reprints of articles by members of the medical profession must not be included in mailings but may be supplied to individual doctors on request. It is permissible to include in promotional material reasonably brief abstracts of, or quotations from, articles by members of the medical profession and to include in such material reference to doctors' names in a bibliography of published works. In no case, however, should doctors' names be used in a prominent manner in promotional material.

Quotations from public broadcasts, e.g. radio and television, may not be used in promotional material. It is permissible to use quotations from private occasions, e.g. medical conferences or symposia, with the written permission of the speaker.

10.2 Quotations from medical literature, or from personal communications received from doctors, must accurately reflect the meaning of the author and the significance of the study.

10.3 The utmost care must be taken to avoid ascribing claims or views to medical authors when such claims or views no longer represent, or may not represent, the current views of the author concerned.

11 Distribution of printed promotional material

11.1 Promotional material should only be sent or distributed to those categories of persons whose need for, or interest in, the particular information can reasonably be assumed.

11.2 Any information designed to encourage the use of medical products in clinics, industrial concerns, clubs or schools must be addressed to the medical adviser or medical officer or to medical auxiliary staff.

11.3 Restraint should be exercised on the frequency of distribution and on the volume of promotional material distributed.

The style of mailings is relevant to their acceptability to doctors and criticism of their frequency is most likely to arise where their informational content is limited or where they appear to be elaborate and expensive. A higher frequency rate will be accepted for mailings on 'new' products than for others.

11.4 Mailing lists must be kept up to date. Requests from doctors to be removed from promotional mailing lists must be complied with promptly and no name may

be restored except at the doctor's request or with his permission.

12 Audio-visual material

12.1 Audio-visual material must comply with all relevant requirements of the Code, with the exception of Clause 6.3.

12.2 When audio-visual material is used to promote a product, copies of the relevant data sheet, or a document with the same content, should be made available to all persons present.

12.3 Audio-visual promotional material is subject to the certification requirements of Clause 13.

13 Certification of printed promotional material

13.1 No promotional material shall be issued unless the final text and layout have been certified by two persons on behalf of the member company in the manner provided by this Clause. One of the two persons shall be a doctor. The other shall be a pharmacist or some other appropriately qualified person or a senior official of the company. The doctor, pharmacist or other qualified person must be a senior employee of the company or an appropriately qualified person whose services are retained for that purpose.

13.2 The names of those nominated, together with their qualifications, shall be notified in advance to the licensing authority. The names and qualifications of designated alternative signatories must also be given. Changes in the names of nominees must be promptly notified.

13.3 The certificate shall certify that the signatories have examined the material in its final form and that in their belief it is in accordance with the requirements of the relevant advertising regulations and this Code of Practice, is consistent with the product licence and the data sheet, and is a fair and truthful presentation of the facts about the product.

13.4 Member companies shall preserve all certificates, together with the material in the form certified, for not less than three years and produce them upon request from the licensing authority or the Association at the instance of the Code of Practice Committee.

13.5 The foregoing procedure shall apply, with the necessary variations, to the certification of briefing material for representatives in accordance with Clause 15.12 and to audio-visual promotional material prepared by or on behalf of member companies.

14 Suspension of advertisements

In the event of the Code of Practice Committee requiring a member company to withdraw an advertisement pending its decision on a complaint by the licensing authority relevant to the safe or proper use of the product, the member company shall at once make every possible endeavour to comply.

15 Medical representatives

15.1 Medical representatives must be adequately trained and possess sufficient medical and technical knowledge to present information on the company's products in an accurate and responsible manner.

15.2 Medical representatives should at all times maintain a high standard of ethical conduct in the discharge of their duties.

15.3 The requirements of the Code which aim at accuracy, fairness, balance, good taste apply to oral representations as well as printed material.

15.4 Unfair or misleading comparisons or comparisons implying a therapeutic advantage which is not in fact justified must be avoided by medical representatives.

15.5 Claims made for products by medical representatives must be limited to the indications permitted by the product licence.

15.6 Medical representatives must not employ any inducement or subterfuge to gain an interview. No payment of a fee should be made for the grant of an interview.

The practice of gaining or extending an interview on the pretext of carrying out a survey is to be avoided. This does not preclude the use of medical representatives to obtain bona fide survey information, but it is essential that the survey should be devised and conducted so as to leave no doubt in the doctor's mind that the survey will produce medically useful information.

15.7 Medical representatives must ensure that the frequency timing and duration of calls on doctors, or on hospitals, together with the manner in which they are made, do not cause inconvenience. The wishes of an individual doctor, or the arrangements in force at any particular establishment, must be observed by medical representatives.

The number of calls made on a medical practitioner and the intervals between successive visits are relevant to the determination of frequency.

Companies should arrange that intervals between visits do not cause inconvenience to practitioners and the number of calls made by a medical representative each year should not normally exceed, on average, three visits to each doctor.

Averages are to be calculated separately for general practitioners and other members of the medical profession to whom visits are made.

The calculation should exclude:

- (i) Attendance by a medical representative at a scientific meeting or an audio-visual presentation given to a group of doctors.
- (ii) A visit which is requested by a doctor or a call which is made in order to respond to a specific enquiry.
- (iii) A visit to follow up a report of an adverse reaction.

A medical representative should not stay in a surgery in which another medical representative is already waiting, except with the doctor's or receptionist's approval.

Medical representatives must always endeavour to treat the doctor's time with the utmost respect and give him no cause to believe that his time might have been wasted. If, for any unavoidable reasons, an appointment with a doctor cannot be kept, the longest possible notice must be given.

Calls on hospital medical staff should generally be limited to matters likely to be of specific interest to them. The majority are specialists and medical representatives should ensure that their specialised interests are borne in mind. It is preferable for most hospital staff to be seen only after making a prior appointment, at which time subjects for discussion should be identified.

15.8 Medical representatives must take adequate precautions to ensure the security of medical products in their possession.

15.9 Medical representatives must not use the telephone to promote products to the medical profession unless prior arrangement has been made with individual doctors.

15.10 Medical representatives should be paid on the basis of a fixed basic salary, and any addition proportional to sales of prescription medicines should not constitute an undue proportion of their remuneration.

15.11 When discussion about a product is initiated by a medical representative, he should place before the doctor for reference either a data sheet in respect of that product or another document with the same content. If, however, the doctor asks a question about a different product, then the medical representative will not be required to produce such data in respect of that other product.

15.12 Companies must prepare detailed briefing material for medical representatives on the technical aspects of any product which the medical representative is to promote. A copy of such material must be made available to the licensing authority on request. Briefing material must comply with the relevant requirements of the Code and, in particular, is subject to the certification requirements of Clause 13.

15.13 Medical representatives should not make a claim for a product based on the regulatory treatment of that product, or of competing products, or based on any warnings issued in relation to other products, unless in accordance with a specific requirement. However, a medical representative may refer to such matters in answer to a specific question.

15.14 A company may only employ as medical representatives persons who have passed the examination established by the Association except that:

- (i) Persons with an acceptable professional qualification, e.g. in pharmacy, medicine or nursing will be exempt from this requirement.
- (ii) Persons employed as medical representatives at the date upon which this edition of the Code comes into operation will be exempt from this requirement.

The operative date for the purposes of Clause 15.14 (ii) is 1 October 1979.

- (iii) Trainee medical representatives may be employed for a period of up to two years from the date of commencing training as a medical representative.

16 Samples

16.1 Samples should be provided to a doctor only in response to a signed request unless intended solely for identification or demonstration purposes.

A company may make available to a doctor a pre-printed request form or card; such a form or card may bear no more than the doctor's name, the company's name and address and an identifying reference, together with guidance as to the further information which the doctor himself must add. This limitation as to the provision of information on a pre-printed request form or card does not apply, however, in the case of a product controlled under the Misuse of Drugs Act 1971.

If such a pre-printed form or card is presented by a representative, then the doctor himself must complete the form by inserting the requisite information.

Wherever practicable, an individual sample should not represent more than four days treatment for a single patient. When samples are provided to assist doctors in

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the recognition or identification of a product, or to demonstrate the use of a particular apparatus or equipment, only the minimum quantity necessary for this purpose should be supplied.

16.2 Where samples of products restricted by law to supply on prescription are distributed by a representative, the sample must be handed direct to the doctor or given to a person authorised to receive the sample on his behalf. A similar practice must be adopted for products which it would be unsafe to use except under medical supervision.

16.3 Samples of products restricted by law to supply on prescription, which are made available to representatives for distribution, should be strictly limited in quantity and an adequate system of accountability should be established.

16.4 Samples sent by post must be packed so as to be reasonably secure against the package being opened by young children.

16.5 Distribution of samples in hospitals should comply with individual hospital regulations, if any.

17 Gifts and inducements

17.1 Subject to Clause 17.2 no gift or financial inducement shall be offered or given to members of the medical profession for purposes of sales promotion.

Schemes designed to test the extent to which mailings are opened and read and which involve a reward, e.g. a reward for the return of a voucher included in the mailing, are unacceptable if the gift is one which would not come within Clause 17.2.

17.2 Gifts in the form of articles designed as promotional aids, whether related to a particular product or of general utility, may be distributed to members of the medical and allied professions provided the gift is inexpensive and relevant to the practice of medicine or pharmacy.

Amongst other items, nail brushes, book matches and pens have been held to be reasonable gifts. Gifts of table mats have been held to be in contravention of the Code as being irrelevant to the practice of medicine or pharmacy.

17.3 The requirements of Clause 6.3 or Clause 6.4 do not apply if a promotional aid of the type mentioned in Clause 17.2 bears no more than one or more of the following particulars:

- (i) The name of the product.
- (ii) The name of the product licence holder or the name of that part of his business responsible for the sale of the product.
- (iii) The address of the product licence holder or the address of the part of his business responsible for the sale of the product.
- (iv) An indication that the product name is a trade mark.

If a promotional aid consists of a note pad in which the individual pages bear advertising material, there is no need for the individual pages to comply with Clause 6 provided that the information required by the clause is given elsewhere in the pad; for example, on the cover.

18 Hospitality

Entertainment or other hospitality offered to members of the medical and allied professions for purposes of sales promotion should always be secondary to the main

purpose of the meeting. It should not extend beyond members of the professions. The level of hospitality should be appropriate and not out of proportion to the occasion; its cost should not exceed that level which the recipients might normally adopt when paying for themselves.

Medical and group meetings are desirable and are to be encouraged. Both the British Medical Association and the Association share the opinion that such meetings should only take place if the advertising content is supported by a clear educational content. If hospitality is offered at meetings attendance should be restricted to members of the medical and allied professions.

It follows, therefore, that invitations to such medical and group meetings should not be extended to wives or husbands unless they themselves are practising members of the medical or allied professions.

When organising a meeting at which hospitality will be offered, a factor to be taken into account is the impression which will be created in the minds of the recipients or those who hear about it. Hospitality which becomes little more than pure entertainment has limited value in terms of the provision of information and promotion; such hospitality can only be regarded, therefore, as irrelevant and wasteful.

19 Marketing research

Marketing research is the collection and analysis of information and must be unbiased and non-promotional. The use to which the statistics or information is put may well be promotional. The two phases should be kept distinct.

19.1 Methods used for marketing research must never be such as to bring discredit upon, or to reduce confidence in, the pharmaceutical industry. The following provisions apply whether the research is carried out directly by the company concerned or by an organisation acting on the company's behalf.

19.2 The following information must be made available to the informant at first approach:

- (i) The nature of the survey.
- (ii) The name and address of the organisation carrying out the work.
- (iii) The identity of the interviewer.
- (iv) The nature and length of the interview.

The requirement in Clause 19.2(ii) does not mean that the organisation is also obliged to reveal the identity of its client. This must depend upon the contract between the client and the organisation.

19.3 Questions intended to solicit disparaging references to competing products or companies must be avoided.

19.4 Any written or oral statement given or made to an informant in order to obtain co-operation must be both factually correct and honoured.

19.5 Any incentives offered to the informants should be kept to a minimum and be commensurate with the work involved.

19.6 Marketing research must not in any circumstances be used as a disguised form of sales promotion and the research *per se* must not have as a direct objective the influencing of the opinions of the informant.

19.7 The identity of an informant must be treated as being confidential, unless he has specifically agreed otherwise.

CODE OF PRACTICE FOR THE PHARMACEUTICAL INDUSTRY

In the absence of this agreement it follows that the information provided (as distinct from the overall results of the research) must not be used as the basis upon which a subsequent approach is made to that informant for the purpose of sales promotion.

19.8 Precautions should be taken to ensure that no embarrassment results for informants following on from an interview, or from any subsequent communication concerning the research project.

20 Relations with the general public and lay communication media

20.1 Requests from individual members of the public for information or advice on personal medical matters must always be refused and the enquirer recommended to consult his or her own doctor.

20.2 Medicines which cannot legally be sold or supplied to the public otherwise than in accordance with a prescription, or which are legally limited to promotion for sale or supply only on prescription, must not be advertised to the general public.

Posters or notices issued for display in doctor's surgeries, pharmacies or anywhere to which the public have access must not include any message likely to arouse a demand for any particular product.

20.3 Statements must never be designed or made for the purpose of encouraging members of the public to ask their doctor to prescribe a product.

20.4 Information about medical products or matters related thereto, including scientific discoveries or advances in treatment, should not in general be made available to the general public either directly or through any lay medium.

The intention is to ensure that arrangements made for a press conference, or the extent of a press release, are such as to confine the disclosure of information about medical products or matters relating thereto to persons who are capable of evaluating the information responsibly and not concerned to exaggerate or even sensationalise its significance.

20.5 The importance of such information and the existence of legitimate public interest in acquiring it may exceptionally justify holding a press conference or the issue of a press release.

Invitations to attend such a conference, or the distribution of such a press release, should be confined

to persons who are either medically qualified or established as the representatives of the medical, pharmaceutical or scientific press, or as the medical correspondents of a responsible medium.

In the circumstances set out above as to the significance of the information, and in response to an unsolicited enquiry from a person of the standing described, information may also be released in an informal manner.

20.6 A further exception may arise when there exists a genuine mutual interest of a financial or commercial nature justifying the disclosure of information about medical products or related matters privately or to a restricted public. Examples are the interests of shareholders, financial advisers, employees and creditors.

When releasing information, it is essential to bear in mind the provisions of Clause 4.3 and, in particular, the extreme caution required in any reference to side-effects; it should also be emphasised that the treatment of a particular individual is solely a matter for decision by his medical practitioner.

20.7 On all occasions the information whether written, or communicated by other means, must be presented in a balanced way so as to avoid the risk of raising unfounded hopes of successful treatment or stimulating the demand for prescription of the particular product.

20.8 An announcement of the introduction of a new medical product must not be made by press conference or formal press release until the appropriate steps have been taken to inform the medical profession of its availability.

21 Transitional provisions

21.1 This Revised Fifth Edition of the Code shall not take effect:

(i) Until 1 October 1982, in relation to any advertisement consisting of four or more pages or advertising on a promotional aid, printed before 1 December 1978 and sent through the post or otherwise delivered to a doctor or a dentist.

(ii) Until 1 April 1982, in relation to any other advertisement and any other matter.

21.2 Until this Code takes effect in relation to any advertisement to which Clause 21.1 (i) applies, the requirements of the Fourth Edition of the Code shall continue to apply to that advertisement.

Abbott Laboratories Limited

Queenborough

Kent ME11 5EL



ABBOCIN®

Presentation Each yellow, sugar-coated tablet contains 250 mg Oxytetracycline Dihydrate BP.

Uses Organisms sensitive to oxytetracycline include a large number of Gram-negative and Gram-positive pathogenic bacteria. Those organisms that are sensitive to tetracycline in the concentrations usually achieved in the body during treatment are *Bacillus anthracis*, *Brucella* spp., *Escherichia coli*, *Haemophilus* spp., *Klebsiella* spp., *Proteus vulgaris*, staphylococci, streptococci, mycoplasma, *Entamoeba histolytica*, *Trichomonas vaginalis*, certain rickettsias and larger viruses. *Pseudomonas aeruginosa*, salmonella spp., and *Mycobacterium tuberculosis* are less susceptible.

Dosage and administration For adults and older children the dose is 250 mg four times daily taken orally. In severe infections this dose may be doubled or trebled.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to the tetracyclines.

Precautions and side-effects: As with other tetracyclines, Abbocin should be administered with great care to individuals with renal or hepatic dysfunction. Because of the staining of teeth and effects on bone development, tetracyclines should not be given in pregnancy or to children under 12 years of age. Tetracyclines should not be administered simultaneously with milk, antacids or preparations containing iron, calcium or magnesium.

Side-effects include nausea, diarrhoea and symptoms resulting from the overgrowth of non-susceptible organisms. Overgrowth of *Candida albicans* in the mouth may cause glossitis and stomatitis which may extend into the trachea and bronchi; overgrowth of *C. albicans* in the bowel results in pruritis ani; overgrowth of resistant coliform organisms such as pseudomonas and proteus may also cause diarrhoea. Occasionally resistant staphylococci may give rise to a fulminating enterocolitis. Allergic reactions and skin rashes are rare.

Treatment of overdose: Gastric lavage. Intensive supportive therapy. In cases of overdose, allergic reactions such as drug fever, anaphylactic shock and rash may occur. For treatment of anaphylaxis immediate administration of adrenaline, oxygen and artificial respiration is necessary.

Adrenaline is given subcutaneously as 0.5–1 ml adrenaline Injection BP 0.1%. For dyspnoea, aminophylline, calcium and antihistamines may be given. General measures, such as administration of plasma, blood, vasopressor drugs or hydrocortisone (100 mg IV) may be necessary.

Incompatible with alkalis and chloramphenicol.

Pharmaceutical precautions Store below 25°C. Keep container tightly closed.

Legal category POM.

Package quantities Abbocin is supplied in containers of 1,000 sugar-coated tablets.

Further information Metabolisable carbohydrate content approx 0.29 g per tablet.

Product licence number 0037/0095.

ABBOKINASE® ▼

Presentation Abbokinase is a highly purified sterile lyophilised formulation of urokinase obtained from cultures of human kidney cells. Urokinase is a plasminogen activator excreted in the urine of normal healthy individuals. Each vial of Abbokinase contains in excess of 250,000 iu so that, following reconstitution with 5.2 ml sterile water for injection, each ml of the 5 ml which can be withdrawn will contain 50,000 iu urokinase, 5 mg mannitol and 5 mg sodium chloride.

Uses Abbokinase *in-vivo* and *in-vitro* produces the release of plasmin by an enzymatic action on human plasminogen.

Abbokinase has only minimal activity in reducing fibrinogen levels but blood plasminogen levels are reduced, the effect being dose-dependent.

Abbokinase is virtually non-antigenic to humans and, in therapeutic doses, is thromboplastin-free.

Thrombolytic therapy is indicated in the treatment of vascular occlusions caused by forming or recently formed fibrin clots. Theoretically the best results will be obtained with thrombi less than 24 hours old.

Abbokinase is indicated as a thrombolytic agent in pulmonary embolism.

Dosage and administration Abbokinase is administered intravenously by continuous infusion, usually for a period of 12 hours.

It is recommended that Abbokinase be given in a solution of normal saline by constant infusion. An initial loading dose to be given during the first ten minutes of therapy is advocated.

This loading dose should be equal to the amount which it is planned to administer over each succeeding period of one hour. Ideally, an infusion pump should be used to maintain a constant rate of infusion.

Abbokinase is reconstituted with 5.2 ml sterile water for injection, without preservatives.

For administration the reconstituted solution should be further diluted with normal saline. It is strongly recommended that the total volume after dilution should be 195 ml, irrespective of the number of vials used, since this provides for a bolus dose of 15 ml followed by the infusion of 15 ml per hour over 12 hours. However, choice of another volume is possible, the physician being guided by considerations of possible effect on the patient of larger volumes and physical difficulties of measurement with smaller volumes. A chart is available detailing volumes of reconstitution and further dilution for use (on

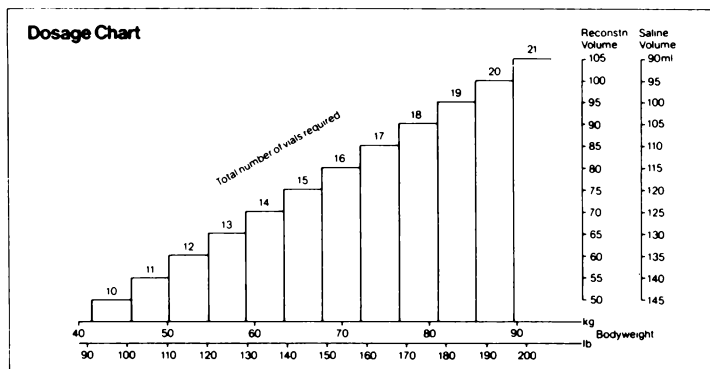


Figure – Number of vials of Abbokinase required according to patient weight and data for reconstitution and further dilution.

the basis of a final volume of 195 ml) in cases where the amount of Abbokinase immediately available is less than that required for the total treatment.

Dosage: It should be noted that patient-to-patient variation in response can be expected, due to individual variation in levels of inhibitory factors. Certain disease states such as uraemia, some malignancies and dyslipidaemias can be associated with an increased plasma level of urokinase or plasmin inhibitors. In other conditions such as massive pulmonary embolism, endogenous fibrinolytic activity may be increased.

The recommended dosage regimen for the treatment of pulmonary embolism is:

Loading dose – 4,400 iu per kg body weight over 10 minutes.

Constant infusion dose – 4,400 iu per kg body weight per hour.

Duration of infusion – 12 hours.

Contra-indications, warnings, etc

Contra-indications: Manifest or recent (i.e. within three days) haemorrhage. Any haemorrhagic diathesis. Severe hypertension. During cardiopulmonary resuscitation. During pregnancy or suspected pregnancy. Menstruation.

Warnings and precautions: The major adverse effect of Abbokinase is haemorrhage, usually associated with too high dosage. A high incidence of bleeding from minor skin lesions, therapeutic and diagnostic puncture sites and pre-existing gastro-intestinal lesions has been observed with high dosages. Any evidence of significant internal bleeding necessitates the cessation of thrombolytic therapy. An antifibrinolytic agent such as tranexamic acid may be used as an antidote if required. It should be available, if necessary, during infusions with Abbokinase when high doses are being administered.

Post-surgery for one month.

Recent surgery (within three days).

Concurrent anticoagulant therapy should be administered cautiously.

Mild temperature increases have been observed during thrombolytic therapy with Abbokinase.

When there is a history of hypersensitivity to drugs, etc., caution is advised and resuscitatory facilities as well

as corticosteroids, adrenaline etc. should be readily available when Abbokinase is infused.

Monitoring: The monitoring of fibrinolytic activity, thrombin clotting time and of plasminogen levels is desirable.

Pharmaceutical precautions The lyophilised powder should be stored at 2–8°C. Reconstituted solution should be used immediately, but the secondarily diluted product in normal saline can be preserved at room temperature, if necessary, for up to 24 hours.

Legal category POM.

Package quantities Available in packs of 2 vials of 250,000 iu each.

Further information The potency of Abbokinase is expressed in International Units (iu). For practical purposes the iu is considered by most authorities to be equivalent to the CTA unit.

The Ploug unit is usually considered to be equal to 1.4 iu.

Product licence number 0037/0096.

AKINETON®

Presentation Akineton is supplied in white scored tablets, with a triangle on the opposite side, containing 2 mg biperiden hydrochloride. Also available in 1 ml ampoules containing 5 mg of biperiden lactate.

Uses In drug-induced extrapyramidal symptoms and all other types of parkinsonism. It is particularly effective against rigidity.

Dosage and administration **Adults:**

1. **Tablets:** Begin with $\frac{1}{2}$ tablet twice daily and gradually increase to 1 tablet thrice a day. After maintenance at this level for a few days, gradually increase until no further symptomatic improvement is obtained. Decrease cautiously to lowest dosage which adequately controls symptoms. The optimum maintenance dose varies from 3–12 mg daily.

2. Ampoules: 1–4 ampoules daily slowly intravenously or intramuscularly.

Children: Not recommended.

Notes:

1. When salivation is reduced the tablets are best taken after meals, in other cases they should be taken during meals.

2. With parenteral administration, the systolic blood pressure may be decreased by 20–30 mm Hg and the diastolic by 5–20 mm Hg.

3. **Combined treatment:** In some cases the response of tremor to the drug may be inadequate. In such cases combined therapy with a preparation effective against tremor should be considered. However, it is advisable to continue with Akineton alone until it has been established that its effect on tremor is inadequate.

4. **Reversal effect:** An increase in parkinsonism symptoms during treatment is a preliminary sign of intoxication due to excessive dosage and should be treated by reduction of the dose.

Contra-indications, warnings, etc

Contra-indications: Sensitivity to Akineton (Biperiden hydrochloride). Narrow angle glaucoma. Intestinal obstruction.

Precautions: Care should be taken when administering Akineton to patients with cardiac arrhythmias. Patients with recent myocardial infarction should be given Akineton only if the heart rate is well controlled.

Occasionally drowsiness may occur, and patients who drive a car or operate any other potentially dangerous machinery which requires concentration should be warned that side-effects of this type are a possibility. As with other drugs acting on the central nervous system, the consumption of alcohol should be avoided during Akineton therapy.

As with every other long-term medication regular blood counts are recommended.

Treatment with Akineton should not be discontinued abruptly. Transfer of patients to Akineton from other anti-parkinsonism agents should be made gradually, the original agent being reduced in dose as Akineton is substituted.

Use during pregnancy: The potential benefits of Akineton therapy should be weighed against possible hazards to the patient as well as to the foetus. No data are available regarding continuous administration in pregnant patients.

Side-effects: Akineton is well tolerated and side-effects are minimal even with prolonged usage. Dryness of the mouth, disturbances of accommodation, fatigue and vertigo may occur. In general these symptoms disappear in a few days without change in dosage; in a few cases a reduction of the dose may be needed, but discontinuation is seldom required. Gastro-intestinal symptoms can be prevented, in most cases, by administering Akineton during or after a meal.

Restlessness, confusion and euphoria may occur, but the incidence is low. Occasionally drowsiness may occur.

On rare occasions, particularly in patients with hypertrophy of the prostate, disturbances of micturition may occur and, even more rarely, retention of urine. Reduction of dosage will usually restore the bladder function to normal.

Overdosage: **Symptoms:** respiratory and cardiac depression.

Treatment: Gastric lavage or emesis should be considered. Vital signs should be closely monitored and appropriate supportive measures taken. Artificial ventilation may be necessary. In the event of cardiac depression, a cardiac stimulant such as dobutamine may be considered.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Akineton 2 mg tablets are supplied in containers of 50.

Akineton ampoules are supplied in boxes of 5 × 1 ml ampoules.

Further information *Metabolisable carbohydrate content:* Approx. 0.16 g per tablet.

Sodium content: 0.13 mmol per ampoule (0.13 mmol per ml).

Product licence numbers

Tablets 0037/5900

Ampoules 0037/5901

CO-FRAM* ▼

© *Approved name:* Co-trifamole

Presentation White, scored tablets each containing 80 mg trimethoprim BP and 400 mg sulphamoxole. Each tablet bears the  logo.

Uses Treatment of infections caused by a wide range of gram-positive and gram-negative organisms. Co-Fram is particularly indicated in the treatment of the following:

Urinary tract infections, including pyelonephritis, pyelitis and cystitis.

Genital tract infections, including prostatitis and non-gonococcal urethritis.

Gastro-intestinal tract infections, such as enteritis, enterocolitis, bacterial dysentery and salmonella infections including typhoid and paratyphoid fevers.

Skin infections, including pyoderma, abscesses, wound infections, furunculosis.

Respiratory tract infections, including acute and chronic bronchitis, pneumonia, broncho-pneumonia, bronchiectasis.

Ear, nose & throat infections, such as tonsillitis, otitis media, sinusitis and pharyngitis.

Other infections due to sensitive pathogens.

Dosage and administration **Adults:** Two tablets initially followed by one tablet every twelve hours. Treatment should continue until two days after the disappearance of all clinical signs of infection.

Children (6–12 years): 1–1½ tablets initially followed by ½–1 tablet every 12 hours. Treatment should continue until 2 days after the disappearance of all clinical signs of infection.

Contra-indications, warnings, etc

Contra-indications: Co-Fram is contra-indicated in severe renal insufficiency where repeated measurements of the plasma sulphonamide concentration are not practicable.

Co-Fram is contra-indicated in patients with severe hepatic disorders or blood dyscrasias.

Co-Fram should not be given to patients with a history of sulphonamide or trimethoprim sensitivity.

Co-Fram should not be given during pregnancy nor should it be given to premature babies or during the first four months of life. The usual caution in prescribing any drug for women of child-bearing age should be exercised with Co-Fram.

Under adverse circumstances Co-Fram could impair folic acid metabolism in humans. Therefore use in patients with haemopoietic disorders should be avoided.

Precautions: It is important to ensure that the patient has an adequate fluid intake. In particular, there must be an adequate daily volume of urine in patients with dehydration due to severe loss of fluid associated with vomiting, diarrhoea and persistent fever. Substances which acidify the urine should not be given during treatment with Co-Fram.

In severe renal insufficiency dosage should be reduced or the interval between doses extended to avoid accumulation of the drug; plasma concentrations of sulphonamide must be monitored during treatment in order to establish optimum dosage.

The blood picture should be checked during long-term treatment with Co-Fram in order to detect possible cases of folic acid deficiency.

Side-effects: Gastro-intestinal side-effects and skin reactions may occur in a small proportion of patients. The possibility of blood dyscrasias of the sort associated with other preparations containing sulphonamides should be borne in mind, particularly in the elderly.

Treatment of overdosage: Gastric lavage and general supportive measures. Forced diuresis and alkalisation of the urine will aid elimination of sulphamoxole. Calcium folinate 3–6 mg for 5–7 days given intramuscularly will counteract the effects of trimethoprim on haemopoiesis.

Pharmaceutical precautions Store at room temperature.

Legal category POM.

Package quantities Containers of 100 tablets.

Further information Metabolisable carbohydrate 75 mg per tablet.

Product licence number 0037/0099

CORDILOX* 120 CORDILOX*

Presentation Cordilox 120 is presented as a yellow Filmtab* (film-coated tablet, Abbott) containing 120 mg Verapamil Hydrochloride BP. Cordilox is also available as yellow Filmtabs containing 40 mg and 80 mg Verapamil Hydrochloride BP. Cordilox 120 and Cordilox are Verapamil Hydrochloride Tablets BP.

Uses Cordilox is a calcium antagonist which blocks the inward movement of calcium in cardiac muscle cells, in smooth muscle cells of the coronary and systemic arteries and in the cells of the intracardiac conduction system. The decrease in systemic and coronary vascular resistance and the sparing effect on intracellular oxygen consumption appear to explain the anti-anginal properties of the product.

Because of its effect on the movement of calcium in the intracardiac conduction system, it reduces automaticity, decreases conduction velocity and increases the refractory period.

Cordilox reduces both systolic and diastolic blood pressure by mechanisms which have not been fully determined.

Cordilox is clinically useful in:

- (1) the treatment and prophylaxis of angina pectoris.
- (2) the treatment and prophylaxis of supraventricular tachycardia (paroxysmal tachycardia, premature supraventricular contractions, atrial fibrillation and flutter) and paroxysmal supraventricular tachycardia, of the reciprocating type, associated with the Wolff-Parkinson-White syndrome.
- (3) the treatment of mild to moderate hypertension and of renal hypertension, used alone or in conjunction with other antihypertensive therapy.

Dosage and administration

1. **Angina: Adults:** 120 mg t.d.s. is recommended. 80 mg t.d.s. can be completely satisfactory in some patients with angina of effort. Less than 120 mg t.d.s. is not likely to be effective in angina at rest and variant angina.

2. **Supraventricular Tachycardias: Adults:** 40–120 mg t.d.s. according to the severity of the condition (in acute cases, Cordilox i.v. is indicated).

Children: Up to 2 years: $\frac{1}{2}$ 40 mg tablet 2–3 times a day.

2 years and above: 1–3 40 mg tablets, 2–3 times a day, according to age and effectiveness.

3. **Hypertension: Adults:** The usual dose range is 80–160 mg t.d.s. The dose should be increased from 80 mg t.d.s. at weekly intervals according to response, either alone or in conjunction with other antihypertensive therapy. A further reduction in blood pressure may be obtained by combining Cordilox with other antihypertensive agents, e.g. thiazide diuretics.

Children: up to 10 mg/kg/day in divided doses, according to severity of disease.

Contra-indications, warnings, etc *Contra-indications:* Hypotension associated with cardiogenic shock, marked bradycardia (less than 50 beats/minute), second or third degree atrioventricular block, sick sinus syndrome, uncompensated heart failure.

Precautions: Cordilox may affect impulse conduction and should be used with caution in patients with first degree atrioventricular block. The effects of Cordilox and beta blockers may be additive both with respect to conduction and contraction, therefore care must be exercised when these are administered concurrently or closely together. This is especially true when either drug is administered intravenously.

Cordilox may affect left ventricular contractility as a result of its mode of action. This effect is small and normally not important but cardiac failure may be precipitated or aggravated if it exists. In cases with poor ventricular function therefore Cordilox should only be given after appropriate therapy for cardiac failure such as digitalis, etc.

Verapamil hydrochloride has been shown to increase the serum concentration of digoxin and caution should be exercised with regard to digitalis toxicity.

Caution should be observed in the acute phase of myocardial infarction.

In patients with impaired liver function, particular attention should be paid to the dosage because of reduced drug metabolism.

Although animal studies have not shown any teratogenic effect, Cordilox should not be given during the first

trimester of pregnancy unless, in the clinician's judgement, it is essential for the welfare of the patient.

Side-effects: Cordilox is generally well-tolerated. Constipation is not uncommon, flushing is observed occasionally, headaches rarely. Nausea and vomiting have seldom been reported and allergic reactions even more rarely.

Overdosage: Usual emergency measures for acute cardiovascular side-effects should be applied, e.g.:

- in the case of cardiac arrest, heart massage, mechanical respiration, followed by appropriate intensive care;
- in the case of the second and third degree AV block, atropine, isoprenaline and, if required, pace-maker therapy;
- in the case of signs of myocardial insufficiency, dopamine, dobutamine, cardiac glycosides or calcium gluconate (10–20 ml of a 10% solution);
- in the case of hypotension, appropriate positioning of patient, dopamine, dobutamine, noradrenaline.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Cordilox 120 is supplied in containers of 100 and 500 tablets.

Cordilox 40 and 80 mg are supplied in containers of 100 tablets.

Further information Metabolisable carbohydrate content: Cordilox 120: approx. 0.12 g per tablet; Cordilox 40 mg and 80 mg: approx. 0.04 g and 0.08 g per tablet respectively.

Product licence numbers

Cordilox 120	0037/0084
Cordilox 40 mg	0037/0098
Cordilox 80 mg	0037/0085

CORDILOX* I.V.

Presentation Cordilox for intravenous administration (Verapamil Hydrochloride Injection BP) is available in 2 ml ampoules each containing 5 mg verapamil hydrochloride.

Uses Cordilox slows AV nodal conduction. This is due to a specific inhibitory effect on the transmembrane passage of calcium ions. Simultaneously, it diminishes the peripheral resistance and so relieves the work load on the heart.

Clinically, Cordilox decreases myocardial oxygen consumption and increases exercise tolerance.

Cordilox is effective in the treatment of supraventricular arrhythmias.

Dosage and administration *By intravenous injection:* For the treatment of tachyarrhythmias 5–10 mg (1–2 ampoules) should be injected over a period of 30 seconds intravenously, with continuous observation of the patient.

In cases of paroxysmal tachyarrhythmias a further 5 mg may, if necessary, be injected 5–10 minutes after the first injection with the same precautions being observed.

Higher doses are not usually necessary.

By intravenous infusion: 5–10 mg of Cordilox per hour may be administered in saline, glucose, laevulose, or similar solutions, until a total dose varying between 25–100 mg per day is reached.

Intravenous dosage in children: *Newborn:* 0.75–1 mg (0.3–0.4 ml).

Infants: 0.75–2 mg (0.3–0.8 ml).

Children aged 1–5 years: 2–3 mg (0.8–1.2 ml) *6–15 years:* 2.5–5 mg (1.0–2.0 ml).

In many cases smaller doses than those mentioned above are sufficient. The injection should be stopped at the onset of the desired effect.

Intravenous injection should desirably be made – and in infancy always – under electrocardiographic control. If necessary, the same dose may be repeated after 5–10 minutes.

Contra-indications, warnings, etc *Contra-indications:* Hypotension associated with cardiogenic shock, marked bradycardia (less than 50 beats/minute), uncompensated heart failure.

Precautions: Cordilox may affect impulse generation or conduction. Thus its use should be cautionary in, for instance, sick sinus syndrome, AV block and patients with prolonged P-R intervals, etc.

Cordilox may affect ventricular contractility as a result of its mode of action. This effect is small and normally not important but cardiac failure may be precipitated or aggravated if it exists. In cases with poor ventricular function therefore Cordilox should only be given after appropriate therapy for cardiac failure such as digitalis, etc.

Verapamil hydrochloride has been shown to increase the serum concentration of digoxin and caution should be exercised with regard to digitalis toxicity.

Caution should be observed in the acute plasma phase of myocardial infarction.

In patients with impaired liver function, particular attention should be paid to the dosage because of reduced drug metabolism.

Although animal studies have not shown any teratogenic effect, Cordilox should not be given during the 1st trimester of pregnancy unless, in the clinician's judgement, it is essential for the welfare of the patient.

Side-effects: Parenteral Cordilox is well tolerated and does not exert a bronchoconstrictor effect.

Due to the mode of action, undesired effects on atrioventricular conduction and blood pressure are possible. This applies particularly to patients with atrioventricular block and/or considerably impaired myocardial function. On rare occasions the intravenous administration of Cordilox may lead to an undesired blocking of conduction, and, in extreme cases, to asystole. The asystole is usually of short duration and cardiac action returns spontaneously after a few seconds, usually in the form of sinus rhythm. However, if on rare occasions this pattern does not ensue, treatment should be carried out as described below.

Cordilox may have an additive effect with other antihypertensive drugs. Thus, in many cases, with Cordilox, a reduction in dose of the antihypertensive drug is possible. During the simultaneous administration of Cordilox and drugs with cardiodepressive effect and/or inhibiting effect on atrioventricular conduction (e.g. beta-adrenergic blocking substances, quinidine), watch should be kept for additive effects.

Intravenous administration of Cordilox may lead to a slight transient fall in blood pressure due to a reduction of peripheral resistance. Rarely this may result in severe hypotension.

Ventricular fibrillation may be precipitated on very rare occasions.

Treatment of acute cardiovascular side-effects: If acute complications occur after the intravenous injection of Cordilox (asystole, total atrioventricular block, or ventricular fibrillation) the usual emergency measures should be applied e.g. cardiac massage, mechanical respiration, the intravenous or intra-cardiac injection of adrenaline, and the intravenous injection of 10–20 ml of calcium gluconate 10% solution. In the event of ventricular asystole usual resuscitative measures should be used. Hypotension following intravenous injection of Cordilox may, if necessary, be controlled without difficulty by the use of vasoconstrictor substances.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Cordilox ampoules are supplied in boxes of 5 × 2 ml ampoules, each ampoule containing 5 mg Verapamil Hydrochloride BP.

Further information *Sodium content:* 0.30 mmol per ampoule (0.15 mmol per ml).

Product licence number 0037/5903.

ENDURON*

Presentation Each square, pink, grooved tablet contains 5 mg methyclothiazide.

Uses Enduron is indicated as a primary measure in the treatment of mild to moderate hypertension and as an adjunct to other drugs in the treatment of resistant hypertension. It is also indicated in the same clinical situations in which benzothiadiazines are of value. It is used in the treatment and control of oedema associated with congestive heart failure, the nephrotic syndrome, hepatic cirrhosis, pre-menstrual tension and the administration of steroids. The use of Enduron permits a reduction in the dosage of more potent antihypertensive agents with a consequent reduction in side-effects.

Dosage and administration The usual oral dosage is 2.5–5 mg daily. This may be increased to 10 mg once daily, if necessary, but doses larger than 10 mg have little additional therapeutic effect.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to thiazide derivatives. It should not be administered in the presence of severe renal or hepatic disease.

Precautions and side-effects: Although the incidence of side-effects with Enduron is extremely low, it is a benzothiadiazine derivative, and the physician should be alert for the side-effects inherent in this type of medication. If potassium depletion occurs, citrus fruit juices should be taken regularly to supplement potassium intake. Patients on digitalis, on corticosteroids, or with impending hepatic coma, cirrhotic oedema or ascites may require potassium supplements, and should be carefully evaluated clinically. Hypochloraemic alkalosis is a possibility with any potent benzothiadiazine, but remote with Enduron because it produces approximately equivalent sodium and chloride excretion. Elevation of

the blood urea nitrogen, serum uric acid and blood sugar have occurred with the use of thiazide drugs. Myocardial sensitivity to digitalis is increased in the presence of reduced potassium uptake and signs of digitalis intoxication may be produced by formerly tolerated doses of digitalis. Blood dyscrasias including thrombocytopenia with purpura, agranulocytosis and aplastic anaemia have also been reported but are rare.

Overdosage: Symptoms: electrolyte imbalance. Dehydration. Hypotension. Signs of potassium deficiency including confusion, dizziness, muscular weakness and gastro-intestinal disturbances may occur.

Treatment: Employ general supportive measures. Replacement of fluids and electrolytes may be indicated.

For recent ingestion gastric lavage or emesis should be considered.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Enduron is supplied in containers of 100 tablets.

Further information *Metabolisable carbohydrate content:* Approx. 0.18 g per tablet.

Product licence number 0037/5028.

ENDURONYL*

Presentation Each square, grooved, yellow Enduronyl tablet contains:

Methyclothiazide	5 mg
Deserpidine	0.25 mg

Also available as Enduronyl Forte in square, grooved, ing:

grey tablets, each containing:

Methyclothiazide	5 mg
Deserpidine	0.5 mg

Uses In the treatment of hypertension.

Dosage and administration One half to two tablets Enduronyl or Enduronyl Forte daily. The dosage should be determined by individual titration of ingredients. Dosage of both components should be carefully adjusted to the needs of the individual patient. Usual daily dosage of Enduronyl or Enduronyl Forte 1 tablet. Grooved tablets are provided to permit considerable latitude in meeting dosage requirements of individual patients. Therapy should be initiated with 1 Enduronyl tablet daily even in patients with severe hypertension. This dosage may be increased to 2 tablets daily, depending upon the result of the initial dosage. Usually a period of ten days to two weeks of therapy is required to determine the full effects of a given dosage. In all cases an effort should be made to determine the lowest effective dose for each patient. A dosage as low as ½-tablet of Enduronyl, once a day, may suffice, whereas up to the maximum of 2 tablets may be required in some cases. Occasionally it may be possible to reduce the dosage when control has been obtained with maximum doses. If Enduronyl is administered with other antihypertensive agents the initial dosage of these drugs should be halved.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to the thiazide derivatives. Enduronyl should not be administered in the

presence of severe renal or hepatic disease. Because of the deserpidine content, Enduronyl is also contra-indicated in patients with mental depression and suicidal tendencies, active peptic ulcer or ulcerative colitis.

Precautions and side-effects: The low incidence of side-effects observed with the use of Enduron and Harmony (deserpidine) individually is applicable to their combined use in Enduronyl. Moreover, the combination exerts equivalent antihypertensive effect, with lesser amounts of each drug than when they are given singly. Nevertheless, the physician should be alert for the side-effects inherent in this type of medication.

Overdosage – Enduron (methyclothiazide)

Symptoms: Electrolyte imbalance. Dehydration. Hypotension. Signs of potassium deficiency including confusion, dizziness, muscular weakness and gastrointestinal disturbances may occur.

Treatment: Employ general supportive measures. Replacement of fluids and electrolytes may be indicated.

For recent ingestion gastric lavage or emesis should be considered.

Harmony (deserpidine)

Symptoms: Mental depression, hypotension, ptosis, miosis and catatonia in severe cases.

Treatment: Suggested treatment is the administration of methylamphetamine hydrochloride 5–15 mg orally for adults. More severe cases will require 10–30 mg intravenously or intramuscularly. Treatment should be initiated with the smaller dose. For children these doses must be reduced in proportion to body weight.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Enduronyl is supplied in containers of 100 and 500 tablets.

Enduronyl Forte is supplied in containers of 100 tablets.

Further information *Metabolisable carbohydrate content:* Enduronyl, approx. 0.18 g per tablet.

Enduronyl Forte, approx. 0.18 g per tablet.

Product licence numbers

Enduronyl 0037/5029

Enduronyl Forte 0037/5030

ERYTHROMID*

Presentation Each 250 mg orange coloured enteric-coated Filmtab* (film-coated tablet Abbott) contains 250 mg erythromycin base. They are Erythromycin Tablets BP.

Uses For the prophylaxis and treatment of infections caused by erythromycin-sensitive organisms.

Clinical indications: Erythromid is highly effective in the treatment of a great variety of clinical infections.

1. **Upper respiratory tract infections:** tonsillitis, peritonsillar abscess, pharyngitis, laryngitis, sinusitis, secondary infections in colds and influenza.

2. **Lower respiratory tract infections:** Tracheitis, acute and chronic bronchitis, pneumonia (lobar pneumonia, bronchopneumonia, primary atypical pneumonia), bronchiectasis, legionnaires' disease.

3. **Ear infections:** Otitis media and otitis externa, mastoiditis.

4. **Oral infections:** Gingivitis, Vincent's angina.

5. **Eye infections:** Blepharitis.

6. **Skin and soft-tissue infections:** Boils and carbuncles, paronychia, abscesses, pustular acne, impetigo, cellulitis, erysipelas.

7. **Gastro-intestinal infections:** Cholecystitis, staphylococcal enterocolitis.

8. **Prophylaxis:** Pre- and post-operative, trauma, burns, rheumatic fever.

9. **Other infections:** Osteomyelitis, urethritis, gonorrhoea, syphilis, lymphogranuloma venereum, diphtheria, prostatitis, scarlet fever.

Note: The antibiotic has also proved to be of value in endocarditis and septicæmia, but in these conditions initial administration of erythromycin lactobionate by the intravenous route is advisable.

Microbiological indications: Erythromid is active against a wide variety of pathogenic organisms, Gram-positive cocci – staphylococci, pneumococci and streptococci (including enterococci) – meningococci, mycoplasma, L-forms, *Haemophilus influenzae*, the agents causing trachoma and lymphogranuloma venereum, chlamydia, clostridia, corynebacteria, neisseria, *Treponema pallidum*, bordetella.

Note: The majority of strains of *Haemophilus influenzae* are susceptible to the concentrations reached after ordinary doses.

Dosage and administration *Adults and older children:* Usual oral dosage 1 tablet every four to six hours, increased to 4 g or more per day in unusually severe infections.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to erythromycin.

Precautions: Erythromycin is excreted principally by the liver, so caution should be exercised in administering the antibiotic to patients with impaired hepatic function or concomitantly receiving potentially hepatotoxic agents.

Recent studies reveal that the use of erythromycin in patients who are receiving high doses of theophylline may be associated with an increase of serum theophylline levels and potential theophylline toxicity.

In case of theophylline toxicity and/or elevated serum theophylline levels, the dose of theophylline should be reduced while the patient is receiving erythromycin therapy.

Use in pregnancy: There is no evidence of hazard from erythromycin in human pregnancy and it has been in wide use for many years without apparent ill consequence. Animal studies have shown no hazard.

Side-effects: There are very few side-effects to any Abbott erythromycin product. There are no reports implicating them with abnormal tooth development and only rare reports of damage to the blood, kidneys, liver or central nervous system. Allergic reactions are rare and mild, although anaphylaxis has occurred. Occasionally there is abdominal discomfort after oral administration, sometimes with nausea and vomiting. It usually subsides after a few days without having to reduce the dosage. The rare possibility of superinfection caused by overgrowth of non-susceptible bacteria or fungi should be kept in mind during prolonged or repeated therapy, especially when other antibacterial agents are simultaneously employed.

Overdosage: **Symptoms:** nausea, vomiting, diarrhoea.

Treatment: Gastric lavage, general supportive measures.

Pharmaceutical precautions Keep bottle tightly closed. Protect from light and store below 30°C.

Legal category POM.

Package quantities Erythromid is supplied in containers of 100, 500 and 1000 tablets.

Further information Contains no metabolisable carbohydrate.

Product licence number 0037/5019.

ERYTHROCIN® 250

Presentation Each 250 mg Erythrocin white Filmtab® (film-coated tablet Abbott) contains 250 mg erythromycin activity as Erythromycin Stearate BP.

Uses For the prophylaxis and treatment of infections caused by erythromycin-sensitive organisms.

Clinical indications: Erythrocin is highly effective in the treatment of a great variety of clinical infections.

1. **Upper respiratory tract infections:** Tonsillitis, peritonsillar abscess, pharyngitis, laryngitis, sinusitis, secondary infections in colds and influenza.
2. **Lower respiratory tract infections:** Tracheitis, acute and chronic bronchitis, pneumonia (lobar pneumonia, bronchopneumonia, primary atypical pneumonia), bronchiectasis, legionnaires' disease.
3. **Ear infections:** Otitis media and otitis externa, mastoiditis.
4. **Oral infections:** Gingivitis, Vincent's angina.
5. **Eye infections:** Blepharitis.
6. **Skin and soft-tissue infections:** Boils and carbuncles, paronychia, abscesses, pustular acne, impetigo, cellulitis, erysipelas.
7. **Gastro-intestinal infections:** Cholecystitis, staphylococcal enterocolitis.
8. **Prophylaxis:** Pre- and post-operative, trauma, burns, rheumatic fever.
9. **Other infections:** Osteomyelitis, urethritis, gonorrhoea, syphilis, lymphogranuloma venereum, diphtheria, prostatitis, scarlet fever.

Note: The antibiotic has also proved to be of value in endocarditis and septicaemia, but in these conditions initial administration of erythromycin lactobionate by the intravenous route is advisable.

Microbiological indications: Erythrocin is active against a wide variety of pathogenic organisms, Gram-positive cocci – staphylococci, pneumococci and streptococci (including enterococci) – meningococci, mycoplasma, L-forms, *Haemophilus influenzae*, the agents causing trachoma and lymphogranuloma venereum, chlamydia, clostridia, *Corynebacterium diphtheriae* (as an adjunct to antitoxin), neisseria, *Treponema pallidum*, bordetella.

Note: The majority of strains of *Haemophilus influenzae* are susceptible to the concentrations reached after ordinary doses.

Dosage and administration **Adults:** 1–2 g per day divided into 6, 8 or 12 hourly doses. May be increased up to 4 g daily in severe infections.

The usual adult dose is one 250 mg tablet four times a day, or twice daily dosage can be given if preferred. Tablets should be taken before or with meals.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to erythromycin.

Precautions: Erythromycin is excreted principally by the liver, so caution should be exercised in administering the antibiotic to patients with impaired hepatic function or concomitantly receiving potentially hepatotoxic agents.

Recent studies reveal that the use of erythromycin in patients who are receiving high doses of theophylline may be associated with an increase of serum theophylline levels and potential theophylline toxicity.

In case of theophylline toxicity and/or elevated serum theophylline levels, the dose of theophylline should be reduced while the patient is receiving erythromycin therapy.

Use in pregnancy: There is no evidence of hazard from erythromycin in human pregnancy. It has been in wide use for many years without apparent ill consequence. Animal studies have shown no hazard.

Side-effects and precautions: There are very few side-effects to any Abbott Erythrocin product. There are no reports implicating Erythrocin with abnormal tooth development and only rare reports of damage to the blood, kidneys, liver or central nervous system. Allergic reactions are rare and mild, although anaphylaxis has occurred. Occasionally there is abdominal discomfort after oral administration, sometimes with nausea and vomiting. It usually subsides after a few days without having to reduce the dosage. The rare possibility of superinfection caused by overgrowth of non-susceptible bacteria or fungi should be kept in mind during prolonged or repeated therapy, especially when other antibacterial agents are simultaneously employed.

Overdosage: **Symptoms:** nausea, vomiting, diarrhoea.

Treatment: Gastric lavage, general supportive measures.

Pharmaceutical precautions Protect Filmtabs from light. Store below 25°C.

Legal category POM.

Package quantities Erythrocin 250 mg is supplied in containers of 100, 500 and 1,000 tablets.

Further information *Metabolisable carbohydrate content:* Approx. 0.07 g per tablet.

Product licence number 0037/5079.

ERYTHROCIN® 500

Presentation Each white Erythrocin 500 Filmtab® (film-coated tablet Abbott) contains 500 mg erythromycin activity as Erythromycin Stearate BP.

Uses For the prophylaxis and treatment of infections caused by erythromycin-sensitive organisms.

Clinical indications: Erythrocin is highly effective in the treatment of a great variety of clinical infections.

1. **Upper respiratory tract infections:** Tonsillitis, peritonsillar abscess, pharyngitis, laryngitis, sinusitis, secondary infections in colds and influenza.
2. **Lower respiratory tract infections:** Tracheitis, acute and chronic bronchitis, pneumonia (lobar pneumonia, bronchopneumonia, primary atypical pneumonia), bronchiectasis, legionnaires' disease.
3. **Ear infections:** Otitis media and otitis externa, mastoiditis.
4. **Oral infections:** Gingivitis, Vincent's angina.
5. **Eye infections:** Blepharitis.
6. **Skin and soft-tissue infections:** Boils and carbuncles, paronychia, abscesses, pustular acne, impetigo, cellulitis, erysipelas.

7. *Gastro-intestinal infections*: Cholecystitis, staphylococcal enterocolitis.

8. *Prophylaxis*: Pre- and post-operative, trauma, burns, rheumatic fever.

9. *Other infections*: Osteomyelitis, urethritis, gonorrhoea, syphilis, lymphogranuloma venereum, diphtheria, prostatitis, scarlet fever.

Note: The antibiotic has also proved to be of value in endocarditis and septicaemia, but in these conditions initial administration of erythromycin lactobionate by the intravenous route is advisable.

Microbiological indications: Erythrocin is active against a wide variety of pathogenic organisms, Gram-positive cocci – staphylococci, pneumococci and streptococci (including enterococci) – meningococci, mycoplasma, L-forms, *Haemophilus influenzae*, the agents causing trachoma and lymphogranuloma venereum, chlamydia, clostridia, *Corynebacterium diphtheriae* (as an adjunct to antitoxin), neisseria, *Treponema pallidum*, bordetella.

Note: the majority of strains of *Haemophilus influenzae* are susceptible to the concentrations reached after ordinary doses.

Dosage and administration Adults 1–2 g daily, divided into 6, 8 or 12 hourly doses. May be increased up to 4 g daily in severe infections.

Tablets should be taken before or with meals.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to erythromycin.

Precautions: Erythromycin is excreted principally by the liver, so caution should be exercised in administering the antibiotic to patients with impaired hepatic function or concomitantly receiving potentially hepatotoxic agents.

Recent studies reveal that the use of erythromycin in patients who are receiving high doses of theophylline may be associated with an increase of serum theophylline levels and potential theophylline toxicity.

In case of theophylline toxicity and/or elevated serum theophylline levels, the dose of theophylline should be reduced while the patient is receiving erythromycin therapy.

Use in pregnancy: There is no evidence of hazard from erythromycin in human pregnancy and it has been in wide use for many years without apparent ill consequence. Animal studies have shown no hazard.

Side-effects: There are very few side-effects to any Abbott Erythrocin product. There are no reports implicating Erythrocin with abnormal tooth development and only rare reports of damage to the blood, kidneys, liver or central nervous system. Allergic reactions are rare and mild, although anaphylaxis has occurred. Occasionally there is abdominal discomfort after oral administration, sometimes with nausea and vomiting. It usually subsides after a few days without having to reduce the dosage. The rare possibility of superinfection caused by overgrowth of non-susceptible bacteria or fungi should be kept in mind during prolonged or repeated therapy especially when other antibacterial agents are simultaneously employed.

Overdosage: *Symptoms*: nausea, vomiting, diarrhoea.

Treatment: Gastric lavage, general supportive measures.

Pharmaceutical precautions Protect Filmtabs from light. Store below 25°C.

Legal category POM.

Package quantities Erythrocin 500 is supplied in blister packs of 15 and containers of 100 and 500 tablets.

Further information *Metabolisable carbohydrate content*: Approx. 0.15 g per tablet.

Product licence number 0037/5044.

ERYTHROCIN* I.V. LACTOBIONATE

Presentation Erythrocin I.V. Lactobionate is a soluble erythromycin salt suitable for intravenous administration. It is in the form of a sterile, lyophilised powder for reconstitution, in vials containing 300 mg erythromycin activity as the lactobionate, and in vials containing 1 g erythromycin activity as the lactobionate. When reconstituted according to the directions the concentration of benzyl alcohol (as a preservative) in the 5% stock solution is 0.9% in both strengths.

Uses *Clinical indications*: Erythrocin is highly effective in the treatment of a great variety of clinical infections. It is indicated in severe cases of infection caused by sensitive organisms and in cases where high blood levels are required at the earliest opportunity, or when the oral route is not available.

1. Upper respiratory tract infections.
2. Lower respiratory tract infections.
3. Skin and soft-tissue infections.
4. Gastro-intestinal infections.
5. Prophylaxis: Pre- and post-operative, trauma, burns and rheumatic fever.
6. Endocarditis and septicaemia.

Microbiological indications: Erythrocin is active against a wide variety of pathogenic organisms, Gram-positive cocci-staphylococci, pneumococci and streptococci (including enterococci) – meningococci, mycoplasma, L-forms, *Haemophilus influenzae*, the agents causing trachoma and lymphogranuloma venereum, chlamydia, clostridia, *Corynebacterium diphtheriae* (as an adjunct to antitoxin), neisseria, *Treponema pallidum*, bordetella.

Adults: Mild to moderate infections: 2 grams daily in divided doses.

Severe infections: 4 grams or more daily in divided doses.

Children: Mild to moderate infections: 30 mg/kg body weight daily in divided doses.

Severe infections: 50 mg/kg body weight daily in divided doses.

Administration: This may be by continuous infusion or by intermittent intravenous injection. The preparation is not suitable for intramuscular use.

For continuous infusion a concentration of 1 mg erythromycin per ml is recommended at final dilution.

For intermittent injection a concentration of 1 to 5 mg erythromycin per ml is recommended. This should be administered at intervals of not more than 6 hours. Injection should be sufficiently slow to avoid pain along the vein (several minutes if necessary).

Preparation of Solution:

1. Preparation of a 5% stock solution. (a) 300 mg vial: Add 6 ml of Water for Injections BP to the vial to obtain a stock solution containing 50 mg erythromycin per ml (5% solution). (b) 1 g vial: Add 20 ml of Water for Injections BP to the vial to obtain a stock solution containing 50 mg erythromycin per ml (5% solution).

Do not use 0.9% w/v Saline or other electrolyte solutions as, at this concentration, a precipitate may form.

Use within 24 hours of reconstitution.

2. Further dilution. The 1 mg erythromycin/ml (0.1% solution) is obtained by diluting the stock solution to 50 times its original volume. Thus, for the 300 mg vial from 6 ml to 300 ml, for the 1 g vial from 20 ml to 1,000 ml.

The 5 mg erythromycin/ml (0.5% solution) is obtained by diluting the stock solution to 10 times its original volume. Thus, for the 300 mg vial from 6 ml to 60 ml, for the 1 g vial from 20 ml to 200 ml.

The following are suitable diluents: Sodium Chloride Injection BP (0.9% saline), Compound Sodium Lactate Injection BP (Hartmann's Solution).

Solutions containing dextrose may also be used but sodium bicarbonate must first be added as a buffer to ensure neutrality.

2.4 ml of sterile 8.4% w/v sodium bicarbonate solution will neutralise one litre each of: Dextrose Injection BP (5%), or of Sodium Chloride and Dextrose Injection BP (usually 0.18% sodium chloride and 4.0% dextrose).

The stability of solutions of Erythrocin Lactobionate is adversely affected below pH 5.5.

To ensure potency, solutions of Erythrocin Lactobionate at final dilution should be administered completely within 8 hours of preparation.

Contra-indications, warnings, etc

Contra-indications: Compatibility with other I.V. additives has not been established. Known sensitivity to erythromycin.

Precautions: Extravasation should be avoided. The injection should be slow (several minutes if necessary) to avoid pain along the vein.

Erythromycin is excreted principally by the liver, so caution should be exercised in administering the antibiotic to patients with impaired hepatic function or concomitantly receiving potentially hepatotoxic agents.

Reversible hearing loss associated with the intravenous infusion of 4 or more grams per day of erythromycin lactobionate has been reported rarely.

Recent studies reveal that the use of erythromycin in patients who are receiving high doses of theophylline may be associated with an increase of serum theophylline levels and potential theophylline toxicity.

In case of theophylline toxicity and/or elevated serum theophylline levels, the dose of theophylline should be reduced while the patient is receiving erythromycin therapy.

Use in pregnancy: There is no evidence of hazard from erythromycin in human pregnancy and it has been in wide use for many years without apparent ill consequence. Animal studies have shown no hazard.

Side-effects: There are very few side-effects to any Abbott Erythrocin product. There are no reports implicating Erythrocin with abnormal tooth development and only rare reports of damage to the blood, kidneys, liver or central nervous system. Allergic reactions are rare and mild, although anaphylaxis has occurred. The rare possibility of superinfection caused by overgrowth of non-susceptible bacteria or fungi should be kept in mind during prolonged or repeated therapy, especially when other antibacterial agents are simultaneously employed.

Pharmaceutical precautions The powder is stable at room temperature. Use within 24 hours of reconstitution.

Legal category POM.

Package quantities Erythrocin I.V. Lactobionate is supplied in 300 mg vials and in 1 g vials.

Further information Contains no sodium.

Product licence numbers

300 mg vials 0037/5063

1 g vials 0037/0092

ERYTHROCIN* ORAL SUSPENSION

Presentation A ready-made caramel-flavoured suspension containing 100 mg erythromycin activity per 5 ml as erythromycin stearate.

Uses For the prophylaxis and treatment of infections caused by erythromycin-sensitive organisms.

Clinical indications: Erythrocin is highly effective in the treatment of a great variety of clinical infections.

1. Upper respiratory tract infections: Tonsillitis, peritonsillar abscess, pharyngitis, laryngitis, sinusitis, secondary infections in colds and influenza.

2. Lower respiratory tract infections: Tracheitis, acute and chronic bronchitis, pneumonia (lobar pneumonia, bronchopneumonia, primary atypical pneumonia), bronchiectasis, legionnaires' disease.

3. Ear infections: Otitis media and otitis externa, mastoiditis.

4. Oral infections: Gingivitis, Vincent's angina.

5. Eye infections: Blepharitis.

6. Skin and soft-tissue infections: Boils and carbuncles, paronychia, abscesses, pustular acne, impetigo, cellulitis, erysipelas.

7. Gastro-intestinal infections: Cholecystitis, staphylococcal enterocolitis.

8. Prophylaxis: Pre- and post-operative, trauma, burns, rheumatic fever.

9. Other infections: Osteomyelitis, urethritis, gonorrhoea, syphilis, lymphogranuloma venereum, diphtheria, prostatitis, scarlet fever.

Note: The antibiotic has also proved to be of value in endocarditis and septicaemia, but in these conditions initial administration of erythromycin by the intravenous route is advisable.

Microbiological indications: Erythrocin is active against a wide variety of pathogenic organisms, Gram-positive cocci – staphylococci, pneumococci and streptococci (including enterococci) – meningococci, mycoplasma, L-forms, *Haemophilus influenzae*, the agents causing trachoma and lymphogranuloma venereum, chlamydia, clostridia, *Corynebacterium diphtheriae* (as an adjunct to antitoxin), neisseria, *Treponema pallidum*, bordetella.

Note: The majority of strains of *Haemophilus influenzae* are susceptible to the concentrations reached after ordinary doses.

Dosage and administration 30–50 mg/kg per day divided into 6-, 8- or 12-hourly doses. For very severe infections the dosage may be increased to 4 g or more per day for adults.

Note: Shake the suspension well before using.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to erythromycin.

Precautions: Erythromycin is excreted principally by the liver, so caution should be exercised in administering the

antibiotic to patients with impaired hepatic function or concomitantly receiving potentially hepatotoxic agents.

Recent studies reveal that the use of erythromycin in patients who are receiving high doses of theophylline may be associated with an increase of serum theophylline levels and potential theophylline toxicity.

In case of theophylline toxicity and/or elevated serum theophylline levels, the dose of theophylline should be reduced while the patient is receiving erythromycin therapy.

Use in pregnancy: There is no evidence of hazard from erythromycin in human pregnancy and it has been in wide use for many years without apparent ill consequence. Animal studies have shown no hazard.

Side-effects and precautions: There are very few side-effects to any Abbott Erythrocin product. There are no reports implicating Erythrocin with abnormal tooth development, and only rare reports of damage to the blood, kidneys, liver or central nervous system. Allergic reactions are rare and mild although anaphylaxis has occurred. Occasionally there is abdominal discomfort after oral administration, sometimes with nausea and vomiting. It usually subsides after a few days without having to reduce the dosage. The rare possibility of super-infection caused by overgrowth of non-susceptible bacteria or fungi should be kept in mind during prolonged or repeated therapy, especially when other antibacterial agents are simultaneously employed.

Overdosage: Symptoms: nausea, vomiting and diarrhoea.

Treatment: Gastric lavage, general supportive measures.

Pharmaceutical precautions Protect from heat. Store below 30°C.

Legal category POM.

Package quantities Erythrocin Suspension is supplied in bottles of 100 and 500 ml.

Further information Metabolisable carbohydrate content: approximately 3.5 g per 5 ml.

Product licence number 0037/5045.

ERYTHROPEP* PI ERYTHROPEP* ERYTHROPEP* FORTE

Presentation Erythromycin ethyl succinate in the form of granules which, when reconstituted, make a cherry-flavoured suspension. It is available in three strengths:

- 1) Erythropep PI which contains 125 mg erythromycin activity per 5 ml.
- 2) Erythropep containing 250 mg erythromycin activity per 5 ml.
- 3) Erythropep Forte containing 500 mg erythromycin activity per 5 ml.

In addition, Erythropep PI is available in single dose sachets each containing 125 mg erythromycin activity. Erythropep is available in single dose sachets each containing 250 mg erythromycin activity.

Uses Clinical indications: Erythropep is highly effective in the treatment of a great variety of clinical infections:

1. **Upper respiratory tract infections:** Tonsillitis, peritonsillar abscess, pharyngitis, laryngitis, sinusitis, secondary infections in colds and influenza.

2. **Lower respiratory tract infections:** Tracheitis, acute and chronic bronchitis, pneumonia (lobar pneumonia, bronchopneumonia, primary atypical pneumonia), bronchiectasis, legionnaires' disease.

3. **Ear infections:** Otitis media and otitis externa, mastoiditis.

4. **Oral infections:** Gingivitis, Vincent's angina.

5. **Eye infections:** Blepharitis.

6. **Skin and soft-tissue infections:** Boils and carbuncles, paronychia, abscesses, pustular acne, impetigo, cellulitis, erysipelas.

7. **Prophylaxis:** Pre- and post-operative, trauma, burns, rheumatic fever.

8. **Genito-urinary infections:** Urethritis, gonorrhoea, syphilis, lymphogranuloma venereum, prostatitis.

9. **Other infections:** Osteomyelitis, diphtheria, scarlet fever.

Note: The antibiotic has also proved to be of value in endocarditis and septicaemia, but in these conditions initial administration of erythromycin lactobionate by the intravenous route may be advisable.

Microbiological indications: Erythropep is active against a wide variety of pathogenic organisms, Gram-positive cocci – staphylococci, pneumococci and streptococci (including enterococci) – meningococci, mycoplasma, L-forms, *Haemophilus influenzae*, the agents causing trachoma and lymphogranuloma venereum, chlamydia, clostridia, corynebacteria, neisseria, *Treponema pallidum*, bordetella.

Note: The majority of strains of *Haemophilus influenzae* are susceptible to the concentrations reached after ordinary doses.

Dosage and administration Reconstitution: Erythropep products are taken orally after being reconstituted as follows:

1. **Erythropep PI:** Add 69 ml water to the granules contained in 100 ml bottle and shake vigorously. This will make 100 ml of the suspension, each 5 ml containing 125 mg erythromycin activity.
2. **Erythropep:** Add 68 ml water to the granules contained in 100 ml bottle and shake vigorously. This will make 100 ml of the suspension, each 5 ml containing 250 mg erythromycin activity.
3. **Erythropep Forte:** Add 61 ml water to the granules contained in 100 ml bottle and shake vigorously. This will make 100 ml of the suspension, each 5 ml containing 500 mg erythromycin activity.
4. **Erythropep PI single dose sachet.** Disperse the contents of the sachet in a little water before taking.
5. **Erythropep single dose sachet:** Disperse the contents of the sachet in a little water before taking.

Recommended dosage:

1. Erythropep PI suspension and single dose sachets for infants and babies up to 2 years of age, 125 mg, four times daily.

2. Erythropep suspension and single dose sachets for children between the ages of 2 and 8 years, 250 mg, four times daily.

3. Erythropep Forte for children above 8 years of age, and adults, 500 mg, four times daily.

When twice daily medication is required for children over 2 years of age, half the total dose may be given every 12 hours.

In terms of mg/kg the usual dose is 30 mg erythromycin/kg/day in divided doses. In very severe infections

this may be increased to 50 mg erythromycin/kg/day in divided doses.

The usual adult dose is 2 g/day in divided doses. For severe infections this may be increased to 4 g or more, per day, in divided doses.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to erythromycin.

Precautions: Erythroped is excreted principally by the liver, so caution should be exercised in administering the antibiotic to patients with impaired hepatic function or concomitantly receiving potentially hepatotoxic agents.

Recent studies reveal that the use of erythromycin in patients who are receiving high doses of theophylline may be associated with an increase of serum theophylline levels and potential theophylline toxicity.

In case of theophylline toxicity and/or elevated serum theophylline levels, the dose of theophylline should be reduced while the patient is receiving erythromycin therapy.

Use in pregnancy: There is no evidence of hazard from erythromycin in human pregnancy and it has been in wide use for many years without apparent ill consequence. Animal studies have shown no hazard.

Side-effects: There are very few side-effects to any Abbott Erythroped product. There are no reports implicating Erythroped with abnormal tooth development and only rare reports of damage to the blood, kidneys, liver or central nervous system. Allergic reactions are rare and mild, although anaphylaxis has occurred. Occasionally there is abdominal discomfort after oral administration, sometimes with nausea and vomiting. It usually subsides after a few days without having to reduce the dosage.

Overdosage: *Symptoms:* nausea, vomiting and diarrhoea.

Treatment: Gastric lavage, general supportive measures.

Pharmaceutical precautions Store in a cool place and keep the container tightly closed. The suspension should be used within 5 days after reconstitution. Shake well before using.

Legal category POM.

Package quantities Erythroped PI is supplied in 100 ml bottles, and in boxes of 200 single dose sachets. Erythroped is supplied in 100 ml bottles, and in boxes of 200 single dose sachets. Erythroped Forte is supplied in 100 ml bottles.

Further information *Metabolisable carbohydrate content:* Erythroped PI, approx. 2.0 g per 5 ml or 0.9 g per sachet.

Erythroped approx. 1.9 g per 5 ml or per sachet.

Erythroped Forte, approx. 2.0 g per 5 ml.

Product licence numbers

Erythroped PI suspension	0037/5015
Erythroped suspension	0037/5014
Erythroped Forte	0037/5016
Erythroped PI single dose sachets	0037/5017
Erythroped single dose sachets	0037/5018

ETHRANE* ▼

Presentation Ethrane (enflurane) is an inhalation anaesthetic with a pleasant ethereal odour. No additives or stabilisers are present.

Actions Induction and recovery are rapid. It does not stimulate excessive salivation, tracheobronchial secretions or cause bronchial constriction. Pharyngeal and laryngeal reflexes are diminished quickly. The level of anaesthesia changes rapidly with Ethrane. Tachypnoea does not usually occur. Spontaneous respiration becomes depressed as the depth of anaesthesia increases.

Ethrane provokes a 'sigh' response reminiscent of that seen with diethyl ether.

During induction there is a decrease in blood pressure followed by a return to near normal levels, which may or may not be associated with surgical stimulation.

Blood pressure tends to fall in direct relation to the depth of anaesthesia but cardiac rate and rhythm remain stable. Ethrane appears to 'sensitise' the myocardium to adrenaline in man to a lesser extent than halothane. Available data indicate that subcutaneous injections of adrenaline may be safely administered to humans in concentrations of 1:100,000 or less at a dose of 10 ml in any given 10 minute period and not more than 30 ml/hour. All the usual precautions in the use of vasoconstrictor substances must be observed.

Good muscular relaxation is obtained with Ethrane, but should greater relaxation be necessary minimal doses of an intravenous muscle relaxant may be used with measures to ensure adequate ventilation.

All commonly used intravenous muscle relaxants are compatible with Ethrane.

Note: Ethrane potentiates the effect of the non-depolarising muscle relaxants which should therefore be used in reduced dosage. Neostigmine does not reverse the direct effect of Ethrane.

Ethrane produces little post operative analgesia.

Ethrane may be used for induction and maintenance of general anaesthesia. Adequate data are not available yet to establish its full place in obstetric anaesthesia other than in caesarean section. High concentrations of Ethrane may produce marked uterine relaxation.

Ethrane may be used for outpatient and dental anaesthesia in view of the rapidity of action and recovery, with stability of the cardiovascular system. Ethrane can be used safely in children.

Metabolism of Ethrane in the human body proceeds at a low rate; inorganic fluoride is formed but serum levels in healthy individuals have not been shown to rise to significant levels.

Dosage and administration Vaporisers calibrated specifically for Ethrane should be used so that the concentration being delivered is known.

Premedication: Drugs used for premedication should be selected for each individual patient. The use of anticholinergic drugs is a matter of choice.

Induction: To avoid excitement a short-acting barbiturate or other intravenous induction agent should be administered, followed by inhalation of the Ethrane mixture. Ethrane and oxygen alone or oxygen-nitrous oxide mixtures may be used.

It is recommended that Ethrane induction be initiated at a concentration of 0.4% and gradually increased by 0.5% increments after every few breaths until surgical anaesthesia is achieved.

The maximum inspired concentrations during induction should be no more than 4.5%. High inspired concentrations should be lowered as rapidly as possible to maintenance levels to prevent overdosage, and the blood pressure carefully observed.

Maintenance: In conjunction with nitrous oxide, surgical

levels of anaesthesia may be maintained with a 0.5%–3% concentration of Éthane. A 3% concentration should not be exceeded for maintenance during spontaneous respiration. With controlled respiration techniques, during prolonged operations, single or supplementary doses of muscle relaxants may be used if required, bearing in mind the possibility of some slight potentiation. Ventilation to maintain the carbon dioxide tension in arterial blood in the 4.7–6.0 kPa (35–45 mmHg) range is preferred to hyper- or hypoventilation, in order to minimise the possibility of CNS excitation.

Blood pressure levels during maintenance depend on Éthane concentration in the absence of other complicating factors. Excessive decreases (unless related to hypovolaemia) may be due to depth of anaesthesia and in such instances should be corrected by reducing the inspired Éthane concentration.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to Éthane.

Precautions: Éthane should be used with caution in patients who by virtue of medical or drug history, may be considered more susceptible to cerebral stimulation produced by this drug. Increasing depth of anaesthesia with Éthane may produce changes in the electroencephalogram characterised by high voltage, fast frequency waves progressing through spike-dome complexes alternating with periods of electrical silence to frank seizure activity patterns. The latter may or may not be associated with motor movement. Motor activity, when encountered, generally consists of twitching or 'jerks' of various muscle groups; it is self-limiting and can be terminated by lowering the anaesthetic concentration. This electroencephalographic pattern associated with deep anaesthesia may be exacerbated by hyperventilation producing low arterial carbon dioxide tension. The pattern serves as a warning that depth of anaesthesia is excessive. Cerebral blood flow and metabolism studies in normal volunteers during seizure patterns show no evidence of cerebral hypoxia, and recovery appears to be uncomplicated.

Since levels of anaesthesia may be altered easily and rapidly, only vaporisers which deliver a predictable output with reasonable accuracy should be used. Hypotension and respiratory exchange can serve as a guide to anaesthetic depth. With deep levels of anaesthesia, more marked hypotension and respiratory depression are encountered.

The action of non-depolarising relaxants is augmented by Éthane, so less than the usual amounts of those drugs should be used.

Overdosage or unduly rapid absorption of adrenaline administered topically or by subcutaneous or submucosal injection during Éthane anaesthesia may give rise to cardiac arrhythmias (see 'Actions' section). Care must be taken to avoid intravenous injection.

Bromsulphthalein (BSP) retention is mildly raised post-operatively in some cases. There is some elevation of blood glucose and white blood cell count intra-operatively.

Use in pregnancy: Reproduction studies have been performed in rats and rabbits. Following single and multiple maternal administrations, no evidence of teratogenicity due to Éthane was found in the developing fetuses in these species. The relevance of these studies to the human is not known. Since there is no adequate experience in pregnant women who have received the drug, safety in pregnancy has not been established.

Adverse reactions:

1. Motor activity exemplified by movement of various muscle groups and seizures may be encountered with deep levels of Éthane anaesthesia, particularly with hyperventilation.

2. Hypotension, respiratory depression and arrhythmias have been reported.

3. Elevation of the white blood cell count has been observed. It has not been determined whether this is related to Éthane or to surgical stress.

4. A mild increase in serum glucose concentration has been observed in some normal and diabetic patients, as with other anaesthetic agents. There seems to be no contra-indication to the use of the agent in these patients for whom rapid recovery is advantageous.

5. Hepatic enzyme changes occur less frequently and to a lesser degree after multiple Éthane anaesthetics when compared with multiple exposures to halothane. While jaundice and significant hepatic enzyme increases occasionally occur after halothane anaesthesia there is, as yet, no report of their appearance after the administration of Éthane in the absence of complicating factors such as blood transfusion or concomitant administration of hepatotoxic drugs.

6. Increased serum inorganic fluoride levels have been found during and immediately after Éthane anaesthesia due to biodegradation of the agent. These levels normally remain well below the postulated threshold for nephrotoxicity and, after reaching a peak within eight hours of the end of the anaesthetic, rapidly return to preoperative values.

Although there is no evidence that Éthane anaesthesia adversely affects the normal or diseased kidney it may be prudent to avoid its use in cases of chronic renal failure.

Side-effects: Nausea, vomiting, hiccups or shivering may occur occasionally.

Pharmaceutical precautions Store away from heat. Keep well closed.

Legal category P.

Package quantities Éthane is supplied in bottles of 250 ml.

Further information Nil.

Product licence number 0037/0053.

EUTONYL*

Presentation Each apricot Eutonyl Filmtab* (film-coated tablet Abbott) contains 25 mg pargyline hydrochloride.

Uses For the treatment of resistant hypertension, particularly when other treatments have failed.

Note: Eutonyl is a monoamine oxidase inhibitor and the usual precautions necessary with this class of drug must be observed.

Dosage and administration Eutonyl is administered orally as a single daily dose; there is no known advantage in prescribing the drug more frequently. Clinical response to the drug is not immediate. Four days to three weeks or more may be required to produce the full effects of a given daily dosage. For this reason it is generally unwise to increase dosage more frequently than once a week. The effects of the drug may persist following reduction of dosage or withdrawal. If therapy must be interrupted

because of undesirable side-effects, the drug should be withheld until all such effects have disappeared. Therapy is then reinstituted at a lower dosage. Because the drug exerts an orthostatic effect on blood pressure, dosage adjustments should be based upon the blood pressure response in the standing position.

The usual adult dosage for initiating therapy in hypertensive patients not receiving other antihypertensive agents is 25 mg once daily. This dosage may be increased once a week until the desired response is obtained, or a maximum of 75 mg per day is reached. Patients over the age of 65, or those who have undergone sympathectomy, may be unusually sensitive to the antihypertensive properties of the drug. When Eutonyl is added to an established antihypertensive regimen, the initial dose should not exceed 25 mg daily (less in sympathectomised or elderly patients).

Eutonyl should not be administered to children under 12 years of age, because of limited experience with this group.

Reduction of blood pressure is often maintained in hypertensive patients with a daily dose of 25–50 mg of Eutonyl alone. Larger doses may be tried in resistant cases. In general, the dosage should be kept at the minimum level required to maintain a desirable reduction in blood pressure without encountering undue side-effects. A few patients may develop a relative tolerance to the antihypertensive effects of the drug.

Contra-indications, warnings, etc

Contra-indications: Phaeochromocytoma, paranoid schizophrenia, hyperthyroidism and advanced renal failure. Eutonyl should not be administered to pregnant patients, those with malignant hypertension, or to children under 12 years of age because significant clinical information concerning the use of the drug in these conditions is not available. In general the following drugs or agents are contra-indicated in patients receiving Eutonyl:

Centrally acting sympathomimetic amines such as amphetamine and its derivatives (also found in anorectic preparations).

Some patients may experience a mood-elevating effect, as may happen with many compounds of this class. However, clinical studies have not clearly differentiated the mood-elevating effects from those which may result from the reduction of blood pressure alone.

Peripherally acting sympathomimetic drugs such as ephedrine and its derivatives (also found in nasal decongestants, cold remedies and hay-fever preparations).

Aged cheese (e.g. Cheddar, Camembert, and Stilton), processed cheese and other foods which require the action of bacteria or moulds for their preparation or preservation (e.g. Chianti wine) because of the presence of pressor substances such as tyramine. Other foods which should be avoided during pargyline therapy because of their high pressor amine content include chocolate, yeast extract, avocado, pickled herring, pods of broad beans, banana peels and chicken livers. Cream cheese and cottage cheese can be allowed in the diet during pargyline therapy since their tyramine content is low.

In some patients receiving pargyline, tyramine may precipitate an abrupt rise in blood pressure accompanied by some or all of the following: severe headache, chest pain, profuse sweating, palpitation, tachycardia or bradycardia, visual disturbances, stertorous breathing, coma and intracranial bleeding (which could be fatal). A

phenothiazine derivative or phentolamine may be administered parenterally for treatment of such an acute hypertensive reaction.

Parenteral administration of reserpine or guanethidine which may cause hypertensive reactions from sudden release of catecholamines. Parenteral use of these drugs is contra-indicated during, and for at least one week following, treatment with pargyline hydrochloride.

Imipramine, amitriptyline, desipramine, nortriptyline or their analogues should not be used with pargyline. The use of these drugs with a monoamine oxidase inhibitor has been reported to cause vascular collapse and hyperthermia which may be fatal. A drug-free interval (at least two weeks) should separate therapy with Eutonyl and use of these agents.

Other monoamine oxidase inhibitors, since they may augment the effects of pargyline hydrochloride.

Methyldopa or dopamine, which may cause hyperexcitability in patients receiving pargyline hydrochloride.

There have been several reports of potentiation of the pressor effects of L-dopa by various monoamine oxidase inhibitors. For this reason concomitant therapy is contra-indicated and at least one month should elapse after discontinuation of a monoamine oxidase inhibitor before L-dopa is given.

Patients' warnings:

1. Patients should be warned against the use of any over-the-counter preparations, particularly 'cold preparations' and antihistamines, or prescription drugs without the knowledge and consent of the physician.

2. Patients should be cautioned on the use of cheese (see contra-indications) and alcoholic beverages in any form.

3. Patients should be warned about the likelihood of the occurrence of orthostatic hypotension.

4. Patients should be instructed to report promptly the occurrence of severe headache or other unusual symptoms.

5. Patients with angina pectoris or coronary artery disease should be especially warned not to increase their physical activities in response to a diminution in anginal symptoms or an increase in well-being occurring during treatment with Eutonyl.

Physicians' warnings:

1. When indicated the following should be cautiously prescribed in reduced dosages: antihistamines; hypnotics, sedatives or tranquillisers; narcotics (pethidine should not be used).

2. Discontinue Eutonyl at least two weeks prior to elective surgery.

3. In emergency surgery the dose of narcotics or other premedication should be reduced to one quarter or one-fifth of the usual amount. Clinical experience has shown that response to all anaesthetic agents can be exaggerated in patients receiving Eutonyl. Therefore the dose of the anaesthetic should be carefully adjusted.

4. Eutonyl may induce hypoglycaemia.

5. Care should be exercised in using Eutonyl in patients with advanced renal failure.

Precautions: The therapeutic response to a variety of drugs may be changed or exaggerated in patients receiving a monoamine oxidase inhibitor such as pargyline hydrochloride. Alcohol, narcotics (pethidine should be avoided), antihistamines, anaesthetics, barbiturates, chloral hydrate and other hypnotics, sedatives, tranquillisers or caffeine should be used cautiously and at a reduced dosage in patients who are taking Eutonyl.

An increased response to central depressants may be

manifested by acute hypotension and increased sedative effect. Pargyline hydrochloride may increase the hypotensive effects of anaesthetic agents and surgery, and so should be discontinued for 10–14 days prior to surgery. In the event of emergency surgery, smaller doses than usual (one-quarter to one-fifth) of narcotics, analgesics and other premedications should be used. If severe hypotension should occur, this can be controlled by small doses of a vasopressor agent such as noradrenaline.

Febrile illnesses may increase the hypotensive effect and it may be advisable to withdraw the drug during such diseases. Eutonyl is a non-hydrazine derivative and has not been shown to damage the kidney, liver or blood-forming organs, or to be associated with optic atrophy. However, laboratory studies including urinalyses, liver function tests and complete blood counts should be performed periodically. The drug should be used with caution in the presence of liver disease. Since pargyline hydrochloride is excreted primarily in the urine, patients with impaired renal function may experience cumulative drug effects. Such patients should also be watched for elevations of blood urea nitrogen and other evidence of progressive renal failure. If such alterations should persist and progress, the drug should be discontinued.

Patients receiving this drug for prolonged periods of time should be examined for any changes in colour perception, visual fields, fundi and visual acuity.

Patients with angina pectoris or coronary artery disease should be warned against an increase in physical activity because of the diminution of anginal symptoms and an increased feeling of well-being with Eutonyl. All patients should be warned about the possible occurrence of orthostatic hypotension. If hypotension develops in these patients, Eutonyl dosage should be reduced or therapy discontinued since severe and/or prolonged hypotension may precipitate cerebral or coronary vessel thrombosis.

Eutonyl should not be used in individuals with hyperactive or hyperexcitable personalities, as some of these patients show an undesirable increase in motor activity with restlessness, confusion, agitation and disorientation.

Clinical studies have shown that pargyline may unmask severe psychotic symptoms such as hallucinations or paranoid delusions in some patients with pre-existing serious emotional problems. This can usually be controlled by judicious administration of chlorpromazine intramuscularly or other phenothiazines, the patient remaining supine for one hour after administration. Pargyline hydrochloride should be used with caution in patients with parkinsonism as it may increase symptoms. In addition great care is required if pargyline hydrochloride is administered in conjunction with anti-parkinsonian agents. Clinical reports state that certain individuals receiving pargyline hydrochloride for a prolonged period of time are refractory to the nerve-blocking effects of local anaesthetics.

Side-effects: Apart from hypotensive symptoms due to overdosage, the side-effects with Eutonyl are relatively infrequent especially if the dosage is kept as low as possible by combining it with a thiazide. Apart from orthostatic hypotension, side-effects include mild constipation, oedema, dry mouth, sweating, increased appetite, arthralgia, nausea and vomiting, headache, insomnia, difficulty in micturition, nightmares, impotence and delayed ejaculation, rash and purpura. Gain in weight may be due to either oedema or increased

appetite. Drug fever is extremely rare. In some patients a reduction of the blood sugar has been noted. Congestive heart failure has been reported in patients with reduced cardiac reserve. Muscular twitching and extrapyramidal-like symptoms have also been reported.

Overdosage: Symptoms: Reported effects of monoamine oxidase inhibitor overdosage include agitation, hallucinations and exaggerated reflexes, hyperpyrexia, convulsions and both hypotension and hypertension.

Treatment: Management must be attempted with great caution because of the possibility of interaction with the drugs used. Conservative treatment to maintain normal temperature, respiration, blood pressure and correct fluid and electrolyte balance is usually successful.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Eutonyl is supplied in containers of 100 Filmtabs.

Further information *Metabolisable carbohydrate content:* approx 0.11 g per tablet.

Product licence number 0037/5032.

FERRO-GRADUMET*

Presentation Each red Filmtab* (film-coated tablet Abbott) contains Dried Ferrous Sulphate BP 325 mg (equivalent to 105 mg elemental iron) in a sustained release form (Gradumet*).

Uses For the prevention and treatment of iron-deficiency anaemia.

The Gradumet device allows sustained release of the active ingredient over a number of hours, which increases iron utilisation and reduces gastro-intestinal intolerance.

The device consists of an inert plastic matrix, honey-combed by thousands of narrow passages which contain the active drug together with a water-soluble channelling agent. As the tablet passes down the gastro-intestinal tract the iron is leached out. The spent matrix is finally excreted in the stools.

Dosage and administration *Recommended adult oral dosage:* 1 tablet daily before food. As gastro-intestinal intolerance is not a problem with Ferro-Gradumet it should be given on an empty stomach, when iron is most effectively absorbed.

Children: Not suitable for children under 12 years of age.

Contra-indications, warnings, etc *Precautions:* As with all iron preparations Ferro-Gradumet should be given with care in patients with haemochromatosis, haemolytic anaemia or haemoglobinopathies. Interaction (chelation) with tetracyclines. Ferro-Gradumet tablets should be kept out of children's reach.

Side-effects: Those associated with conventional oral iron preparations, such as nausea, vomiting, diarrhoea and/or constipation, are less likely to occur. Because of the sustained release pattern, only a small amount of the iron is released in the stomach which is never exposed to large amounts of iron as is the case with ordinary tablets. The clinical advantages which follow are twofold – minimal side-effects and efficient absorption.

Overdosage: Symptoms: The initial symptoms of massive ferrous sulphate overdosage are absent, the delayed release allowing sufficient time for gastric lavage and

other forms of treatment to be effective before absorption occurs to any extent. Treatment should not be delayed, therefore, even if immediate symptoms are absent. Symptoms may include gastro-intestinal irritation, lassitude, haematemesis, diarrhoea, cardiovascular collapse. A transient recovery followed by a relapse 24–48 hours after ingestion may occur.

Treatment: The ingested Gradumet matrix cannot be readily aspirated through a stomach tube and there is no known chemical which will dissolve the Gradumet without harming the gastric mucosa. Accordingly, when overdosage is discovered early, the following procedure is recommended.

1. Administer an emetic by stomach tube.
2. Withdraw the stomach tube and wait for the patient to vomit.
3. Keep the patient under constant surveillance to detect possible aspiration of vomitus; maintain suction apparatus and standby emergency oxygen in case of need.
4. Examine the vomitus for returned Gradumet tablets.
5. Administer a saline cathartic. By the time toxic signs have appeared, Gradumet tablets are in most cases past the pylorus so that emesis is of no value. Gastric lavage may be considered to remove amounts of the drug already released in the stomach. A saline cathartic then should be given to speed the Gradumet tablets along the alimentary canal so as to minimise or prevent further absorption of the medication.
6. The use of an iron chelating agent such as oral desferrioxamine should be considered. In severe cases parenteral desferrioxamine may be necessary.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Ferro-Gradumet is supplied in 5 carton packs, each carton containing 30 (2 × 15) tablets.

Further information *Metabolisable carbohydrate content:* Approx. 0.02 g per tablet.

Product licence number 0037/5000.

FERROGRAD® C

Presentation Each two-layered, red Filmtab® (film-coated tablet Abbott) contains Dried Ferrous Sulphate BP 325 mg (equivalent to 105 mg elemental iron) in a sustained release form (Gradumet®) and 500 mg vitamin C, as sodium ascorbate.

Uses For the prevention and treatment of iron-deficiency anaemia and for the simultaneous treatment of vitamin C deficiency.

The Gradumet device allows sustained release of ferrous sulphate over a number of hours, which increases iron utilisation and reduces gastro-intestinal intolerance. The Gradumet consists of an inert plastic matrix honey-combed by thousands of narrow passages which contain the active drug together with a water-soluble channelling agent. As the tablet passes down the gastro-intestinal tract the iron is leached out. The spent matrix is finally excreted in the stools.

Ferrograd C combines the advantages of ferrous sulphate in the Gradumet matrix with a large dose of vitamin C further to enhance absorption and is indicated in iron-deficiency anaemia, especially when poor ab-

sorption is a problem, and to promote haemopoiesis in patients where an underlying Vitamin C deficiency limits optimal haemoglobin formation. In patients whose haemoglobin has returned to normal, Ferrograd C may be of particular value in replenishing the depleted stores of iron.

Dosage and administration *Recommended adult oral dosage:* 1 tablet a day before food.

Children: not recommended for children under 12 years of age.

Contra-indications, warnings, etc *Warning:* The administration of therapeutic doses of ascorbic acid may interfere with the Clinistix test for glycosuria giving a false negative result.

Side-effects: Those associated with conventional oral iron preparations, such as nausea, vomiting, diarrhoea and/or constipation, are less likely to occur. Because of the sustained release pattern only a small amount of the iron is released in the stomach, which is never exposed to large amounts of iron as is the case with ordinary tablets. The clinical advantages which follow are two-fold – minimal side-effects and efficient absorption.

Precautions: As with all iron preparations Ferrograd C should be given with care in patients with haemochromatosis, haemolytic anaemias or haemoglobinopathies. Interaction (chelation) with tetracyclines. Ferrograd C Tablets should be kept out of children's reach.

Overdosage: Symptoms: The initial symptoms of massive ferrous sulphate overdosage are absent, the delayed release allowing sufficient time for gastric lavage and other forms of treatment to be effective before absorption occurs to any extent. Treatment should not be delayed, therefore, even if immediate symptoms are absent.

Symptoms may include: gastro-intestinal irritation, lassitude, haematemesis, diarrhoea, cardiovascular collapse. A transient recovery followed by a relapse 24–48 hours after ingestion may occur.

Vitamin C overdosage may cause acidosis and haemolytic anaemia in predisposed individuals (glucose 6-phosphate dehydrogenase deficiency). Renal failure may occur in massive Vitamin C overdosage.

Treatment: The ingested Gradumet matrix cannot be readily aspirated through a stomach tube and there is no known chemical which will dissolve the Gradumet without harming the gastric mucosa. Accordingly, when overdosage is discovered early, the following procedure is recommended:

1. Administer an emetic by stomach tube.
2. Withdraw the stomach tube and wait for the patient to vomit.
3. Keep the patient under constant surveillance to detect possible aspiration of vomitus; maintain suction apparatus and standby emergency oxygen in case of need.
4. Examine the vomitus for returned Gradumet tablets.
5. Administer a saline cathartic. By the time toxic signs have appeared, Gradumet tablets are in most cases past the pylorus so that emesis is of no value. Gastric lavage may be considered to remove amounts of the drug already released in the stomach. A saline cathartic then should be given to speed the Gradumet tablets along the alimentary canal so as to minimise or prevent further absorption of the medication.
6. The use of an iron chelating agent such as oral desferrioxamine should be considered. In severe cases parenteral desferrioxamine may be necessary.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Ferrograd C is supplied in 5 carton packs, each carton containing 30 (2 × 15) tablets.

Further information *Metabolisable carbohydrate contents:* Approx. 0.01 g per tablet.

Product licence number 0037/5001.

FERROGRAD* FOLIC

Presentation A two-layered (red and yellow), round, bi-convex Filmtab* (film-coated tablet Abbott). Each tablet contains Dried Ferrous Sulphate BP 325 mg (equivalent to 105 mg elemental iron) in a sustained release form (red half – Gradumet*) and 350 mcg Folic Acid BP (yellow half).

Uses Ferrograd Folic is indicated:

1. For the prevention and treatment of iron-deficiency anaemia of pregnancy.
2. For the prophylaxis of megaloblastic anaemia of pregnancy.

The Gradumet device allows sustained release of ferrous sulphate over a number of hours, which increases iron utilisation and reduces gastro-intestinal intolerance. The device consists of an inert plastic matrix, honey-combed by thousands of narrow passages which contain the active drug together with a water-soluble channelling agent. As the tablet passes down the gastro-intestinal tract the iron is leached out. The spent matrix is finally excreted in the stools. Folic acid requirements in pregnancy can be met with supplements of between 300 and 400 mcg daily. Without such supplements folate deficiency may develop leading to megaloblastic anaemia with attendant obstetric risks. Doses over 400 mcg may mask undiagnosed primary B₁₂ deficiency.

In the extremely unlikely event of this condition occurring in a pregnant woman, the safe prophylactic dose is considered to be 350 mcg.

Dosage and administration *Recommended adult oral dosage:* 1 tablet daily before food throughout pregnancy and during the first month of the puerperium. *Children:* not applicable.

Contra-indications, warnings, etc

Contra-indications: Megaloblastic anaemia due to primary vitamin B₁₂ deficiency.

Side-effects: Those associated with conventional oral iron preparations such as nausea, vomiting, diarrhoea and/or constipation, are less likely to occur. Because of the sustained release pattern, only a small amount of the iron is released in the stomach, which is never exposed to large amounts of iron as is the case with ordinary tablets. The clinical advantages which follow are twofold – minimal side-effects and efficient absorption.

Precautions: As with all iron preparations Ferrograd Folic should be given with care in patients with haemochromatosis, haemolytic anaemias or haemoglobinopathies. Interaction (chelation) with tetracyclines. Ferrograd Folic tablets should be kept out of children's reach.

Overdosage: *Symptoms:* The initial symptoms of massive ferrous sulphate overdosage are absent, the delayed release allowing sufficient time for gastric lavage and

other forms of treatment to be effective before absorption occurs to any extent. Treatment should not be delayed, therefore, even if immediate symptoms are absent. Symptoms may include gastro-intestinal irritation, lassitude, haematemesis, diarrhoea, cardiovascular collapse. A transient recovery followed by a relapse 24–48 hours after ingestion may occur.

Treatment: The ingested Gradumet matrix cannot be readily aspirated through a stomach tube and there is no known chemical which will dissolve the Gradumet without harming the gastric mucosa. Accordingly, when overdosage is discovered early, the following procedure is recommended:

1. Administer an emetic by stomach tube.
2. Withdraw the stomach tube and wait for the patient to vomit.
3. Keep the patient under constant surveillance to detect possible aspiration of vomitus; maintain suction apparatus and standby emergency oxygen in case of need.
4. Examine the vomitus for returned Gradumet tablets.
5. Administer a saline cathartic. By the time toxic signs have appeared, Gradumet tablets are in most cases past the pylorus so that emesis is of no value. Gastric lavage may be considered to remove amounts of the drug already released in the stomach. A saline cathartic then should be given to speed the Gradumet tablets along the alimentary canal so as to minimise or prevent further absorption of the medication.
6. The use of an iron chelating agent such as oral desferrioxamine should be considered. In severe cases, parenteral desferrioxamine may be necessary.

Pharmaceutical precautions Store below 20°C.

Legal category POM.

Package quantities Ferrograd Folic is supplied in 5 carton packs, each carton containing 30 (2 × 15) tablets.

Further information *Metabolisable carbohydrate content:* Approx. 0.3 g per tablet.

Product licence number 0037/5002.

HARMOGEN*

Presentation Each scored, peach coloured, flat, elongated tablet contains 1.5 mg Harmogen (piperazine oestrone sulphate), equivalent to 0.93 mg of oestrone. The tablets are marked LV.

Uses Oestrogen replacement therapy and relief of oestrogen deficiency symptoms at or after the menopause, and following surgical or radiotherapeutic oophorectomy for example:

- (a) vasomotor symptoms – hot flushes, palpitations, nocturnal sweating.
- (b) urogenital symptoms – senile atrophic vaginitis, urethritis and urethral syndrome, pruritus vulvae.
- (c) psychomotor symptoms – depression, irritability, sleep disturbances including insomnia.

Dosage and administration 1.5–4.5 mg daily, taken orally as a single dose, or may be divided. As with most drugs the dosage should be adjusted to the minimum required to control symptoms. It may be necessary to divide the daily dose if gastro-intestinal irritation becomes a problem. Replacement therapy: clinical studies indicate that two Harmogen tablets daily is a satisfactory

starting dose. Daily dose should be increased or decreased according to clinical response. The scored tablet can be easily broken in half, facilitating small adjustments of dose. The maintenance dose should be the lowest that controls the symptoms adequately. If breakthrough bleeding, breast tenderness or abdominal cramps occur, the dose should be reduced until the symptoms are just suppressed. Maintenance dosage is usually prescribed for periods of three to four weeks alternating with rest periods for five to seven days. Withdrawal bleeding may occur towards the end of the rest period. It may be preferable in some patients to give Harmogen continuously and to add a progestational agent every four to six weeks to evoke a menstrual period. Harmogen's effectiveness can be determined by both symptomatic improvement and an improvement in the vaginal cytology.

For senile vaginitis, kraurosis and pruritus vulvae, a dose of one to three Harmogen tablets is given daily according to the needs of the individual patient. The usual dose is one tablet twice daily.

Contra-indications, warnings, etc

Contra-indications: Genital or mammary malignancy. Liver dysfunction. Existing or previous thromboembolic disease. Disorders of carbohydrate or lipid metabolism. Undiagnosed abnormal bleeding from the genital tract. Pregnancy. Renal insufficiency. Even though oestrogens have proved useful in the palliation of some cases of disseminated carcinoma of the breast, they may actually accelerate the spread and growth of the tumour in other cases.

Precautions: Oestrogen withdrawal bleeding during cyclical therapy of female patients is a natural occurrence. However, bleeding while on oestrogens could be 'breakthrough' if daily oestrogen dosage needs adjusting, or it could indicate the development of a pathological condition unrelated to oestrogen therapy, e.g. fibroids, malignancy, etc. The occurrence of irregular bleeding or spotting should be thoroughly investigated in premenopausal and post-menopausal women.

Prolonged exposure to unopposed oestrogens may increase the risk of the development of endometrial carcinoma.

Adverse effects of oestrogen therapy on blood pressure and gall bladder function have been reported.

Side-effects: Studies with Harmogen have shown that the incidence of side-effects is low in women treated for menopausal symptoms. Nausea is the most frequent side-effect, but this seldom interferes with eating and tends to subside with continued therapy or reduction of dosage. With oestrogens in general, less common side-effects include sodium and water retention, breast swelling and tenderness, anorexia, vomiting, headaches, changes in liver function and breakthrough bleeding. Rare reactions include allergies, jaundice, increased blood sugar levels, decreased glucose tolerance and loss or increase of libido. Oestrogens may precipitate or aggravate porphyria cutanea tarda in predisposed individuals.

Overdosage: Symptoms: nausea, vomiting, breast enlargement, vaginal bleeding.

Treatment: Gastric lavage, emesis and general supportive measures.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Harmogen is supplied in containers of 100 tablets.

Further information *Metabolisable carbohydrate content:* Approx. 0.2 g per tablet.

The amount of piperazine in Harmogen is not sufficient to exert a pharmacological action but its addition ensures solubility, stability and uniform potency.

Product licence number 0037/5064.

HARMONYL*

Presentation Harmony is a crystalline alkaloid isolated from the root of *Rauwolfia canescens*. Each grooved, pink tablet contains 0.25 mg deserpidine.

Uses Harmony can be used alone in the management of mild essential hypertension. It can be combined with benzothiadiazines such as methyclothiazide or other potent antihypertensive agents in the treatment of more severe cases. Such a combination often proves beneficial in the management of hypertension which is unresponsive to diuretic or Rauwolfia therapy alone.

Dosage and administration Treatment may start with one 0.25 mg tablet daily either as a single oral dose or 0.125 mg (half of the scored tablet) twice daily. This dose can be increased if necessary up to 0.25 mg four times daily. As 10–14 days are required for the drug to produce its full effect, adjustments in dosage should not be made more frequently. If the therapeutic response is not adequate it is advisable to add another antihypertensive to the therapy.

For children, doses are reduced in proportion to body weight.

Contra-indications, warnings, etc

Contra-indications: Patients with severe suicidal tendencies, active peptic ulcer and ulcerative colitis.

Precautions: Harmony should be used cautiously in patients who have a history of peptic ulcer because the drug causes a rise in free and total hydrochloric acid and an increase in the volume of gastric secretion. Some authorities suggest withdrawal or dose reduction two weeks prior to elective surgery. An unexpected degree of hypotension and bradycardia has been reported in patients undergoing anaesthesia while under treatment with Rauwolfia alkaloids. When emergency surgical procedures are necessary, parenteral administration of vagal blocking agents to prevent or reverse hypotension and/or bradycardia may be considered. In epileptic patients therapy may necessitate dosage adjustments of anticonvulsant medication: Rauwolfia alkaloids lower the convulsive threshold and shorten the latent period between stimulus and seizure. This factor should be taken into account in patients undergoing electro-shock treatment. As with all Rauwolfia preparations, severe mental depression has appeared in a small percentage of patients. When Harmony is discontinued depression usually disappears but active treatment is sometimes required. Watch for symptoms of depression, particularly in patients whose histories are questionable. Alert responsible members of the family to the problem.

Side-effects: Adverse effects encountered with Harmony are infrequent and usually mild in character. Qualitatively similar to those reported for reserpine, the incidence of these untoward effects, particularly lethargy and depression, is lower. They may include nasal

stuffiness, diarrhoea, nausea, headache, weight gain, reduction in libido and potency, aggravation of peptic ulcer, epistaxis and skin eruptions. Other side-effects are excessive drowsiness, fatigue, weakness, dizziness, anorexia, asthma in susceptible persons, nightmares which may be early signs of mental depression and eventually may lead to suicidal attempts. Any antihypertensive agent, including Harmonyl, which can cause significant hypotension may precipitate angina in patients with arteriosclerosis who are prone to angina pectoris. Electrolyte imbalance and excessive salivation have been reported during deserpidine therapy. When adverse reactions occur, they are usually reversible and disappear when the drug is discontinued.

Overdosage: Symptoms: Central depression, hypotension, ptosis, miosis and catatonias in severe cases.

Treatment: Administration of methylamphetamine hydrochloride, in a dosage of 5–15 mg orally for adults. More severe cases may require 10–30 mg intravenously or intramuscularly.

Treatment should be initiated with the smaller dose.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Harmonyl is supplied in containers of 100 tablets.

Further information *Metabolisable carbohydrate content:* Approx. 0.12 g per tablet.

Product licence number 0037/5071.

IBERET* 500 ▼

Presentation Each red Filmtab* (film-coated tablet Abbott) contains, in a sustained release form (Gradumet*):

Dried Ferrous Sulphate BP	325 mg
(equivalent to 105 mg elemental iron)	
Ascorbic acid (vitamin C, as Na salt)	500 mg
Nicotinamide BP	30 mg
Thiamine Mononitrate USP (vitamin B ₁)	6 mg
Riboflavin (vitamin B ₂)	6 mg
Calcium Pantothenate USP	10 mg
Pyridoxine Hydrochloride BP (vitamin B ₆)	5 mg

Uses Iberet 500 combines the advantages of ferrous sulphate in the Gradumet form with a large dose of vitamin C. It also contains water-soluble B vitamins.

It is indicated in the treatment of iron-deficiency anaemia and for the simultaneous treatment of vitamin C deficiency. Vitamin C enhances the absorption of iron and is therefore valuable where poor absorption is a problem. It also promotes haemopoiesis in patients where an underlying deficiency of the vitamin limits optimal haemoglobin formation.

Iberet 500 is also indicated in the prophylaxis of iron and vitamin B and C deficient states arising particularly from dietary factors, for example in the elderly person.

The Gradumet device consists of an inert plastic matrix, honeycombed by thousands of narrow passages which contain the active drug, together with a water-soluble channelling agent. As the tablet passes down the gastro-intestinal tract the iron is leached out. The spent matrix is finally excreted in the stools.

The device releases only a small amount of iron in the stomach which is never exposed to large amounts as is the case with ordinary tablets. The clinical advantages

are twofold: minimal side-effects and efficient absorption.

The vitamins are in a layer enclosing the matrix.

Dosage and administration *Adults:* One tablet daily before food. The tablet must be swallowed whole, with a little water if necessary.

Children: Not suitable for children under twelve years of age.

Contra-indications, warnings, etc The usual care should be taken in the use of this product in patients with haemoglobinopathies, haemochromatosis and haemolytic anaemias.

In high doses pyridoxine is known to interfere with prolactin release and may be contra-indicated in nursing mothers.

Pyridoxine is known to interfere with levodopa.

Interaction (chelation) with tetracyclines.

Iberet 500 tablets should be kept out of children's reach.

Side-effects: The side-effects associated with conventional oral iron preparations, e.g. nausea, vomiting, diarrhoea or constipation, are less likely to occur.

Overdosage: In achievable overdose, the only constituents which will cause concern are the iron and, possibly, vitamin C which may cause acidosis and haemolytic anaemia in predisposed individuals (glucose-6-phosphate dehydrogenase deficiency). Renal failure may occur in massive vitamin C overdose.

Iron overdose symptoms: The initial symptoms of massive ferrous sulphate overdose are absent, the delayed release allowing sufficient time for gastric lavage and other forms of treatment to be effective before absorption occurs to any extent. Treatment should not be delayed therefore, even if immediate symptoms are absent.

Symptoms may include: gastro-intestinal irritation, lassitude, haematemesis, diarrhoea, cardiovascular collapse. A transient recovery followed by a relapse 24–48 hours after ingestion may occur.

Treatment: The ingested Gradumet cannot be readily aspirated through a stomach tube and there is no known chemical which will dissolve the matrix without harming the gastric mucosa. An emetic may return the Gradumets from the stomach. When toxic signs have appeared, the tablets are likely to have passed the pylorus and emesis will be of no use. A saline cathartic may speed passage along the gut and reduce the time available for iron absorption.

The patient should be kept under observation and due consideration given to the use of standard treatments for iron overdose, including the use of chelating agents such as oral desferrioxamine. In severe cases parenteral desferrioxamine may be necessary.

Warning: Administration of therapeutic doses of ascorbic acid may interfere with the Clinistix test for glucosuria giving a false negative result.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Iberet 500 is supplied in packs of five cartons, each carton containing 30 (2 × 15) tablets.

Further information Iberet 500 does not contain vitamin B₁₂. Metabolisable carbohydrate content: nil.

Product licence number 0037/0097.

IBEROL*

Presentation Each red Filmtab* (film-coated tablet Abbott) contains:

Dried Ferrous Sulphate BP	325 mg
(equivalent to 105 mg elemental iron)	
Ascorbic acid (as sodium ascorbate)	75 mg
Liver fraction 2 NF XI	100 mg
Thiamine Mononitrate USP	3 mg
Riboflavin BP	3 mg
Nicotinamide BP	15 mg
Pyridoxine Hydrochloride BP	1.5 mg

Uses Iberol is indicated for the treatment of iron-deficiency and nutritional anaemias: during convalescence (especially after gastrectomy) and in old age.

Dosage and administration Recommended oral adult dose is 2 tablets daily.

Not recommended for children under 12 years of age.

Contra-indications, warnings, etc As with all iron preparations Iberol should be given with care in patients with haemochromatosis, haemolytic anaemias or haemoglobinopathies. In high doses pyridoxine is known to interfere with prolactin release and may be contra-indicated in nursing mothers. Tablets should be kept out of the reach of children.

Overdosage: Symptoms: gastro-intestinal irritation, lassitude, haematemesis, diarrhoea, cardiovascular collapse. A transient recovery followed by a relapse 24–48 hours after ingestion may occur.

Treatment: Gastric lavage or induced emesis. The use of an iron chelating agent such as oral desferrioxamine should be considered. In severe cases parenteral desferrioxamine may be necessary.

Pharmaceutical precautions Keep the bottle tightly closed.

Legal category P.

Package quantities Iberol is supplied in containers of 100 tablets.

Further information *Metabolisable carbohydrate content:* Approx. 0.12 g per tablet.

Product licence number 0037/5004.

IROFOL* C

Presentation Each two-layered, red Filmtab* (film-coated tablet Abbott) contains Dried Ferrous Sulphate BP 325 mg (equivalent to 105 mg elemental iron) in a sustained release form (the Gradumet*), 500 mg vitamin C (as sodium ascorbate) and 350 mcg Folic Acid BP.

Uses

1. For the prevention and treatment of iron-deficiency anaemia during pregnancy.
2. For the prophylaxis of megaloblastic anaemia during pregnancy.
3. For the simultaneous treatment of vitamin C deficiency.

The Gradumet device allows sustained release of ferrous sulphate over a number of hours which increases iron utilisation and reduces gastro-intestinal intolerance. The device consists of an inert plastic matrix, honey-combed by thousands of narrow passages which contain the active drug together with a water soluble channelling agent. As the tablet passes down the gastro-intestinal

tract the iron is leached out. The spent matrix is finally excreted in the stools. Irofol C combines the advantages of ferrous sulphate in the slow release form with a large dose of vitamin C further to enhance iron absorption, and to produce haemopoiesis in patients where an underlying Vitamin C deficiency limits optimal haemoglobin formation.

During pregnancy folic acid requirements can be met with between 300–400 mcg daily. Without such supplementation folate deficiency may develop leading to megaloblastic anaemia with attendant obstetric risks. Doses over 400 mcg may mask undiagnosed primary B₁₂ deficiency, in the extremely unlikely event of this condition occurring in a pregnant woman, so the safe prophylactic dose is considered to be 350 mcg.

Dosage and administration *Recommended oral dosage:* 1 tablet a day before food throughout pregnancy. Children not applicable.

Contra-indications, warnings, etc

Contra-indications: Megaloblastic anaemia due to vitamin B₁₂ deficiency.

Precautions: As with all iron preparations Irofol C should be given with care in patients with haemochromatosis, haemolytic anaemia or haemoglobinopathies. Interaction (chelation) with tetracyclines. Irofol C should be kept out of children's reach.

Warning: Administration of therapeutic doses of ascorbic acid may interfere with the Clinistix test for glucosuria giving a false negative result.

Side-effects: Those associated with conventional oral iron preparations, such as nausea, vomiting, diarrhoea and/or constipation, are less likely to occur. Because of the sustained release pattern only a small amount of the iron is released in the stomach, which is never exposed to large amounts of iron as is the case with ordinary tablets. The clinical advantages which follow are twofold – minimal side-effects and efficient absorption.

Overdosage: Symptoms: The initial symptoms of massive ferrous sulphate overdosage are absent, the delayed release allowing sufficient time for gastric lavage and other forms of treatment to be effective before absorption occurs to any extent. Treatment should not be delayed, therefore, even if immediate symptoms are absent. Symptoms may include gastro-intestinal irritation, lassitude, haematemesis, diarrhoea, cardiovascular collapse. A transient recovery followed by a relapse 24–48 hours after ingestion may occur.

Vitamin C overdosage may cause acidosis and haemolytic anaemia in predisposed individuals (glucose 6 – phosphate dehydrogenase deficiency). Renal failure may occur in massive Vitamin C overdosage.

Treatment: The ingested matrix cannot be readily aspirated through a stomach tube and there is no known chemical which will dissolve the matrix without harming the gastric mucosa. Accordingly, when overdosage is discovered early, the following procedure is recommended.

1. Administer an emetic by stomach tube.
2. Withdraw the stomach tube and wait for the patient to vomit.
3. Keep the patient under constant surveillance to detect possible aspiration of vomitus, maintain suction apparatus and standby emergency oxygen in case of need.
4. Examine the vomitus for returned Gradumet tablets.
5. Administer a saline cathartic. By the time toxic

signs have appeared, Gradumet tablets are in most cases of no value. Gastric lavage may be considered to remove amounts of the drug already released in the stomach. A saline cathartic should be given to speed the Gradumet tablets along the alimentary canal so as to minimise or prevent further absorption of the medication.

6. The use of an iron chelating agent such as oral desferrioxamine should be considered. In severe cases parenteral desferrioxamine may be necessary.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Irofol C is supplied in 5 carton packs, each carton containing 30 (2 × 15) tablets.

Further information *Metabolisable carbohydrate content:* Approx. 0.01 g per tablet.

Product licence number 0037/5003.

NEMBUTAL*

Presentation Nembutal is available in yellow capsules, each capsule containing 100 mg Pentobarbitone Sodium BP.

Uses Nembutal is indicated for severe intractable insomnia.

Dosage and administration Recommended oral dose 100–200 mg.

Contra-indications, warnings, etc

Contra-indications: Uncontrolled pain; children and young adults; the elderly and debilitated; pregnancy and breast feeding; patients with a history of alcohol or drug abuse; porphyria.

Precautions: Reduce dose in patients with renal or hepatic failure. (See also under Adverse Effects).

Drug interactions: Barbiturates cause induction of liver enzymes, so that the availability and blood concentrations of drugs given concurrently that are metabolised in the liver may be affected. These include the following: coumarin-type anticoagulants; systemic steroids (including oral contraceptives); phenytoin; griseofulvin; rifampicin; phenothiazines such as chlorpromazine; tricyclic antidepressants.

Adverse effects: Common adverse effects include drowsiness, sedation, unsteadiness, vertigo and incoordination. Performance and alertness may be impaired during the first week of administration. Patients should be warned of the possible hazard when driving or operating machinery. These effects may be potentiated by alcohol. Other adverse reactions may include a 'hangover' effect, paradoxical excitement, confusion, memory defects, and rashes in patients who may be sensitive to this type of drug.

Overdosage: Symptoms: Stupor, coma, respiratory depression. Hypothermia, hypotension and bradycardia may be observed in severe cases.

Treatment: Gastric lavage and general supportive treatment as in poisoning by other barbiturates. The use of amphetamines may be considered. The use of anaesthetic drugs is controversial, but it is generally agreed that their administration represents at the best an emergency measure, additional to but not replacing the all important

supportive therapy. Peritoneal dialysis and the artificial kidney have been successfully employed.

Further information: Addiction potential: Barbiturates have a high addiction potential. Long-term use or use of high dosage for short periods may lead to tolerance and subsequently to physical and psychological dependence. Symptoms of dependence include confusion, defective judgement and loss of emotional control. Withdrawal symptoms occur after long-term normal use (and particularly after abuse) on rapid cessation of barbiturate treatment. Symptoms include nightmares, irritability and insomnia and, in severe cases, tremors, delirium, convulsions and death. Withdrawal symptoms have been reported in neonates after barbiturate treatment during pregnancy and labour.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Nembutal Capsules 100 mg are supplied in containers of 500 and 1,000.

Further information *Metabolisable carbohydrate content:* Nembutal 100 mg, approx. 0.02 g per capsule.

Product licence number 0037/5005.

PARADIONE*

Presentation Paraldione is supplied in red, soft gelatine capsules, each capsule containing 300 mg paraldione.

Uses Paraldione is indicated in the treatment of the petit mal triad (petit mal, akinetic and myoclonic epilepsy) diagnosed clinically or by the typical spike and dome wave on the electroencephalograph or both. The drug does not control grand mal seizures.

Paraldione is most effective in idiopathic epilepsy, but may be used in seizures due to organic brain damage if the symptoms associated with petit mal epilepsy are present. In patients exhibiting both grand mal and petit mal seizures, Paraldione may be used with a suitable grand-mal anticonvulsant.

Note: Paraldione appears to be somewhat less potent than Tridione against clinical petit mal, but may be preferred because it produces a lower incidence of visual disturbances. Paraldione has in general been associated with a lower incidence of serious side-effects than Tridione.

Dosage and administration The dosage of Paraldione must be adjusted for each patient at the level which controls symptoms without producing undesirable effects.

Initial dosage for adults and older children: 0.9 g daily in divided doses.

Initial dosage for children 2–6 years: 0.6 g daily in divided doses.

The initial dosage should be increased at weekly or fortnightly intervals by 300 mg per day until relief is obtained, until toxic symptoms appear, or until double the initial dose is being administered. Maintenance dosage should be adjusted to the minimum required to maintain control.

Contra-indications, warnings, etc

Contra-indications: Severe hepatic or renal impairment

and blood dyscrasias. Known hypersensitivity to paramethadione.

Warning – usage in pregnancy: Recent reports suggest that certain anticonvulsant drugs including Paradione are associated with an increased incidence of congenital malformations among the offspring of women receiving these drugs at the time of conception and subsequent pregnancy. Therefore the usage of these drugs in pregnant women or in women of childbearing age should be avoided if possible. The safety of Paradione for use during lactation has not been established.

Precautions: Paradione should be withdrawn promptly at the appearance of a skin rash, because of the grave possibility of exfoliative dermatitis or erythema multiforme. Even a minor acne-like or morbilliform rash should be allowed to clear completely before treatment with the drug is resumed, and in such cases therapy should be reinstituted cautiously. A moderate degree of neutropenia with or without a corresponding drop in the leucocyte count may occur, but this does not call for withdrawal of therapy unless the total number of neutrophils drops to 2,500 per mm³ or below; frequent blood examination should be made when the count is less than 3,000. More severe haematological complications, including fatal aplastic anaemia, have occurred.

A nephrotic syndrome and hepatitis have been reported with fatalities. It is essential, therefore, that strict medical supervision be maintained during the initial period of treatment, and that examinations including laboratory tests of the blood and urine be conducted at monthly intervals. Albuminuria is an indication for withdrawing the medication. If jaundice or other signs of hepatitis appear, therapy should be discontinued. Paradione should not be used in patients with severe hepatic or renal impairment or blood dyscrasias. Caution is necessary in patients with diseases of the retina or optic nerve. If scotomata are encountered therapy should be discontinued. Other drugs known to cause toxic effects should be avoided or used only with extreme caution during therapy with Paradione.

Side-effects: The most common side-effects are drowsiness (sedation) and blurring of vision in bright light (hemeralopia). The latter also has been described as the 'glare phenomenon'. Drowsiness tends to subside with continued therapy or can be overcome by the concurrent administration of an amphetamine, without loss of anti-epileptic effect. Hemeralopia occurs mainly in adult patients, the effect being much less frequently encountered in children. This disturbance of vision results from a retinal rather than a central action of the drug, is not due to toxic damage, and disappears when therapy is withdrawn or the dosage is reduced. This sensitivity to bright light can usually be tolerated if dark glasses are worn. Gastro-intestinal effects reported are hiccups, nausea, vomiting, abdominal pain and gastric disturbances.

Anorexia and weight loss have also been reported. Skin rashes, bleeding gums, epistaxis, retinal and petechial haemorrhages, vaginal bleeding and certain blood dyscrasias including leucopenia, neutropenia, thrombocytopenia, pancytopenia, agranulocytosis and hypoplastic anaemia have been reported in patients given Paradione. A lupus erythematosus syndrome has been reported to be associated with administration of Paradione.

Other reactions include changes in blood pressure albuminuria and nephrosis, hepatitis, and precipitation of grand-mal seizures. Hair loss has been reported to

occur in some patients receiving Paradione and only rarely in patients on Tridione; in such instances, consideration should be given to alternative medication.

Overdosage: Symptoms: These include nausea, drowsiness, dizziness, ataxia and visual disturbances. Coma may follow massive overdosage.

Treatment: Vomiting should be induced or gastric lavage instituted. General supportive measures will be necessary. A careful evaluation of liver and renal function and of the blood-forming organs should be made following recovery.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Paradione is supplied in containers of 100 capsules.

Further information Contains no metabolisable carbohydrate.

Product licence number 0037/5077.

PEGANONE*

Presentation Each grooved, white tablet contains 500 mg of ethosin.

Uses Peganone is an anticonvulsant of the hydantoin series, indicated primarily in grand mal epilepsy, and to a lesser extent in the management of psychomotor seizures. It may be of benefit to some patients with petit mal and petit mal variant seizures. In patients with grand mal seizures not previously treated, Peganone may give excellent control with a minimum of side-effects. Peganone may be added to existing therapy when treatment is proving unsuccessful. This may permit a reduction in dosage of the other medications, the incidence of side-effects may be reduced and the therapeutic effect improved.

Dosage and administration In adults the initial oral dosage of Peganone is 1 g daily, increasing by 500 mg at intervals of several days until a level of 2–3 g daily is reached. This should be given in 4–6 divided doses, after food. Less than 2 g per day has been found to be ineffective in most adults. In children the initial dose should be 500 mg per day in divided doses increasing up to 1 g daily or more if necessary. If the patient is already receiving another anticonvulsant it should not be discontinued when Peganone therapy is started. The dosage of the other drug should be reduced gradually as that of Peganone is increased. Peganone may eventually replace the other drug or the optimum dosage of both anticonvulsants may be established. Peganone is compatible with other commonly used anticonvulsants.

Contra-indications, warnings, etc **Warning—usage in pregnancy:** The safety of Peganone during pregnancy, lactation and in women of childbearing age has not been established. Therefore the use of this drug in pregnant women or in women of childbearing age should be avoided if possible.

Evidence suggests that hydantoin compounds may interfere with folic acid metabolism, precipitating a megaloblastic anaemia. If this should occur during gestation, folic acid therapy should be considered.

Its use in combination with other drugs known to adversely affect the haemopoietic system should be avoided if possible.

Side-effects: The published incidence of side-effects is low, but, as Peganone is a hydantoin compound, blood counts and urine examinations should be carried out at monthly intervals, for several months from the start of therapy. As in patients receiving other hydantoin compounds blood dyscrasias have been reported, on rare occasions, in patients receiving Peganone. Its use in combination with other drugs known adversely to affect the haemopoietic system should be avoided if possible.

Although the causative role of Peganone has not been definitely established, physicians should be alert for general malaise, sore throat and other symptoms indicative of early blood dyscrasias. If clinical evidence suggests an hepatic disorder, liver function tests should be undertaken. Signs of liver damage or marked depression of the blood count are indications for withdrawal of the drug.

Occasionally, nausea or vomiting after ingestion of Peganone has been reported, but, if the drug is administered after meals, the incidence of gastric disturbances is very low. Other side-effects include fatigue, dizziness, headache, diplopia, nystagmus, skin rash, numbness, fever, diarrhoea and chest pain. Ataxia and gum hypertrophy have occurred rarely – usually in patients receiving an additional hydantoin derivative. Ataxia and gum hypertrophy produced by other hydantoins can subside when Peganone is substituted. Isolated cases of lymphadenopathy and systemic lupus erythematosus have been reported in patients taking hydantoin compounds, and lymphadenopathy has occurred with Peganone. The withdrawal of therapy can result in remission of the clinical and pathological findings. If a lymphoma-like syndrome develops, therefore, the drug should be withdrawn and the patient closely observed for regression before treatment is reinstituted.

Overdosage: Symptoms: Drowsiness, visual disturbance, nausea, ataxia. Coma is theoretically possible at very high dosage but has not been reported.

Treatment: Provoke vomiting or undertake gastric lavage. General supportive measures. The follow-up should include careful evaluation of blood-forming organs.

Compatibility: Peganone is compatible with all commonly employed anticonvulsant medications. In grand mal seizures use of the drug with phenobarbitone may be beneficial. Peganone may be used in combination with drugs such as troxidone or paramethadione, as an adjunct in those patients with petit mal associated with grand mal.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Peganone is supplied in containers of 100 tablets.

Further information *Metabolisable carbohydrate content:* Approx. 0.1 g per tablet.

Product licence number 0037/5054.

PENTHRANE*

Presentation Penthrane (Methoxyflurane BP) is an anaesthetic agent for inhalation. It is a clear, almost colourless liquid with a characteristic fruity odour. An antioxidant, butylated hydroxytoluene 0.01% w/w is added to ensure stability on standing.

Uses When used for obstetric patients, light planes of

Penthrane anaesthesia have little effect on uterine contractions. There are no known contra-indications to the concomitant use of Penthrane and oxytocic agents.

During general anaesthesia bronchial constriction and laryngeal spasm are not usually produced by Penthrane.

Characteristically during Penthrane anaesthesia satisfactory cardiovascular stability is maintained. The myocardium is only minimally sensitised by Penthrane to adrenaline. Some decrease in blood pressure often accompanies light planes of anaesthesia. This may be associated with bradycardia. This hypotension, usually of not more than 20 mm Hg, is accompanied by a reduced contractile force of the heart muscle and reduced cardiac output.

Following surgical anaesthesia with Penthrane, analgesia and drowsiness may persist after consciousness has returned. This may obviate or reduce the need for sedation in the immediate post-operative period.

Penthrane provides analgesia or anaesthesia.

Indications for analgesia: For the relief of pain during labour.

The Central Midwives Boards and the Joint Nursing and Midwives Council for the Northern Ireland Authority have approved the use of Penthrane in conjunction with the specifically designed Cardiff Inhaler for use by midwives for analgesia during labour.

Indications for anaesthesia: Penthrane is an inhalation agent indicated for general anaesthesia. It is recommended to be used with nitrous oxide, but it may be administered as the sole inhalation agent when nitrous oxide is not available. When Penthrane is used alone with oxygen or air as the carrier gas, increased concentrations must be used.

Dosage and administration *For analgesia:* Vapour concentrations in the range of 0.3–0.8% are recommended. Penthrane may be self-administered by draw-over inhalers (such as Cyprane) if the patients are kept under close observation. The patient in labour may receive a fixed optimal concentration of 0.35% Penthrane in air from a Cardiff Inhaler. Compensatory devices within the instrument prevent significant variations in respiratory rate and volume and ambient temperature which may occur in clinical practice. Penthrane does not interfere with uterine action and the progress of labour is not slowed.

Important note: For intermittent administration from this inhaler, the dosage for each patient must be limited to the vapour from not more than 15 ml of liquid Penthrane. In practice this is rarely exceeded during use of the inhaler for the indication listed. If anaesthesia is required then the recommendations given below should be followed.

For general anaesthesia: The lowest effective dosage of Penthrane should be used in order to minimise the possibility of renal dysfunction and to allow for optimal recovery time. Deeper planes of anaesthesia should be avoided. It is recommended that Penthrane should be administered with a carrier gas consisting of at least 50% nitrous oxide.

1. **Levels and signs:** See the table opposite.

2. **Apparatus:** Penthrane should be administered with calibrated temperature compensated out-of-circle vaporisers (e.g. Pentec Mk II Penlon) or by other methods which provide accurate vapour concentrations or precise measurements of dose. The uptake of the anaesthetic by rubber tubing, bags and soda lime which may prolong induction and recovery time can be reduced by the use

of non-adsorbent plastic circuit material (not polyvinyl chloride) and fresh moist soda lime. The fresh gas inlet should be located downstream of the CO₂ absorber in order to avoid excessive absorption of anaesthetic, and the rebreathing bag and expiratory valve should be located on the expiratory side.

3. *Pre-medication:* The usual pre-anaesthetic medications may be administered prior to Penthrane anaesthesia.

4. *Carrier gas:* For general surgery, Penthrane should be administered with a carrier gas flow consisting of oxygen and at least 50% nitrous oxide in a semi-closed circuit, in order to reduce to a minimum the total Penthrane dose, unless nitrous oxide is contra-indicated.

5. *Muscle relaxation:* Adequate relaxation should be obtained by using a muscle relaxant, e.g. succinylcholine chloride, tubocurarine or pancuronium. The usual dosage of non-depolarising muscle relaxants should be reduced by approximately half. Penthrane alone should not be administered at levels required to achieve muscle relaxation.

6. *Induction:* Rapid induction should be accomplished by an ultra-short-acting barbiturate, such as thiopentone sodium for injection. Initially Penthrane concentrations may be increased as tolerated, to the maximum possible vapour concentration, i.e. approximately 3%. This maxi-

mum concentration should only be continued for about two to five minutes according to the patient's weight, or until the desired level of Penthrane anaesthesia is reached.

7. *Maintenance:* The concentration of Penthrane should then be reduced at frequent intervals to the lowest concentration which will maintain adequate anaesthesia. In general, after an hour of anaesthesia, concentrations of 0.2–0.4% should be sufficient for this purpose, with a gas flow of 5 litres/minute.

8. *Recovery:* When administration has been prolonged, Penthrane should be discontinued before the expected end of surgery by a length of time equivalent to 10 minutes for each hour the Penthrane was in use. Elimination of Penthrane is greatly aided by flushing with pure oxygen. Most patients recover quietly and without delirium or hypotension and with a minimum incidence of nausea and vomiting.

9. *Anaesthetic level and signs:*

- (a) Analgesic level – for pain relief in labour.
- (b) Light anaesthetic level – in minor surgical procedures.
- (c) Moderate anaesthetic level – for general surgical use.
- (d) Deep anaesthetic level – this level must be avoided.

PENTHRANE-LEVELS AND SIGNS

	<i>Analgesia</i>	<i>Light anaesthesia</i>	<i>Moderate anaesthesia</i>	<i>Deep anaesthesia</i>
<i>State of consciousness</i>	Drowsy	Unconscious (possible slow movements)	Unconscious (no movement)	
<i>Response to painful stimulus</i>	Decreased	Further decreased	Absent	
<i>Eyeball activity</i>	Normal	Sluggish	Fixed and central	
<i>Pupillary reaction to light</i>	Present			Absent
<i>Lid reflex</i>	Present		Absent	
<i>Tearing (after lid manipulation)</i>	Absent	Present	Absent	
<i>Skin colour</i>	Normal			Pallor
<i>Capillary refill</i>	Good			Poor to absent
<i>Blood pressure</i>	Unchanged	May drop 20 to 40 mm Hg	Usually recovers	Progressive hypotension
<i>Pulse</i>	Stable			Possible tachy- or bradycardia
<i>Respiration</i>	Stable	Irregular, long expiratory pause	Stable, shorter expiratory pause	Decreasing minute and tidal volumes
<i>Swallowing and protective reflexes</i>	Present		Absent	
<i>Muscle relaxation</i>	None	Superficial (e.g. jaw)	Mild	Fair to good

† Not recommended with Penthrane.

- (e) Signs – the signs of Penthrane anaesthesia should be observed closely as a guide to a proper depth. Signs of each level are clearly identifiable (see the table opposite).

Contra-indications, warnings, etc

Contra-indications: Penthrane should not be used when previous exposure to this agent or to other halogenated anaesthetics has been followed by jaundice and/or unexplained fever, because of the possibility of hepatic toxicity. Cross-sensitivity between Penthrane and halothane has been reported.

Important note: *Penthrane should not be readministered within a month.*

Precautions: Occurrence of renal dysfunction has been associated with *excessive dosage of Penthrane*. This has ranged in severity from transient alterations in biochemical values to irreversible renal failure. It is believed that these effects are associated with elevated serum inorganic fluoride levels. After Penthrane anaesthesia, serum inorganic fluoride and urinary inorganic fluoride and oxalate concentrations increase, indicating that these substances are products of Penthrane metabolism. These are dose-related effects. Therefore, the recommended dosage should be followed, unless, in the judgement of the physician, the potential benefits outweigh the risks. The lowest effective dosage should be administered especially in aged or obese patients and in surgical procedures of long duration, bearing in mind that the total dose delivered to the patient is in the main a factor of duration of administration and vapour concentration.

Polyuric renal insufficiency associated with excessive total dosage of Penthrane is characterised by the development, early in the post-operative period, of the following manifestations:

- High urine volume in relation to fluid intake.
- Weight loss.
- Elevation of serum sodium, chloride, uric acid, creatinine, osmolality and blood urea nitrogen (BUN).

Oliguric renal dysfunction associated with excessive total dosage of Penthrane is characterised by the following manifestations:

- Low urine volume in relation to fluid intake.
- Increased values of BUN, and serum creatinine, uric acid, chloride, and decreased values of sodium.

The guiding principles for minimising the possibility of renal involvement are:

- Avoid using Penthrane alone to achieve muscular relaxation.
- Patients with pre-existing renal disease or impairment of renal function, toxæmia of pregnancy and patients undergoing vascular surgery involving the renal vessels should not receive Penthrane unless in the judgement of the clinician the benefits outweigh the increased risk of nephrotoxic effects.
- Light or moderate anaesthesia with Penthrane should not be repeated within one month.
- All patients who receive Penthrane should be monitored for urinary output and possible laboratory signs of renal dysfunction, as indicated. Losses of fluids and electrolytes in urine or by other routes should be promptly replaced.
- The concurrent use of tetracyclines and Penthrane has been reported to result in fatal renal toxicity. Penthrane may enhance the adverse renal effects of other known nephrotoxic drugs.

Caution should be exercised in using Penthrane in patients with prolonged histories of treatment or exposure to enzyme-inducing agents (e.g. barbiturates and insecticides) as such agents may enhance the metabolism of Penthrane. Cirrhosis, a history of viral hepatitis or other abnormalities involving liver dysfunction may be the basis for selecting an anaesthetic other than a halogenated agent. Penthrane anaesthesia can possibly aggravate or superimpose renal impairment in diabetic patients with renal dysfunction, polyuria or obesity, or who are not optimally controlled.

The risk of renal toxicity is greater in obese patients because of the lipophilic properties of Penthrane and the weight-related recommended dose.

Ventilation should be assessed carefully and, if depressed, should be augmented to ensure adequate oxygenation and carbon dioxide removal. Barbiturates and narcotics, used as adjuncts, should be administered in conservative doses to avoid ventilatory depression. Penthrane causes a slight metabolic acidosis.

Penthrane augments the effect of non-depolarising muscle relaxants, therefore, their usual dosage should be reduced by approximately half.

Adrenaline or noradrenaline should be employed cautiously during Penthrane anaesthesia.

Use in pregnancy: Safe use of Penthrane other than for obstetrics has not been established with respect to adverse effects upon foetal development. Therefore, Penthrane should not be used in women of childbearing potential and particularly during early pregnancy unless, in the judgement of the physician, the potential benefits outweigh the possible hazards.

Usage in obstetrics: Attention should be given to the directions shown under dosage and administration.

The effect of inorganic fluoride in the infant is not known.

Controlled studies together with world-wide clinical experience have demonstrated that the occurrence of renal dysfunction associated with high levels of serum inorganic fluoride in either the mother or child must be considered unlikely.

Adverse reactions: Renal dysfunction (see Contra-indications, warnings, etc. Dosage and administration).

Hepatic dysfunction, jaundice, and fatal hepatic necrosis have occurred rarely following Penthrane anaesthesia. Such reactions appear to represent a sensitivity reaction to halogenated anaesthetics. Also as with other anaesthetics, transient alterations in liver function tests may follow Penthrane administration.

Some patients exhibit pallor during recovery after excessive dosage of Penthrane.

As with other anaesthetic agents for inhalation, adverse reactions which have been reported include cardiac arrest, malignant hyperpyrexia, prolonged post-operative somnolence, respiratory depression, laryngospasm, bronchospasm, nausea, vomiting, post-operative headache, hypotension and emergence delirium.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Penthrane is available in 125 ml bottles.

Further information Nil.

Product licence number 0037/5066.

SURBEX T*

Presentation Each orange-yellow ovaloid tablet contains:

Riboflavin BP	10 mg
Nicotinamide BP	100 mg
Pyridoxine Hydrochloride BP	5 mg
Ascorbic acid BP	500 mg
Thiamine Mononitrate USP	15 mg

Uses Surbex-T is indicated in vitamin B complex and vitamin C deficiencies including those arising from: debility after illness or operation, chronic alcoholism, renal dialysis, prolonged antibiotic therapy, old age and associated poor diet.

Dosage and administration Recommended oral dosage: one tablet daily, or more depending on clinical need. Children 6-12 years 1 tablet daily.

Contra-indications, warnings, etc In high doses, pyridoxine is known to interfere with prolactin release and may be contra-indicated in nursing mothers. Keep all tablets out of the reach of children.

Warning: The administration of therapeutic doses of ascorbic acid may interfere with the Clinistix test for glycosuria giving a false negative result.

Overdosage: Symptoms: In achievable overdose, the only constituent which may cause concern is Vitamin C which may cause acidosis and haemolytic anaemia in predisposed individuals (glucose 6-phosphate dehydrogenase deficiency). Renal failure may occur following massive overdose.

Treatment: Gastric lavage or induced emesis.

Pharmaceutical precautions Store in a cool place.

Legal category GSL.

Package quantities Surbex-T is supplied in containers of 100 tablets.

Further information Contains no metabolisable carbohydrate.

Product licence number 0037/5012.

THEOGRAD*

Presentation Each white Filmtab* (film-coated tablet Abbott) contains 350 mg Theophylline BP in a sustained release form (Gradumet*).

Uses For the prevention or relief of bronchospasm. The Gradumet consists of a plastic matrix, honeycombed by thousands of narrow passages which contain the active drug together with a water soluble channelling agent. As the tablet passes down the gastro-intestinal tract, the theophylline is leached out; this action is quite independent of intestinal variables such as pH and enzyme effect, viscosity, ion concentration, surface tension and motility. The spent matrix is finally excreted in the stools.

Quite apart from providing a more uniform and prolonged clinical effect, the controlled release of theophylline reduces gastric irritation, often a problem with conventional preparations, to a minimum.

Dosage and administration Usual dosage: 1 tablet every 12 hours. In patients with acute symptoms 2 tablets initially, followed by 1 tablet at 12-hourly intervals.

Some patients may require to have the dose titrated to produce the desired therapeutic effect, which is usually

obtained with a serum concentration of 10-20 mcg/ml. These patients will require higher and more frequent doses.

Contra-indications, warnings, etc

Contra-indications: Theophylline is relatively non-toxic and there are no clear cut contra-indications.

Precautions: As with all adrenergic stimulants, Theograd should be used with caution in patients with cardiac arrhythmias.

Recent studies reveal that the use of erythromycin in patients who are receiving high doses of theophylline may be associated with an increase of serum theophylline levels and potential theophylline toxicity.

In case of theophylline toxicity and/or elevated serum theophylline levels, the dose of theophylline should be reduced while the patient is receiving erythromycin therapy.

Side-effects: As with all theophylline preparations, some patients may experience gastro-intestinal side-effects. However, the incidence has been reduced to a minimum by the sustained release formulation.

Overdosage: Symptoms: The delayed release of the theophylline gives extra time in which gastric lavage and general treatment may be instituted. Treatment should not be delayed, therefore, even if immediate symptoms are absent. Symptoms may include nausea, vomiting, gastro-intestinal irritation, tachycardia, hypotension.

Treatment: The ingested Gradumet cannot be readily aspirated through a stomach tube and there is no known chemical which will dissolve the Gradumet without harming the gastric mucosa. Accordingly, when overdosage is discovered early, the following procedure is recommended:

1. Administer an emetic by stomach tube.
2. Withdraw the stomach tube and wait for the patient to vomit.
3. Keep the patient under constant surveillance to detect possible aspiration of vomitus; maintain suction apparatus and standby emergency oxygen in case of need.
4. Examine vomitus for returned Gradumet tablets.
5. Administer a saline cathartic.

By the time toxic signs have appeared, Gradumet tablets are in most cases past the pylorus so that emesis is of no value. Gastric lavage may be considered to remove amounts of the drug already released in the stomach. A saline cathartic then should be given to speed the Gradumet tablets along the alimentary canal so as to minimise or prevent further absorption of the medication.

General supportive measures should be employed.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Theograd is supplied in 5 carton packs, each carton containing 30 (2 by 15) tablets.

Further information *Metabolisable carbohydrate content:* Approx. 0.02 g per tablet.

Product licence number 0037/5059.

TRIDIONE*

Presentation Tridione is supplied in white capsules containing 300 mg of Troxidone BP.

Uses Tridione is indicated in the treatment of the petit mal triad (petit mal, akinetic and myoclonic epilepsy) diagnosed clinically, or by the typical spike and dome wave on the electroencephalograph or both. The drug does not provide control of grand mal seizures. Tridione is most effective in idiopathic epilepsy, but may be used in seizures due to organic brain injury if the symptoms associated with petit mal epilepsy are present. In patients exhibiting both grand mal and petit mal seizures Tridione may be used with a suitable grand mal anticonvulsant.

Tridione appears to be somewhat more potent than Paradione against clinical petit mal, but Paradione may be preferred because it produces a lower incidence of visual disturbances. Paradione has in general been associated with a lower incidence of serious side-effects than Tridione.

Dosage and administration The dosage of Tridione must be adjusted for each patient at the level which controls symptoms without producing undesirable effects.

Initial dosage for adults and older children: 0.9 g daily in divided doses.

Initial dosage for children 2-6 years: 0.6 g daily in divided doses.

The initial dosage should be increased at weekly or fortnightly intervals by 300 mg per day until relief is obtained, until toxic symptoms appear, or until double the initial dose is being administered. Maintenance dosage should be adjusted to the minimum required to maintain control.

Contra-indications, warnings, etc

Contra-indications: Severe hepatic or renal impairment and blood dyscrasias. Known hypersensitivity to troxidone.

Warning - usage in pregnancy: Recent reports suggests that certain anticonvulsant drugs including Tridione are associated with an increased incidence of congenital malformations among the offspring of women receiving these drugs at the time of conception and subsequent pregnancy. The use therefore of these drugs in pregnant women or in women of childbearing age should be avoided if possible. The safety of Tridione for use during lactation has not been established.

Precautions: Tridione should be withdrawn promptly at the appearance of a skin rash, because of the grave possibility of exfoliative dermatitis or erythema multiforme. Even a minor acne-like or morbilliform rash should be allowed to clear completely before treatment with the drug is resumed and in such cases therapy should be reinstituted cautiously. A moderate degree of neutropenia with or without a corresponding drop in the leucocyte count may occur, but this does not call for withdrawal of therapy unless the total number of neutrophils drops to 2,500 per mm³ or below; frequent blood examination should be made when the count is less than 3,000. More severe haematological complications, including fatal aplastic anaemia, have occurred. A nephrotic syndrome and hepatitis have been reported with fatalities. It is, therefore, essential that strict medical supervision be maintained during the initial period of treatment, and that examinations including laboratory tests of the blood and urine be conducted at monthly intervals. Albuminuria is an indication for withdrawing the medication. If jaundice or other signs of hepatitis appear, therapy should be discontinued. Tridione should

not be used in patients with severe hepatic or renal impairment or blood dyscrasias. Caution is necessary in patients with disease of the retina or optic nerve. If scotomata are encountered, therapy should be discontinued. Other drugs known to cause toxic effects should be avoided or used only with extreme caution during therapy with Tridione.

Side-effects: The most common side-effects are drowsiness (sedation) and blurring of vision in bright light (hemeralopia). The latter also has been described as the 'glare phenomenon'. Drowsiness tends to subside with continued therapy or can be overcome by concurrent administration of an amphetamine without loss of anti-epileptic effect. Hemeralopia occurs mainly in adult patients, the effect being much less frequently encountered in children. This disturbance of vision results from a retinal rather than a central action of the drug, is not due to toxic damage, and disappears when therapy is withdrawn or dosage is reduced. This sensitivity to bright light can usually be tolerated if dark glasses are worn. Gastro-intestinal effects reported are hiccups, nausea, vomiting, abdominal pain and gastric disturbances.

Anorexia and weight loss have also been reported. Skin rashes, bleeding gums, epistaxis, retinal and petechial haemorrhages, vaginal bleeding and certain blood dyscrasias including leucopenia, neutropenia, thrombocytopenia, pancytopenia, agranulocytosis and hypoplastic anaemia have been reported in patients given Tridione. As with certain other anticonvulsants, a lupus erythematosus syndrome has been reported to be associated with the administration of Tridione. Similarly, lymphadenopathy simulating malignant lymphoma has occurred in patients where Tridione was among the drugs administered. If a lupus-like manifestation or lymph node enlargement should appear, therapy should be discontinued and the patient observed for improvement before specific treatment for lupus erythematosus or lymphoma is instituted. A myasthenia gravis-like syndrome also has been associated with chronic administration of Tridione. Symptoms suggestive of this condition are an indication for discontinuance of therapy.

Other reactions include changes in blood pressure, and precipitation of grand-mal seizures. Hair loss has been reported to occur in some patients receiving Paradione, but only rarely in patients on Tridione; in such instances, consideration should be given to alternative medication.

Overdosage: Symptoms: These include nausea, drowsiness, dizziness, ataxia and visual disturbances. Coma may follow massive overdosage.

Treatment: Vomiting should be induced or gastric lavage instituted. General supportive measures will be necessary. A careful evaluation of liver and renal function and of the blood-forming organs should be made following recovery.

Pharmaceutical precautions Store in a cool dry place.

Legal category POM.

Package quantities Tridione capsules 300 mg are supplied in containers of 100.

Further information *Metabolisable carbohydrate content:* Tridione capsules, 0.15 g per capsule.

Product licence number 0037/5053.

UREAPHIL®

Presentation Ureaphil is supplied as anhydrous, lyophilised sterile urea powder in 150 ml Abbott Non-Vac® containers, containing 40 g of the powder.

Uses

1. To reduce cerebral oedema and raised intracranial pressure resulting from trauma, surgery or disease.
2. To counteract oliguria following burns, surgery or other trauma.
3. To promote an abundant flow of urine following prostatectomy and so reduce the need for frequent irrigation of the bladder.
4. To induce therapeutic abortion in the mid-trimester of pregnancy.

Note: Although urea acts as an osmotic diuretic, it is not considered the drug of choice for the management of oedema in cardiac failure.

Dosage and administration

Administration: Ureaphil is administered by slow intravenous infusion. The rate of injection should not exceed 60 drops (3–4 ml depending on drop size) per minute. Extreme care is essential to prevent accidental extravasation of the solution at the site of injection, since this may cause local reactions ranging from mild irritation to tissue necrosis. Ureaphil may be reconstituted by the addition of 5 or 10% dextrose or 10% invert sugar in water. It is administered in hypertonic concentrations of 30% (w/v) or 4% (w/v) depending upon clinical indications. To prepare a 30% solution 105 ml of diluent are added to the contents of one 40 g bottle producing 135 ml of solution.

To prepare a 4% solution, the contents of one 40 g bottle are added to 1 l of dextrose in water, producing 1,030 ml of solution. Since the dissolution is an endothermic reaction, the diluent should be warmed slightly, or the solution allowed to reach room temperature, before use. Urea will decompose if the diluent is warmed above 40°C.

Dosage: The amount to be administered is generally estimated on the basis of 1 g of urea per kg of body weight. The dosage must also take into account the clinical condition of the patient, especially the state of hydration, electrolyte balance and integrity of renal function. The total daily dose should not exceed 120 g of urea.

1. **Increased intracranial or cerebrospinal fluid pressure:** For the reduction of cerebral oedema, and increased intracranial or cerebrospinal fluid pressure, a 30% solution is usually employed. The adult dose ranges from 1.0 to 1.5 g (3.3 to 5.0 ml) per kg of body weight (0.45–0.68 g [1.5–2.3 ml] per lb). In children the dosage is from 0.5 to 1.5 g/kg of body weight. In young children up to 2 years of age as little as 0.1 g/kg can be effective.
2. **Oliguria:** To combat antidiuresis following surgery, burns or other trauma a 4% solution has produced satisfactory results. In the adult, the dose ranges from 1.0 to 1.5 g/kg of body weight. This is approximately equivalent to a volume of 1,500–3,000 ml. In children up to 5 years of age, the usual dose of the 4% solution is 1 g/kg/day, administered by slow intravenous drip. Larger doses may be required in older children.
3. **Prostatectomy:** Following prostatectomy, urea is employed as a 4% solution. Depending upon clinical circumstances, 3 litres of solution may be administered daily for three days following surgery. This is equivalent to a daily dose of 120 g of urea.

4. **Therapeutic abortion: Methods:** A sterile, suprapubic, drainage catheter is passed into the amniotic cavity, the liquor drained-off and the volume measured.

- (a) Ureaphil alone: 80 g Ureaphil dissolved in 140 ml 5% dextrose (final volume 200 ml) is given through the cannula into the amniotic cavity.

The time required to induce therapeutic abortion can be reduced by the addition of either oxytocin or prostaglandin E₂ given by methods described below:

- (b) Combined intra-amniotic Ureaphil (80 g dissolved in 140 ml 5% dextrose) and a simultaneous intravenous infusion of oxytocin (100–200 units in 500 ml Compound Sodium Lactate Injection BP – Hartmann's solution.)
- (c) Intra-amniotic Ureaphil 140 ml (80 g Ureaphil dissolved in 80 ml Hartmann's solution). When the administration of the Ureaphil solution is complete either 2.5 mg, 5 mg or 10 mg of prostaglandin E₂ in alcohol is injected. This method is particularly successful in inducing mid-trimester abortion within 24 hours.

Note: When Ureaphil is used alone, some clinicians have increased the amount of 5% dextrose solution to 210 ml (final volume 270 ml).

Contra-indications, warnings, etc

Contra-indications: Urea should not be used in patients with severely impaired renal function, active intracranial bleeding or marked dehydration. Frank liver failure is also a contra-indication for use. Ureaphil should not be infused in the veins of the lower limbs of elderly patients, since phlebitis and thrombosis of superficial veins may occur.

Precautions: Urea may cause depletion of electrolytes, which can result in hyponatraemia and hypokalaemia. Early signs of such depletion may indicate the need for supplementation before serum levels are reduced. An indwelling urethral catheter should be used in comatose patients receiving Ureaphil, to ensure bladder emptying. The rapid intravenous administration of hypertonic solutions of urea may be associated with haemolysis as well as a direct effect on the cerebral vasomotor centres, and as a result there may be increased capillary bleeding. These effects usually can be avoided by not exceeding an infusion rate of 60 drops per minute. Solutions of urea should not be administered through the same set by which blood is being infused. Although arterial oozing has been reported as a nuisance when intracranial surgery is performed on patients after they have been treated with urea, it has not been a significant problem. However, Ureaphil should not be used in the presence of active intracranial bleeding unless such use is preliminary to prompt surgical intervention to control haemorrhage. It should be borne in mind that the reduction in brain oedema induced by urea may result in reactivation of intracranial bleeding.

In the presence of kidney disease, urea should be administered with caution. Mild elevation of non-protein nitrogen does not preclude its use or continued use, but frequent laboratory studies should be made to determine if kidney function is adequate to eliminate the infused urea, as well as that produced endogenously.

Patients exhibiting a temporary reduction in urine volume are generally able to maintain a satisfactory elimination of urea. However, if diuresis does not follow the injection of urea in such patients within 6–12 hours, the drug should be withdrawn pending further evaluation.

of renal function. As with other infused solutions. Ureaphil may temporarily maintain circulatory volume and blood pressure in spite of considerable blood loss. Consequently, when excessive blood loss occurs within a short period of time, blood replacement should be adequate and simultaneous with the infusion of urea.

Hypothermia when used with urea infusion may increase the risk of venous thrombosis and haemoglobinuria.

Side-effects: Headaches (reported to be similar to those which occur in some patients following lumbar puncture), nausea, vomiting, occasional syncope and disorientation have been known to follow intravenous administration of urea. Less often reported is a transient agitated confusional state. No serious reactions have been noted when solutions have been infused slowly provided renal function is not seriously impaired and there is no evidence of active intracranial bleeding. Chemical phlebitis and thrombosis near the site of injection have been reported infrequently.

Pharmaceutical precautions Ureaphil should be used immediately after reconstitution. It should not be stored for any length of time, even in a refrigerator.

Legal category POM.

Package quantities Ureaphil is supplied in 150 ml Abbott Non-Vac[®] single use containers containing 40 g.

Further information Small quantities of sodium hydroxide may have been added to some batches for adjustment of pH.

Product licence number 0037/5072.

VI-DAYLIN[®]

Presentation A citrus-flavoured vitamin syrup formulated for infants and children. Each 5 ml contains:

Vitamin A palmitate	3,000 iu
Vitamin D (Ergocalciferol BP)	400 iu
Thiamine Hydrochloride BP	1.5 mg
Riboflavin BP	1.2 mg
Nicotinamide BP	10 mg
Pyridoxine Hydrochloride BP	1 mg
Ascorbic Acid BP	50 mg

Uses Vi-Daylin is indicated for the prevention and treatment of vitamin deficiencies in infants and children.

Dosage and administration Vi-Daylin is administered orally, and as it will not curdle milk, it may be added to an infant's feed or mixed with cereal or fruit juice.

The prophylactic dose is 2.5–5 ml daily for infants, and 5–10 ml daily for children. The therapeutic dosage is two or three times larger or as directed by the physician.

Contra-indications, warnings, etc Keep all medicines out of the reach of children. Avoid overdosage of vitamins A and D.

In the unlikely event of overdosage gastric lavage or induction of emesis should be considered.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities Vi-Daylin is supplied in 100 ml and 500 ml bottles.

Further information *Metabolisable carbohydrate content:* Approx. 5.5 g per 5 ml.

Product licence number 0037/5011.

**Trade Mark*

Albert Products

A division of Hoechst UK Ltd
50 Salisbury Road
Hounslow
Middlesex TW4 6JH



FRISIUM* ▼

Presentation Frisium capsules each contain 10 mg clobazam. Frisium is presented as hard gelatin capsules coloured powder blue opaque with 'Frisium' printed on both cap and body.

Uses Frisium is a 1,5-benzodiazepine minor tranquilizer and is indicated for the relief of acute or chronic anxiety, tension and agitation. Physical symptoms associated with an underlying anxiety state, phobias and psychosomatic disorders may all respond to treatment with Frisium as may symptoms of anxiety associated with underlying organic disease. Frisium may be used together with antidepressants in the treatment of anxiety associated with depression. Frisium has also been shown to have a beneficial effect in the treatment of sleep disturbances associated with anxiety. Frisium may be used as adjunctive therapy in epilepsy.

Dosage and administration The usual dose for adults is 20–30 mg daily in divided doses or as a single dose given at night. The lower dosage recommendation applies particularly to the elderly who are usually more sensitive to the effects of psychoactive agents.

Doses of up to 60 mg daily have been used in the treatment of hospitalised adult patients with severe anxiety states.

In epilepsy a starting dose of 20–30 mg/day is recommended, increasing as necessary up to a maximum of 60 mg daily. A break in therapy may be beneficial if drug exhaustion develops, recommencing therapy at a low dose.

Children: When prescribed for children over three years of age, dosage should not exceed half the recommended adult dose. Frisium capsules are not recommended for children under three years of age.

Contra-indications, warnings, etc *Contra-indications:* Frisium should not be used in patients known to be hypersensitive to benzodiazepines.

Precautions, warnings: Frisium is a benzodiazepine derivative and, in common with other members of this group, may potentiate the effects of central nervous system depressant drugs, such as alcohol, analgesics, hypnotics and neuroleptics. Addition of Frisium to established anticonvulsant medication may cause a change in plasma levels but no clinical effects have been reported.

The ability to drive or operate machinery may be impaired in individuals who are particularly sensitive to the effects of Frisium or in patients taking high doses.

Frisium should be used in reduced doses in patients with impaired renal or hepatic function.

There is no information on the use of Frisium in early pregnancy but no untoward effects have been found in animal studies. However, there are reports of a possible

association between malformations in infants and the administration of other benzodiazepines in early pregnancy.

Nursing mothers: Clobazam may appear in the breast milk of nursing mothers.

Overdosage: Muscle weakness, ataxia, drowsiness and sedation may occur and, after very high doses, the patient may lose consciousness. The treatment of overdosage is symptomatic. The stomach should be emptied as soon as possible by gastric lavage and general supportive measures should be undertaken as necessary.

Side-effects: Frisium is generally well tolerated. Side-effects such as drowsiness, dizziness or dryness of the mouth have been reported. These are more likely to occur at the beginning of treatment and often disappear with continued treatment or a reduction in dose.

Pharmaceutical precautions Frisium capsules should be stored in a cool, dry place in the original containers or in containers similar to those of the manufacturer.

Legal category POM.

Package quantities Frisium is available as 10 mg capsules packed in blister packs of 100 capsules.

Further information Experimental evidence shows that, in general, when given as a single dose of up to 20 mg or in divided doses of up to 30 mg Frisium does not affect psychomotor function. However, individuals who are sensitive to the effects of Frisium may be adversely affected, particularly at the beginning of treatment.

Product licence number 0086/0065.

MERITAL* 50 CAPSULES ▼

MERITAL* 25 CAPSULES ▼

MERITAL* AM TABLETS ▼

Presentation Merital 50 Capsules each contain 50 mg nomifensine hydrogen maleate. The capsules have a medium orange opaque body and a caramel cap with 'Merital 50' printed on both cap and body.

Merital 25 Capsules each contain 25 mg nomifensine hydrogen maleate. The capsules are coloured medium orange opaque with 'Merital 25' printed on both cap and body.

Merital AM Tablets each contain 100 mg nomifensine hydrogen maleate. They are coloured salmon.

Uses Merital is an antidepressant indicated for the treatment of a wide range of depressive illness, including depression in which anxiety is an accompanying feature.

Initial studies have indicated that Merital is particularly suitable for patients who exhibit symptoms and signs of retardation and, in these patients, may be expected to produce a rapid beneficial effect.

Dosage and administration Many depressed patients will benefit from an initial dose of 50 mg twice or three times a day, and this may be adjusted according to response after 7–10 days. Doses of up to 100 mg may be given as a single daily dose in the morning.

For some patients, particularly the elderly, who are known to be sensitive to the effects of psychotropic drugs, the recommended initial dose is 25 mg three times a day. The normal dose range is 75–200 mg Merital daily.

Children: At the present time there is insufficient experience of the use of Merital in children to enable any dosage recommendation to be made.

Contra-indications, warnings, etc

Contra-indications: At the present time there are no known specific contra-indications to the use of Merital.

Warnings: Merital may antagonise the antihypertensive effects of adrenergic neurone-blocking drugs (e.g. bethanidine, guanethidine and debrisoquine); patients taking these drugs may require restabilisation on a higher dose of their antihypertensive therapy.

Precautions: Merital has been shown to be of value as an antidepressant in patients with Parkinson's disease but may potentiate both the therapeutic and adverse effects of levodopa and other dopamine agonists used in the treatment of this condition. When depression is a component of schizophrenic illness, Merital should be used in conjunction with a neuroleptic (e.g. a phenothiazine). In some cases, Merital has been shown to ameliorate the extra-pyramidal side-effects of this group of drugs.

All available evidence has indicated that Merital is exceptionally well tolerated, and there have been few cardiovascular effects other than mild palpitations. However, until more specific information is obtained, Merital should be used with caution in patients with ischaemic heart disease.

Merital has not been used in conjunction with electroconvulsive therapy but there is no reason to believe that such a combination will lead to any adverse effects.

Since Merital inhibits the synaptic re-uptake of biogenic amines, it should not be given concurrently

with monoamine oxidase inhibitors (MAOIs) or within two weeks of the cessation of MAOI therapy.

There is no information on the use of Merital in pregnancy but no untoward effects have been found in animal studies.

Nursing mothers: Nomifensine has been detected in breast milk in very small quantities; the effect of this low dose of nomifensine on the neonate is not known.

Overdosage: The treatment of overdosage with Merital is symptomatic. The stomach should be emptied as soon as possible by gastric lavage and the patient admitted to hospital. General supportive measures should be undertaken where indicated. However, reports of overdoses with Merital, including one patient who took 3.5 g nomifensine, have shown no serious sequelae directly attributable to the drug.

Side-effects: Merital has been shown to be exceptionally well tolerated and side-effects, when they occur, tend to be mild and transient. Reported side-effects have included sleep disturbance, restlessness, nausea, headache, palpitations, dry mouth, dizziness and a rise in body temperature. In rare cases, increases in liver enzymes (serum transaminases and alkaline phosphatase) have been observed; haemolytic anaemia has also been reported in rare cases.

Pharmaceutical precautions Merital 50 and Merital 25 Capsules should be stored in a cool, dry place in the original containers or in containers similar to those of the manufacturer.

Legal category POM.

Package quantities Merital 50 is available in blister strips packed in cartons of 100 capsules.

Merital 25 is available in blister strips packed in cartons of 100 capsules. Merital AM is available in blister strips packed in cartons of 30 and 100 tablets.

Further information Nil.

Product licence numbers

Merital 25 0086/0052

Merital 50 0086/0053

Merital AM 0086/0085

**Trade Mark*

Alcon Laboratories (UK) Limited
Imperial Way
Watford
Hertfordshire, WD2 4YR

Alcon

ADSORBOTEAR*

Presentation A sterile, clear, colourless, buffered, isotonic, ophthalmic drop containing polyvinylpyrrolidone 1.5%, macrogol 0.2%, hydroxyethylcellulose 0.44%, and preserved with thiomersal 0.002% and disodium edetate 0.05%.

Clinical use For dry eyes or where tears are absent or inadequate due to congenital or acquired conditions.

For use in dry eyes, especially where there is a defect in mucus production after erythema multiforme, chemical injuries and cicatrizing disease.

Dosage and administration Apply 1 or 2 drops to the eye(s) 3 times a day or as needed.

Contra-indications, warnings, etc Known sensitivity to any ingredient. If discomfort or irritation persists, discontinue use.

Warning: Do not touch the dropper tip as this may contaminate the solution.

Pharmaceutical precautions Keep the container tightly closed. Keep in a cool place, and out of the reach of children.

Legal category P.

Package quantities 10 ml.

Further information Nil.

Product licence number 3447/0004.

ALCOMICIN*

Presentation Alcomicin is a sterile, clear, colourless to slightly straw coloured solution for use as eye drops, and packed in 5 ml Drop-Tainers. It contains Gentamicin Sulphate equivalent to 0.3% w/v or 3 mg/ml of Gentamicin base, as a sterile, aqueous, isotonic, buffered solution preserved with 0.01% benzalkonium chloride.

Clinical use Alcomicin (gentamicin) is a bactericidal antibiotic with a broad spectrum of activity against the Gram-negative and Gram-positive bacteria, and its use is indicated in the treatment of external ocular infections caused by eye wounds, bacterial infection, acute conjunctivitis, dacryocystitis, corneal ulcers, blepharitis, keratitis and infections following surgery.

Dosage and administration 1 or 2 drops instilled topically into the conjunctival sac every 4 hours or as necessary.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to any of its ingredients.

Precautions: Prolonged use of antibiotics may occasionally result in overgrowth of non-susceptible organisms, including fungi. If new infections appear during treatment

the drops should be discontinued and appropriate measures taken.

Adverse reactions: Occasional transient irritation may occur.

Warning: Alcomicin Ophthalmic Solution is not for injection.

Pharmaceutical precautions Store away from heat. Do not freeze. Keep the container tightly closed, and out of the reach of children. Discard contents one month after opening.

Legal category POM.

Package quantities 5 ml in Drop-Tainer dispensers.

Further information Alcomocin (gentamicin) eye drops are contained in an unbreakable semi-rigid plastic dropper bottle with a screw-on cap, and containing 5 ml of the preparation.

Product licence number 0649/0040.

BALANCED SALT SOLUTION ALCON BSS*

Presentation A sterile physiological balanced salt solution which is isotonic to the tissues of the eye. It is a lint free solution containing essential ions for normal cell metabolism. Each ml contains Sodium Chloride 0.49%, Potassium Chloride 0.075%, Calcium Chloride 0.048%, Magnesium Chloride Hexahydrate 0.030%, Sodium Acetate 0.39%, Sodium Citrate 0.17% and Water for Injection.

Clinical use As a physiologic irrigating solution.

Dosage and administration Sufficient to produce the required irrigation. The adaptor plug is designed to accept an ophthalmic irrigating needle. Intra-ocular tissue may be irrigated by attaching the needle to the Steri-Unit Drop-Tainer Bottle as follows:

1. Aseptically remove the Drop-Tainer by peeling off the paper backing.
2. Snap on surgical irrigator needle. Push well to ensure it is firmly in place.
3. Test patency of the assembly before inserting into the eye. External irrigation may be performed without the irrigating needle.

Contra-indications, warnings, etc

Contra-indication: There are no specific contra-indications for this product.

Warning: If the blister or paper backing is damaged or broken sterility of the enclosed bottle cannot be assured. Open under aseptic conditions only.

Pharmaceutical precautions This solution contains no preservative and should not be re-used. Prior to intra-ocular use check the following: tip should be firmly in place, irrigating needle should be properly seated. Squeeze out several drops before inserting into the

anterior chamber. The needle should be removed from the anterior chamber prior to releasing pressure to prevent suction.

Storage: Store under normal conditions at 46° to 75°F. The enclosed Steri-Unit Drop-Tainers are sterile and may be safely handled by the surgeon.

Legal category P.

Package quantities 15 ml Steri-Unit Drop-Tainer dispenser.

Further information Nil.

Product licence number 0649/0007.

DENDRID*

Presentation Idoxuridine 0.1% in a sterile buffered isotonic, ophthalmic solution, preserved with benzalkonium chloride 0.01%.

Clinical use For Herpes simplex infections of the eye.

Dosage and administration To be instilled into the affected eye every hour during the day, with continued application every two hours during the night until the lesion does not stain; then every two hours during the day and once at night for an additional 5-7 days.

N.B. Since idoxuridine interferes with the metabolic processes of the virus, only its continued presence can ensure therapeutic effectiveness. Therefore, it is important that a rigid administration schedule be utilized in order to obtain the desired results. Recurrences may occur if therapy is not continued for at least 5-7 days beyond the apparent healing time. If improvement is not obtained within 4-5 days other forms of therapy should be considered for concurrent use.

Contra-indications, warnings, etc There are no specific contra-indications. Some individuals may be sensitive to one or more of the components of this preparation. If any reaction occurs which is uncontrollable with anti-allergic therapy, treatment should be discontinued. Some individuals have experienced irritation or burning from the application of this drug; however, clinical response was not significantly altered in these cases. Care needs to be exercised when steroids are administered concurrently. This product contains benzalkonium chloride and should not be used when soft contact lenses are being worn.

Pregnancy Warning: It has been reported that idoxuridine has teratogenic effects on animals when instilled into the eye. Therefore it should be administered with caution in pregnancy or in women with child-bearing potential.

Adverse reactions: Acute ocular irritation including burning, corneal stippling and clouding has been reported. Following prolonged use of Idoxuridine, ocular irritation characterised by follicular conjunctivitis, blepharitis with punctal swelling, bulbar conjunctival hyperemia, and corneal epithelial staining has also been reported. In either case, the drug should be discontinued.

Precautions: For topical use only. Do not exceed the frequency or duration of recommended dosage. Idoxuridine is not effective in corneal inflammations following herpes simplex keratitis in which the virus is not present. Some strains of herpes simplex appear resistant to the action of Idoxuridine.

Pharmaceutical precautions Store between 3 to 25° C. Protect from light. The contents should be discarded one month after opening. Keep out of reach of children.

Further information The preservative system in Dendrid has been improved so that it is no longer necessary to store the product in a refrigerator. It has also been possible to use the convenient opaque plastic white Drop-Tainer dispenser with the dropper nozzle, instead of the amber glass bottle.

Legal category POM.

Package quantities 15 ml white opaque plastic Droptainer.

Further information Nil.

Product licence number 0649/5910.

ISOPTO* ALKALINE

Presentation Isopto Alkaline is a sterile clear, colourless solution containing hydroxypropyl methylcellulose (hypromellose) 1.0%, preserved with benzalkonium chloride 0.01%.

Clinical uses Isopto Alkaline is an emollient solution used as a physiologic ophthalmic vehicle or suspending agent, and as a tear replacement in tear deficiency, Keratoconjunctivitis sicca and for ocular lubrication.

Dosage and administration It is suitable for use both by adults and children. The dose depends upon the desired amount of lubrication, the usual dosage being one or two drops to be instilled into the eyes three times daily, or as needed.

Contra-indications, warnings, etc If an irritation persists or increases use of the drops should be discontinued. In order to help preserve sterility the dropper should not be allowed to touch the eyelashes or any other surface. This product contains benzalkonium chloride and should not be used when soft contact lenses are being worn.

Pharmaceutical precautions The eyedrops should be stored in a cool place (8° to 25°C). Keep out of reach of children. Discard one month after opening.

Legal category P.

Package quantities 10 ml containers.

Further information Isopto Alkaline eye-drops are contained in an unbreakable semi-rigid plastic dropper bottle with a screw-on cap, containing 15 ml of the preparation. This container bears the label and is itself in a rigid capped plastic outer.

Product licence number 0649/5900.

ISOPTO* ATROPINE 1.0%

Presentation Atropine sulphate U.S.P. 1.0% in the Isopto vehicle of hydroxypropyl methylcellulose (hypromellose) 0.5%. A sterile, isotonic, ophthalmic solution, preserved with benzalkonium chloride 0.01%.

Clinical uses Atropine is a powerful mydriatic and cycloplegic. It is used in refraction, especially in children, and in uveitis.

Dosage and administration For uveitis - one drop to be instilled into the eye three times daily. For refraction - one drop to be instilled into the eye twice daily for one or two days before examination and one hour before examination. In young children maintain pressure over lacrimal sac occluding lacrimal duct for one minute after instillation.

Contra-indications, warnings, etc This preparation is for ophthalmic use only. It should not be used in individuals with hypersensitivity to belladonna alkaloids, or with glaucoma. Prolonged use may produce local irritation and excessive use in children or in certain individuals may produce systemic symptoms of atropine poisoning.

Treatment of overdose: Physostigmine salicylate 1 or 2 mg subcutaneously to control the central or peripheral effects of atropine. This injection may need repeating every 1 or 2 hours as necessary.

Excitement may be controlled by small doses of short acting barbiturate, e.g. thiopentone sodium 100 mg.

Additional warning: This product contains benzalkonium chloride and should not be used when soft contact lenses are worn.

Pharmaceutical precautions Isopto Atropine should be stored in a cool place away from direct sunlight. Keep the container tightly closed. The contents should be discarded one month after opening.

Legal category POM.

Package quantities 5 ml containers.

Further information Isopto Atropine eye drops are contained in an unbreakable semi-rigid, plastic dropper bottle with screw-on cap, containing 5 ml of the preparation. This container bears the label and is in a rigid capped plastic outer.

Product licence number 0649/5901.

ISOPTO* CARBACHOL 3%

Presentation Isopto Carbachol is a clear colourless sterile solution, containing 3% Carbachol and 1% hydroxypropyl methylcellulose (hypromellose), and preserved with benzalkonium chloride 0.005%.

Clinical uses To reduce intraocular pressure. May be used to control intraocular pressure where control by pilocarpine has been lost or in cases of pilocarpine sensitivity.

Dosage and administration *Route of Administration:* Topical ocular use.

Recommended Dosage: Isopto Carbachol is suitable for use only in adults at a dose of two drops three times daily.

Contra-indications, warnings, etc Overdosage may cause systemic symptoms of anticholinesterase poisoning. Use with care in corneal abrasion. Contra-indicated where constriction is undesirable. This product contains benzalkonium chloride and should not be used when soft contact lenses are being worn.

Treatment of overdose: Atropine sulphate 1 or 2 mg subcutaneously or i.m. to control muscarine like effects; repeating the dose every 2-4 hours if necessary. Convulsions may be controlled with a short acting

barbiturate; muscle twitching with tubocurarine (oxygen may be necessary).

Pharmaceutical precautions Isopto Carbachol eye drops should be stored in a cool place away from direct sunlight. Keep the container tightly closed. Contents should be discarded one month after opening.

Legal category POM.

Package quantities 10 ml containers.

Further information Isopto Carbachol eye drops are contained in an unbreakable semi-rigid plastic dropper bottle with screw-on cap, containing 15 ml of the preparation. This container bears the label and is itself in a rigid capped plastic outer.

Product licence number 0649/5902.

ISOPTO* CARPINE

0.5%, 1.0%, 2.0%, 3.0%, 4.0%

Presentation Contains Pilocarpine hydrochloride USP in the following concentrations: 0.5%, 1.0%, 2.0%, 3.0% and 4.0%. The vehicle is a sterile, isotonic, ophthalmic solution containing hydroxypropyl methylcellulose (hypromellose) 0.5%, and preserved with benzalkonium chloride 0.01%.

Clinical uses Isopto Carpine is a miotic and its main use is in the treatment of glaucoma.

Dosage and administration Two drops to be instilled into the eye three times daily or as prescribed.

Contra-indications, warnings, etc Isopto Carpine is contra-indicated where constriction is undesirable such as in acute iritis. There are no known side effects except slight ciliary spasms with resultant temporary reduction of visual acuity. Sensitivity is infrequently observed. If reaction occurs discontinue use.

Side effects from eye-drops are usually controlled by reducing dosage and compressing the lacrimal sac for 5 minutes after each instillation. This product contains benzalkonium chloride and should not be used when soft contact lenses are worn.

Isopto Carpine should be stored in a cool place away from direct sunlight. Keep the container tightly closed. The contents should be discarded one month after opening.

Legal category POM.

Package quantities 10 ml containers.

Further information Isopto Carpine eye drops are contained in an unbreakable semi-rigid, plastic dropper bottle with screw-on cap, containing 15 ml of the preparation. This container bears the label and is itself in a rigid capped plastic outer.

Product licence numbers

0.5%	0649/5903
1.0%	0649/5904
2.0%	0649/5905
3.0%	0649/5906
4.0%	0649/5907

ISOPTO* CETAMIDE 15%

Presentation Isopto Cetamide is a clear, colourless sterile solution, of 0.5% tetrahydroxypropyl methylcellulose

(hypromellose) containing Sulphacetamide Sodium 15%, and preserved with methylparaben 0.05% and propylparaben 0.01%.

Clinical uses As an anti-infective.

Dosage and administration *Route of Administration:* Topical ocular use.

Recommended Dosage: Acute infection: two drops every 2 hours or as prescribed.

Chronic Infections: two drops every 4 hours or as prescribed. Isopto Cetamide is suitable for use by both adults and children.

Contra-indications, warnings, etc Should not be used on patients who have shown hypersensitivity to sulphonamides.

Pharmaceutical precautions Isopto Cetamide eye drops should be stored in a cool place away from direct sunlight. Keep the container tightly closed. Contents should be discarded one month after opening.

Legal category POM.

Package quantities 15 ml.

Further information Isopto Cetamide eye drops are contained in an unbreakable semi-rigid container. This container bears the label and is itself in a rigid capped plastic outer.

Product licence number 0649/5909.

ISOPTO* EPINAL 0.5% and 1.0%

Presentation Isopto Epinal is a clear, colourless to light yellow, sterile, aqueous solution containing 0.5% or 1% Adrenaline, (as the borate complex). Hydroxypropyl methylcellulose (hypromellose), and preserved with benzalkonium chloride 0.01%.

Clinical uses Isopto Epinal is indicated for the control of simple open angle glaucoma. It may be used with miotics. Carbonic Acid Anhydrase inhibitors may be used with this drug in selected cases.

Dosage and administration *Route of Administration:* Instillation into the eye(s).

Recommended Dosage: The dosage must be adjusted to tonometric readings before and during therapy. The usual dosage is one drop in the eye(s) once or twice daily. When used to complement miotic therapy this drug should be instilled 5 to 10 minutes after the miotic drug.

Contra-indications, warnings, etc Do not use in narrow angle glaucoma. Do not use until the diagnosis of glaucoma has been verified. For ophthalmic use only. Not for injection.

Treatment of severe reaction: A severe reaction to adrenaline is rapid in onset and of short duration. In such an event give individuals I.V. injection of quick acting α -adrenergic blocking agent such as 5 to 10 mg pentolamine mesylate, followed by a β -blocking agent such as 2.5 to 5 mg propranolol.

Adverse Reactions: Isopto Epinal drops should be used with caution in patients with hypertensive cardiovascular disease. Prolonged use may produce extra-cellular pigmentation. On rare occasions systemic side-effects have been observed such as headaches, palpitation, pallor, tachycardia, trembling and perspiration. Stinging

may occur after instillation with rebound redness. This product contains benzalkonium chloride and should not be used when soft contact lenses are worn.

Pharmaceutical precautions Contents should be discarded one month after opening. After dispensing, the patient is advised to observe the following precautions:

1. Store the bottle in an up-right position with the dropper tightly sealed.
2. Protect from excessive heat and light. Keep in a cool, dark place.
3. Prevent the dropper tip from touching the eye-lid or other surfaces since this may contaminate the solution. Do not rinse the dropper in tap water.
4. If the clear solution changes colour, obtain a fresh supply from the pharmacist.

Legal category P.

Package quantities 7.5 ml amber glass bottles with dropper.

Further information Nil.

Product licence numbers

1% 0649/0001
0.5% 0649/0002

ISOPTO* FRIN 0.12%

Presentation Isopto Frin is a clear, colourless sterile solution, containing Phenylephrine Hydrochloride 0.12% in a hydroxypropyl methylcellulose (hypromellose) 0.5% aqueous base, preserved with benzalkonium chloride 0.01%.

Clinical uses As an emollient lubricant with vasoconstrictive effect.

Dosage and administration *Route of Administration:* Topical ocular use.

Recommended Dosage: Isopto Frin is suitable for use by both adults and children. One or two drops three times a day or as necessary.

Contra-indications, warnings, etc If the irritation persists or increases its use should be discontinued. Slight dilation of the pupil may occur in some patients. For this reason it should be used with care where narrow angle glaucoma may be present, since its use may precipitate angle closure, or in those with a shallow anterior chamber. This packet contains benzalkonium chloride and should not be used when soft contact lenses are being worn.

Pregnancy Warning: This product should only be used during pregnancy if considered essential by the physician.

Precautions: Care should be exercised in its use in small children, pressure should be put on the inner canthus of the eye for a few minutes after instillation to decrease systemic absorption via the naso lacrimal duct.

Use with caution on an inflamed eye, as hyperaemia greatly increases the rate of systemic absorption through the conjunctiva.

Pharmaceutical precautions Isopto Frin eye drops should be stored in a cool place away from direct sunlight. Keep the container tightly closed. Contents should be discarded one month after opening.

Legal category P.

Package quantities 10 ml containers.

Further information Isopto Frin eye drops are contained in an unbreakable semi-rigid plastic dropper bottle with a screw-on cap, containing 15 ml of the preparation.

Product licence number 0649/5911.

ISOPTO* PLAIN

Presentation Isopto Plain is a sterile, clear, colourless solution containing hydroxypropyl methylcellulose (hypromellose) 0.5%, and preserved with benzalkonium chloride 0.01%.

Clinical uses Isopto Plain is a soothing emollient solution used in cases of tear deficiency as a lubricant, and as an artificial tear and may be used with hard contact lenses.

Dosage and administration It is suitable for use both by adults and children. The dose is one or two drops topically instilled into the eyes three times daily as needed, or as prescribed by the doctor.

Contra-indications, warnings, etc If an irritation persists or increases, use of the drops should be discontinued. In order to help preserve sterility the dropper should not be allowed to touch the eyelids or any other surface. This product contains benzalkonium chloride, and should not be used when soft contact lenses are being worn.

Pharmaceutical precautions The eye-drops should be stored in a cool place (8° to 25°C). Keep the container tightly closed. Keep out of reach of children. Discard contents one month after opening.

Legal category P.

Package quantities 10 ml containers.

Further information Isopto Plain eye-drops are contained in an unbreakable semi-rigid plastic dropper bottle with a screw-on cap, containing 15 ml of the preparation. This container bears the label and is itself in a rigid capped plastic outer.

Product licence number 0649/5920.

MAXIDEX*

Presentation Dexamethasone 0.1% in a vehicle containing 0.5% hydroxypropyl methylcellulose (hypromellose). A sterile, isotonic, ophthalmic suspension, preserved with benzalkonium chloride 0.01%.

Clinical uses Maxidex is indicated in the treatment of certain inflammatory conditions of the anterior segment. Acute and chronic anterior uveitis, iritis, iridocyclitis, cyclitis, herpes zoster ophthalmicus. External diseases: non specific superficial keratitis, phytotenular keratoconjunctivitis, vernal conjunctivitis, allergic, catarrhal and non purulent conjunctivitis.

Recurrent marginal ulceration of toxic or allergic aetiology. Thermal or chemical burns. Post-operatively to reduce inflammatory reactions.

Dosage and administration For severe to acute inflammations 1 or 2 drops to be instilled into the eye every 30-60 mins. for at least 3-4 days or until a satisfactory response is made. Then every 2 to 3 hours

for one to two weeks. If a favourable response is not obtained in 3-4 days subconjunctival or systemic therapy should be instituted.

Contra-indications, warnings, etc

Contra-indications: Herpes simplex and other viral diseases of the cornea and conjunctiva. Fungal disease. Tuberculosis and acute purulent untreated infections.

Warnings: Extended use of topical steroids may increase intraocular pressure which should be checked frequently. In those diseases causing thinning of the cornea, perforation has been known to occur with the use of topical steroids. If the inflammation does not respond within a reasonable period other forms of therapy should be instituted. If any reaction indicating sensitivity is observed, discontinue use. In cases of bacterial infections concomitant use of antibiotics or chemotherapeutics is mandatory.

Intensive or prolonged topical corticosteroid therapy is a possible factor in the formation of posterior subcapsular cataracts. This product contains benzalkonium chloride and should not be used when soft contact lenses are being worn.

Pregnancy Warning: Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnancy has not been absolutely established, therefore it is advisable not to use this product for long term treatment of pregnant patients.

Pharmaceutical precautions Maxidex should be stored in a cool place away from direct sunlight. Keep the container tightly closed. The contents should be discarded one month after opening. Shake well before using.

Legal category POM.

Package quantities 10 ml and 15 ml containers.

Further information Maxidex eye drops are contained in an unbreakable semi-rigid, plastic dropper bottle with a screw-on cap, containing 5 ml or 15 ml of the preparation. This container bears the label and is itself in a rigid capped plastic outer. Maxidex is a highly penetrating form of dexamethasone, a 0.1% microfine suspension especially formulated to provide maximum corneal absorption.

Product licence number 0649/5914.

MAXITROL* EYE DROPS MAXITROL* EYE-OINTMENT

Presentation Drops: Dexamethasone BP 0.1% Polymyxin B Sulphate USP 6,000 units/ml and Neomycin Sulphate equivalent to Neomycin 3.5 mg/ml in a vehicle containing 0.5% hydroxypropyl methylcellulose (hypromellose). A sterile, isotonic, ophthalmic suspension, preserved with benzalkonium chloride 0.004%.

Ointment: Dexamethasone BP 0.1% Polymyxin B Sulphate USP 6,000 units/g and Neomycin Sulphate equivalent to Neomycin 3.5 mg/g in an ointment base, preserved with methylparaben 0.05% and propylparaben 0.01%.

Clinical uses Management of infectious ocular inflammations produced by organisms which are sensitive to Neomycin Sulphate and Polymyxin B Sulphate.

Acute or chronic non-purulent conjunctivitis, blepharo-conjunctivitis, kerato-conjunctivitis, non-specific superficial keratitis, deep keratitis, and acne rosacea keratitis, herpes zoster ophthalmicus iridocyclitis, mild acute iritis, recurrent marginal ulceration, corneal ulcer, non-purulent blepharitis, scleritis, episcleritis and sclero-conjunctivitis. Post-operatively to prevent ocular infection.

Dosage and administration *Drops:* One or two drops to be instilled into the conjunctival sac, 4-6 times daily. Dosage may be reduced after 3-4 days when a satisfactory response has been obtained.

Ointment: Apply a small amount of ointment into the conjunctival sac, 3-6 times a day. When a favourable response is observed, the dosage may be reduced to 3-4 applications per day. This may be followed by once a day applications for several more days.

Contra-indications, warnings, etc

Contra-indications: This drug is contra-indicated in tuberculous, fungal and most viral lesions of the eye (herpes simplex/dendritic keratitis); vaccinia; varicella; acute purulent conjunctivitis and acute purulent blepharitis; and in those persons who have shown hypersensitivity to any of its components.

Warnings: Extended use of topical therapy may cause increased intraocular pressure in certain individuals. It is advisable that intraocular pressure be checked frequently. In those diseases causing thinning of the cornea, perforation has been known to occur with the use of topical steroids.

Prolonged use may result in overgrowth of non-susceptible organisms, including fungi. If the condition does not respond within a reasonable period other forms of therapy should be instituted.

Appropriate measures should be taken when this occurs. A few individuals may be sensitive to one or more components of this product. If any reactions indicating sensitivity are observed discontinue use. Extended use of topical steroids is a possible factor in the formation of subcapsular cataracts. Maxitrol drops contain benzalkonium chloride and should not be used when soft contact lenses are being worn.

Pregnancy Warning: Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnancy has not been absolutely established, therefore it is advisable not to use this product for long term treatment of pregnant patients.

Pharmaceutical precautions Maxitrol eye-drops and eye-ointment should be stored in a cool place away from direct sunlight. Keep the container tightly closed. Contents should be discarded one month after opening. Drops should be well shaken before use.

Legal category POM.

Package quantities *Drops:* 5 ml container
Ointment: 3.5 g

Further information *Drops:* Maxitrol eye-drops are contained in an unbreakable semi-rigid, plastic dropper bottle with screw-on cap, containing 5 ml of the preparation. This container bears the label and is itself in a rigid capped plastic outer.

Ointment: Maxitrol eye-ointment is contained in a tube with a screw-on cap. This tube bears the label and is itself in a rigid capped plastic outer.

Product licence numbers

Maxitrol Eye-Drops 0649/5915
Maxitrol Eye-Ointment 0649/5916

MYDRIACYL 0.5% w/v and 1.0% w/v

Presentation Mydriacyl is a sterile clear, colourless solution containing Tropicamide 0.5% w/v or 1.0% w/v, packed in 5 ml Droptainers, and preserved with benzalkonium chloride 0.01%.

Clinical use As a mydriatic and cycloplegic.

Dosage and administration *Topically:* For refraction, 1 or 2 drops of 1.0% solution in the eye(s), repeated in 5 minutes. If patient is not seen within 20 to 30 minutes, an additional drop may be instilled to prolong mydriatic effect. For examination of fundus, 1 or 2 drops of 0.5% solution 15 or 20 minutes prior to examination.

Contra-indications, warnings, etc

Contra-indications: The use of Mydriacyl in narrow angle glaucoma is contraindicated as it may precipitate angle closure.

Warnings: This preparation may cause CNS disturbances, and care should be exercised in its use in infants and small children. Pressure should be put on the inner canthus of the eye for a few minutes after the instillation to decrease systemic absorption via the naso lacrimal duct.

The possibility of the occurrence of psychotic reaction and behavioural disturbance due to hypersensitivity to anticholinergic drugs should be borne in mind. This product contains benzalkonium chloride and should not be used where soft contact lenses are being worn.

Pregnancy Warning: There is no evidence as to the drug safety in human pregnancy, nor is there evidence from animal work that it is free from hazard. This product should only be used during pregnancy if considered essential by the physician.

Precautions: In the elderly and others where increased intra-ocular pressure may be encountered, mydriatics and cycloplegics should be used cautiously. To avoid inducing angle closure glaucoma, an estimation of the depth of the angle of the anterior chamber should be made.

The lacrimal sac should be compressed by digital pressure for 1 minute after instillation to avoid excessive systemic absorption.

Use with caution on an inflamed eye, as hyperaemia greatly increases the rate of systemic absorption through the conjunctiva.

Adverse Reactions: Increased intra-ocular pressure. Psychotic reactions, behavioural disturbances, and cardiorespiratory collapse in children with this class of drugs has been reported.

Transient stinging, dryness of the mouth, blurred vision, photophobia with or without corneal staining, tachycardia, headache, parasympathetic stimulation or allergic reaction may occur.

Treatment of Severe Reaction: A severe reaction to tropicamide is rapid in onset and of short duration. In such an event give immediate I.V. injection of quick acting α -adrenergic blocking agent such as 5 to 10 mg pentolamine mesylate, followed by a β -blocking agent such as 2.5 mg of propranolol.

Pharmaceutical precautions Mydriacyl eye drops should be stored in a cool place, away from direct

sunlight, but do not refrigerate. Keep the container tightly closed. Discard one month after opening.

Legal category POM.

Package quantities 5 ml containers.

Further information Mydriacyl eye drops are contained in a semi-rigid plastic dropper bottle with a screw-on cap.

Product licence numbers 0649/5917
0649/5918

ALCON OPULETS* ATROPINE 1%

Presentation Single dose clear, colourless, sterile eye drops containing 1% w/v of atropine sulphate BP.

Clinical uses Mydriatic and cycloplegic.

Atropine is used both pre-operatively and post-operatively and may also be used in the treatment of keratitis, iritis and cyclitis, and in refractive work in children.

Dosage and administration One drop as required. Dilatation of the pupil occurs within half an hour on local application.

Uveitis: two of three drops to be instilled four hourly initially and reducing to twice daily when pupil is dilated.

Refraction: two or three drops to be instilled two or three times daily prior to examination.

Contra-indications, warnings, etc Because of the irreversible mydriasis produced by atropine there is a risk that it may precipitate an acute glaucoma episode in cases of latent narrow angle glaucoma. If there is any doubt, the weaker homatropine should be used since its action is reversible by eserine or pilocarpine.

Pharmaceutical precautions Alcon Opulets should be stored in a cool place and protected from strong light.

Legal category POM.

Package quantities Alcon Opulets are available in packs of 20 units each containing 0.25 ml.

Further information Nil.

Product licence number 0649/0061

ALCON OPULETS* BENOXINATE

Presentation Single dose, clear, colourless sterile eye drops containing 0.4% w/v oxybuprocaine hydrochloride (Benoxinate).

Clinical uses Local anaesthetic.

Dosage and administration One drop.

Benoxinate is less irritant than amethocaine in similar concentrations.

Tonometry: One drop is sufficient to anaesthetise the surface of the eye to allow tonometry after 60 seconds.

Fitting Contact Lenses: A further drop after 90 seconds provides adequate anaesthesia for the fitting of contact lenses.

Removal of Foreign Body and/or Incision of Meibomian Cyst: Three drops at 90 second intervals provides sufficient anaesthesia after five minutes for a foreign body to be removed from the corneal epithelium or incision of a Meibomian cyst through the conjunctival

surface. Corneal sensitivity is normal again after about one hour.

Children: Dosage is at the discretion of the physician.

Contra-indications, warnings, etc The anaesthetised eye should be protected from dust and bacterial contamination. Prolonged application of anaesthetic eye drops may damage the cornea.

Pharmaceutical precautions Alcon Opulets should be stored in a cool place and protected from strong light. Solutions of Benoxinate and fluorescein sodium should not be mixed as a precipitate may be formed.

Legal category POM.

Package quantities Alcon Opulets are available in packs of 20 units each containing 0.25 ml.

Further information Benoxinate produces very little conjunctival irritation or hyperaemia and has no effect on the pupil.

The sensitivity of the cornea returns to normal about one hour after administration of Benoxinate drops.

Product licence number 0649/0056.

ALCON OPULETS* CHLORAMPHENICOL 0.5%

Presentation Single dose, clear, colourless, sterile eye drops containing 0.5% w/v Chloramphenicol BP.

Clinical uses Chloramphenicol is a broad spectrum bacteriostatic antibiotic effective against a wide range of Gram negative and Gram positive organisms.

Dosage and administration *Adult:* One or more drops as required.

Children: One drop as required.

Contra-indications, warnings, etc Treatment should be discontinued on the appearance of toxic symptoms or allergic skin rashes. Such a general allergy should be treated with antihistamines by mouth.

Pharmaceutical precautions Alcon Opulets containing Chloramphenicol should be stored at 5°C and away from strong light.

Legal category POM.

Package quantities Alcon Opulets are available in packs of 20 units each containing 0.25 ml.

Further information Nil.

Product licence number 0649/0047.

ALCON OPULETS* CYCLOPENTOLATE 1%

Presentation Single dose, clear, colourless, sterile eye drops containing 1% w/v cyclopentolate hydrochloride BP.

Clinical uses Mydriatic and cycloplegic.

Dosage and administration One or two drops as required.

Maximum effect achieved 30–60 minutes after instillation.

Contra-indications, warnings, etc Recovery of accommodation occurs within 24 hours but may be achieved more rapidly if 1 or 2 drops of a 2% w/v solution of pilocarpine nitrate are instilled.

Use may precipitate a case of latent narrow angle glaucoma into an acute attack.

Pharmaceutical precautions Alcon Opulets should be stored in a cool place and should not be exposed to strong light.

Legal category POM.

Package quantities Alcon Opulets are available in packs of 20 units each containing 0.25 ml.

Further information Nil.

Product licence number 0649/0058.

ALCON OPULETS* FLUORESCEIN SODIUM 1%

Presentation Single dose, clear orange/red sterile solution of 1% w/v fluorescein sodium BP.

Clinical uses As a diagnostic stain. Fluorescein does not stain the normal cornea.

Corneal and conjunctival abrasions or ulcers are stained a bright green and foreign bodies are surrounded by a green ring.

Dosage and administration Sufficient solution should be applied to stain the damaged areas. Excess solution may be washed away with sterile saline solution.

Contra-indications, warnings, etc Special care should be taken to avoid bacterial contamination.

Pharmaceutical precautions Alcon Opulets should be stored in a cool place and not exposed to strong light.

Legal category P.

Package quantities Alcon Opulets are available in packs of 20 units each containing 0.25 ml.

Further information The use of single dose contained preparations of fluorescein sodium are to be preferred according to Martindale (Extra Pharmacopoeia).

Product licence number 0649/0048.

ALCON OPULETS* SODIUM CHLORIDE

Presentation Single dose, clear, colourless, sterile eye drops containing 0.9% w/v sodium chloride BP.

Clinical uses Irrigating agent for the eye.

Dosage and administration Use sufficient solution to adequately irrigate the eye.

Contra-indications, warnings, etc None.

Pharmaceutical precautions Alcon Opulets should be stored in a cool place and should not be exposed to strong light.

Legal category P.

Package quantities Alcon Opulets are available in packs of 20 units each containing 0.25 ml.

Further information Nil.

Product licence number 0649/0055.

ORATROL* TABLETS

Presentation White, circular, bi-convex tablets with a breakline, each containing 50 mg Dichlorphenamide USP.

Uses For adjunctive treatment of chronic simple (open-angle) glaucoma, secondary glaucoma, and preoperatively in acute angle closure glaucoma where delay of surgery is desired in order to lower intraocular pressure.

Oratrol is an orally effective carbonic anhydrase inhibitor. Renal excretion of sodium, potassium and bicarbonate is increased, resulting in an alkaline urine. It also causes a definite increase in chloride excretion. This enhanced excretion of chloride explains at least in part the continued efficacy of Oratrol with repeated administration and the lesser possibility for the development of metabolic acidosis. As is the case with all carbonic anhydrase inhibitors, dichlorphenamide, in high doses, causes some decrease in renal blood flow and glomerular filtration rate.

Oratrol administered orally reduces intraocular pressure by inhibiting the formation of aqueous humour in normal as well as in glaucomatous eyes. The onset of action following a single dose is within an hour and maximal effect is observed within 2 to 4 hours. The reduced intraocular pressure may be maintained for approximately 6 to 12 hours.

Oratrol therapy is most successful, when employed in conjunction with miotics.

Dosage and administration Must be adjusted carefully to meet the requirements of the individual patient. A priming dose of 100 to 200 mg (2 to 4 tablets) is suggested to be administered to adults followed by 100 mg (2 tablets) every 12 hours until the desired response has been obtained. For maintenance therapy dichlorphenamide may be administered to adults in a dosage of 25 to 50 mg ($\frac{1}{2}$ to 1 tablet) one to three times daily.

Contra-indications, warnings, etc

Contra-indications: Hepatic insufficiency, renal failure, hyperchloremic acidosis, adrenocortical insufficiency.

Pregnancy Warning: Dichlorphenamide has caused birth anomalies in experimental animals; therefore, it should be used in pregnant patients or in women of child bearing age only when, in the judgement of the physician, its use is deemed essential to the welfare of the patient.

Warning: Cases with extensive peripheral anterior synechiae and marked impairment of outflow, i.e., haemorrhagic glaucoma, respond very poorly to secondary inhibitors.

Precautions: A close check on the electrolyte balance of the patient is essential during therapy with dichlorphenamide as with patients on any other carbonic anhydrase inhibitor type of compound. In the presence of pulmonary infection where there is severe loss of pulmonary ventilation, therapy with dichlorphenamide should be employed cautiously. Blood counts should be taken regularly to determine the possibility of agranulocytosis or thrombocytopenia.

Adverse Reactions: Side effects which will occur particularly in the high dosage range include gastrointestinal disturbances (anorexia, nausea and vomiting), nervousness, globus hystericus, lassitude, ataxia, tremor, tinnitus, paresthesia (numbness and tingling) of the hands, feet, tongue, mild skin eruption, pruritus, agranulocytosis, and thrombocytopenia. Renal calculi may occur.

Treatment of overdose: The stomach should be emptied by emesis or gastric lavage. Fluids and electrolytes should, if necessary, be replenished. The most likely electrolyte disturbance is a hyperchloraemic acidosis that may respond to bicarbonate administration.

Pharmaceutical precautions Keep out of reach of children.

Legal category POM.

Package quantities 100 tablets.

Further information The product is supplied in 'blister pack' strips each containing 25 tablets, and 4 strips to a carton, it is also packed in amber screw capped tablet bottles.

Product licence number 0649/5919.

TEARS Naturale*

Presentation Tears Naturale is a clear, colourless sterile solution, presented in a 15 ml Drop-Tainer Dispenser, and contains the Duasorb water soluble polymeric system Dextran 70 USP 0.1% and Hydroxypropyl Methylcellulose (Hypromellose 0.3%), and preserved with benzalkonium chloride 0.01% and disodium edetate 0.05%.

Clinical uses A soothing solution for use as an artificial tear and lubricant in the relief of dry eye syndromes associated with deficient tear secretion or deficient mucous.

Dosage and administration Instill 1 or 2 drops into the eye(s), as frequently as to relieve eye irritation symptoms.

Contra-indications, warnings, etc

Contra-indications: This product contains benzalkonium chloride, and should not be used when soft contact lenses are being worn.

Precautions: If irritation persists, discontinue use.

Pharmaceutical precautions To avoid contaminating the solution, do not let the dropper tip touch any surface. Keep the container tightly closed. Discard the contents 1 month after opening.

Legal category P.

Package quantities 15 ml in a special dropper container.

Further information Tears Naturale eye-drops are contained in an unbreakable semi-rigid plastic dropper bottle with a screw-on cap, containing 15 ml of the preparation. The cap is secured to the container by a seal which is broken when first opened.

Product licence number 0649/0031.

ZINCIFRIN*

Presentation Zincfrin is a clear, colourless sterile solution containing Zinc Sulphate 0.25% w/v and Phenylephrine Hydrochloride 0.12% w/v, preserved with benzalkonium chloride 0.01% w/v.

Clinical uses For the treatment of mild, non-specific conjunctivitis, ocular irritation and allergies.

Dosage and administration *Route of Administration:* Topical ocular use.

Recommended Dosage: Zincfrin is suitable for use in both adults and children. 1 or 2 drops in the eyes 3 times daily for adults, and children or as directed by physician.

Contra-indications, warnings, etc If irritation per-

sists or increases the use of Zincfrin should be discontinued. It causes slight dilatation of the pupil and should be used with care in cases of narrow angle glaucoma, since its use may precipitate angle closure, or in those with a shallow anterior chamber.

This product contains benzalkonium chloride and should not be used when soft contact lenses are being worn.

Pregnancy Warning: This product should only be used during pregnancy if considered essential by the physician.

Precautions: Care should be exercised in its use in small children, pressure should be put on the inner canthus of the eye for a few minutes after instillation to decrease systemic absorption via the naso-lacrimal duct.

Use with caution on an inflamed eye, as hyperaemia greatly increases the rate of systemic absorption through the conjunctiva.

Pharmaceutical precautions Zincfrin eye drops should be stored in a cool place away from direct sunlight. Keep the container tightly closed. Discard contents one month after opening.

Legal category P.

Package quantities 15 ml containers.

Further information Zincfrin eye drops are contained in an unbreakable semi-rigid plastic dropper bottle with screw-on cap.

Product licence number 0649/5921.

ALCODERM* CREAM/LOTION

Presentation *Cream:* A white, thick smooth cream.

Lotion: A creamy white, smooth, viscous lotion.

Alcoderm contains liquid paraffin, purified water, cetylalcohol, stearyl alcohol, sodium lauryl sulphate, carbomer, polysorbate 60, triethanolamine, methylparaben, propylparaben.

Clinical use Dry, chafed or irritated skin – Alcoderm is indicated in any condition where the moisture content of the horny layer has decreased below the normal level and the skin is no longer soft and pliable.

Also recommended:

- in acute inflammatory conditions where the skin is intact, such as sunburn and windburn.
- as a smoothing, hydrating agent in certain inflammatory skin conditions where there is dryness and scaling, such as ichthyosis, atopic eczema, winter itch etc.
- as a vehicle for other active constituents.

Additional information: Alcoderm is a specially formulated emulsion with a double acting moisturizing effect. The lotion is suitable for large areas of skin, the cream for smaller drier areas. Alcoderm has a double moisturizing action which can be provided only by oil-in-water emulsions. It hydrates rapidly the surface layers of the skin, and at the same time the oil droplets form a thin, protective layer on the skin. This film gives Alcoderm its special characteristics; it is highly hydrostatic and protects the skin against excessive evaporation of the water. Only 0.6% of the film-forming surface active agents in Alcoderm are water-soluble. No other oil-in-water emulsion contains such a small quantity of water soluble ingredients.

Administration Apply topically to the skin. As required to alleviate the abovementioned skin conditions or as directed by a doctor.

Contra-indications, warnings, etc Avoid contact with the eyes.

Legal category P.

Package quantities

Cream: 60 g
Lotion: 120 ml

Further information Nil.

Product licence numbers

0649/0004 Cream
0649/0005 Lotion

DEBROXIDE*

Presentation Debroxide is a topical aqueous gel containing benzoyl peroxide 5%/10%, dioctyl sodium sulfosuccinate, ederate disodium, poloxamer 182, carbomer 940, propylene glycol, silicon dioxide, purified water, citric acid and/or sodium hydroxide to adjust pH.

Clinical use Debroxide is recommended for adjunctive topical treatment of acne vulgaris. Benzoyl peroxide is an established and effective keratolytic agent with antibacterial properties. It has been shown to be effective in reducing the local population of *Propionibacterium* acnes leading to a reduction in the production of irritant fatty acids in the sebaceous glands.

Administration After washing with a mild cleanser and water, apply once or twice daily to the affected area. The degree of drying and peeling can be adjusted by modification of the dosage schedule.

Contra-indications, warnings, etc

Contra-indication: Persons having known sensitivity to benzoyl peroxide.

Precaution: Avoid contact with the eyes, eyelids and other mucous surfaces.

Warning: May bleach hair and coloured fabrics.

FOR EXTERNAL USE ONLY.

Overdosage: Symptoms: The skin may become excessively red and sore during the first few days of treatment.

Treatment: Apply less often until this phase has passed.

Pharmaceutical precautions Store at room temperature.

Legal category P.

Package quantities Debroxide 5 – 60 g plastic tubes.

Debroxide 10 – 60 g plastic tubes.

Further information Nil.

Product licence numbers

Debroxide 5 0649/0051
Debroxide 10 0649/0062

IONAX* SCRUB

Presentation A pale yellow semi-translucent abradant gel with a fresh odour of lemon for external application. The active ingredients are polyethylene granules, benzalkonium chloride, macrogol (4) lauryl ether, macrogol

(23) lauryl ether, alcohol and foaming agents in an aqueous gel base.

Clinical use An abradant cleanser for the control and hygiene of acne. Use Ionax Scrub to cleanse skin prior to acne or oily skin treatment.

Administration Apply to wet face. Massage on the skin for one or two minutes, then rinse thoroughly.

Use once or twice daily, or as directed by your physician.

Contra-indications, warnings, etc **Caution:** Avoid contact with the eyes.

Upon accidental contact, flush with water and avoid rubbing.

If the skin gets too dry or too reddened discontinue use temporarily.

For external use only. Keep out of reach of children.

Pharmaceutical precautions There are no special pharmaceutical precautions.

Legal category P.

Package quantities 60 g packs in plastic collapsible tubes with plastic screw caps.

Further information Nil.

Product licence number 0649/0006.

IONIL T* SHAMPOO

Presentation A clear brown liquid shampoo with a slight odour of coal tar, for external use. It contains salicylic acid, benazalkonium chloride, coal tar solution USP 5% with polyoxyethylene ethers in an hydro-alcoholic shampoo base.

Clinical use For seborrhoeic dermatitis of the scalp.

Administration Massage Ionil T Shampoo into wet hair.

Do not expect much initial lather as the shampoo is formulated for low foaming.

Rinse, and then apply Ionil T shampoo again and massage into a lather. Allow to remain in the hair for about five minutes before rinsing.

This shampoo may be used daily or as directed by the physician.

For best results do not use soap, detergent or other shampoo on the hair immediately before or after using Ionil T.

Contra-indications, warnings, etc **Caution:** Avoid contact with the eyes.

Upon accidental contact, flush with clear water.

For external use only. Keep out of reach of children.

Pharmaceutical precautions Store away from internal preparations and foods.

Legal category P.

Package quantities 120 ml and 240 ml in cylindrical plastic containers with plastic screw caps.

Further information Nil.

Product licence number 0649/0003.

NUTRAPLUS* Cream

Presentation A smooth white, unperfumed cream for

topical external application. It contains 10% Urea, purified water, blend of light mineral oil, glyceryl monostearate, propylene glycol, methylparaben, propylparaben.

Clinical use An emollient, moisturising and protective cream for the treatment of dry or damaged skin. The presence of 10% urea in the product assists in providing a 'moisturising' effect lasting 5-6 hours, as shown by experiments measuring 'trans-epidermal water loss', in addition to providing the recognised actions of urea for dermatological purposes.

Dosage and administration Apply evenly to dry skin areas 2 to 3 times daily, or as necessary.

Contra-indications, warnings, etc If irritation occurs to any ingredient, discontinue use temporarily. Avoid contact with eyes.

Pharmaceutical precautions For external use only. Keep out of reach of children. Store in a cool place. Replace cap after use.

Legal category P.

Package quantities Nutraplus Cream 60 g.

Further information Nil.

Product licence number 0649/0041.

PSORIGEL*

Presentation A clear thin brown gel with a slight characteristic odour of tar, for topical external application. It contains Solution of coal tar USP 7.5%, 33% alcohol, carbomer 946, propylene glycol, ethanol, laureth 4, diisopropanolamine, and purified water. The hydroalcoholic gel base which is emollient, provides a moist film with the minimum of tar odour and staining potential.

Clinical use For the relief and treatment of inflammatory manifestations of tar responsive dermatoses. Among these are eczema, psoriasis, inflammation, erythema, scaling, pruritus and induration that accompanies various forms of dermatitis.

It also helps to relieve the itching that accompanies psoriasis, and eczema, and helps control the flaking and scaling as well.

Dosage and administration Rub into the affected areas once or twice daily. The gel may be applied more frequently if necessary.

Rub in well, allow to dry and remove any excess by patting with a paper tissue.

Contra-indications, warnings, etc *Caution:* Avoid contact with eyes. Upon accidental contact, flush with water.

After using, avoid exposure to direct sunlight, unless its action is specifically required.

Do not use on highly inflamed or broken skin.

The product contains alcohol.

If undue irritation develops, reduce the frequency of use, or suspend use until irritation subsides.

The staining potential of the product is minimal, but if it does occur, standard laundry procedure will remove most stains.

Pharmaceutical precautions For external use only. Keep out of reach of children.

Legal category P.

Package quantities 90 g in plastic collapsible tubes.

Further information Nil.

Product licence number 0649/0039.

*Trade Mark

Allen & Hanburys Limited

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Oldfield Lane North

Greenford, Middlesex UB6 0HB



AMINOGRAN* FOOD SUPPLEMENT

Presentation Aminogran Food Supplement provides a mixture of L-amino acids, including all the essential amino acids except phenylalanine. It is intended for use with Aminogran Mineral Mixture (see separate Data Sheet for Aminogran Mineral Mixture).

Content per 100 g = 1,675 kJ (400 calories)

	g	mmol
L-Alanine	2.44	27.4
L-Arginine (as glutamate)	4.20	24.1
L-Aspartic acid	6.10	45.8
L-Cystine	1.45	6.0
L-Glutamic acid (total)	12.19	82.9
Glycine	6.10	81.3
L-Histidine (as monohydrochloride)	3.40	21.9
L-Isoleucine	8.53	65.0
L-Leucine	9.95	75.9
L-Lysine (as glutamate)	6.61	45.2
L-Methionine	2.96	19.8
L-Proline	4.26	37.0
L-Serine	8.39	79.8
L-Threonine	5.71	47.9
L-Tryptophan	1.45	7.1
L-Tyrosine	6.42	35.4
L-Valine	7.01	59.8

Aminogran Food Supplement is packed as 500 g in a white polythene bag in a cylindrical plastic container with cardboard carton. The mixture is a white powder. A white measuring scoop is provided which contains 5 g when levelled with a knife edge.

Uses Aminogran Food Supplement is indicated in conjunction with Aminogran Mineral Mixture for the dietary management of phenylketonuria in infants and children, and in phenylketonuric women during pregnancy. It may be used for bottle feeding phenylketonuric infants, but if available, a preparation based on a low-phenylalanine protein hydrolysate is more practicable. Prior to weaning bottle feeds can more easily be prepared from a preparation based on a low-phenylalanine protein hydrolysate, together with carbohydrates and fats to supply energy requirements. Once weaning is started a gradual change to Aminogran should be made, as it proves more acceptable than the protein hydrolysate and reduces feeding problems.

Dosage and administration The aim of treatment with Aminogran preparations is to provide an adequate diet in which there is a reduced intake of phenylalanine so that the blood levels of this amino acid are maintained at 0.2–0.5 mmol/litre (3–8 mg/100 ml).

In sucklings this is best obtained with a preparation based on a low-phenylalanine protein hydrolysate as there are practical difficulties associated with the administration of Aminogran in bottle form due to its low energy value and high osmolality. However, once spoon-feeding is started Aminogran has the advantages of

smaller bulk and superior palatability. Aminogran Food Supplement and Aminogran Mineral Mixture can be used, in appropriately reduced dosage, in conjunction with low-phenylalanine protein hydrolysate during weaning. As the quantity of Aminogran is increased so the low-phenylalanine protein hydrolysate is decreased and eventually omitted once adequate energy is being taken from solids. Thereafter Aminogran preparations are given mixed as a paste or drink as described for older children. Gradually the Aminogran paste can be spoon-fed and given at feed times with the other foods necessary for the phenylalanine and the energy content of the diet.

For older children Aminogran Food Supplement, in the required calculated quantity for the day, together with the daily dose of Aminogran Mineral Mixture, is mixed into a drink or paste with water and/or an appropriate volume of natural vegetable oil or a 50% vegetable oil emulsion (Prosparol; Duncan, Flockhart & Co. Ltd), sugar and/or natural or synthetic protein-free flavouring, such as milk-shake syrup or concentrate. Sugar or milk-shake flavouring must be added if the oil or emulsion is used, to counteract the ketogenic effect of the fat content. The mixture is divided into three equal portions with one portion being given within 20 minutes of each of the three main meals, which should contain a proportion of the daily phenylalanine allowance. A separate drink should be given if the Aminogran mixture is administered as a paste because of the high solute content of the mixture. Administration with a meal is important as some phenylalanine is necessary to ensure that the amino-acid mixture (dietary nitrogen) is utilised for growth.

From school age the Aminogran mixture may be more practically given as two doses daily with two meals.

The daily requirements of energy, Aminogran Food Supplement and phenylalanine are shown in the table.

1. Approximately 1–1.5 g or as appropriate according to natural protein intake to give 1.5–2.0 g protein plus amino acids per kg per day.

2. Approximately 1 g or as appropriate according to natural protein intake to give 1.5 g protein plus amino acids per kg per day.

The daily dose of Aminogran Food Supplement is calculated on the actual body weight in kilograms. The required quantity can be easily measured with the scoop provided, which, when levelled off with a knife edge, contains 5 g. Aminogran Food Supplement should be prescribed to the nearest half-scoop measurement. Aminogran Food Supplement is phenylalanine free so that it is essential it is not used as the sole source of protein nitrogen but that the diet should contain sources of phenylalanine from natural foods together with low-protein foods and energy foods such as sugar, protein-free starches, fat or oil. Special low-protein foods such as breads and biscuits are also available. As phenylalanine is an essential amino acid it is of particular

importance that the growing child is not exposed to phenylalanine deficiency which can easily arise from an increased requirement in association with accelerated growth rate, inadequate absorption of phenylalanine due to vomiting, refusal of diet or inadequate replacement of phenylalanine, or inaccurate measurement of concentrated phenylalanine sources.

Although the exact threshold levels of maternal blood phenylalanine that can prove injurious to the foetus are not known it is recommended that blood phenylalanine levels of 0.2–0.5 mmols/litre (3–8 mg/100 ml) be maintained throughout pregnancy of women with phenylketonuria. Ideally the blood phenylalanine level should be maintained within the recommended range prior to

Guide to daily requirements in dietary management of classical phenylketonuria

Age (years)	Energy per kg actual body weight kilo Joules (Calories)	Aminogran Food Supplement per kg actual body weight (g)	Initial dose of phenylalanine* per kg actual body weight from other foods (mg)
0–1	420–630 (100–150)	3	50 to 60 and if necessary up to 110
1–2	380–420 (90–100)	2–3	30–40
2–4	330–420 (80–100)	2	25–40
4–6	330–420 (80–100)	2	25
6–8	290–380 (70–90)	2	15–25
8–14	230–310 (55–75)	see footnote 1	As tolerance
Over 14	190 (45)	see footnote 2	As tolerance

* This suggested initial starting dose must subsequently be adjusted according to the results of initially very frequent and then regular tests of blood phenylalanine levels.

1. Approximately 1 to 1.5 g or as appropriate according to natural protein intake to give 1.5 to 2.0 g protein plus amino acids per kg per day.

2. Approximately 1 g or as appropriate according to natural protein intake to give 1.5 g protein plus amino acids per kg per day.

Infections or any other situation causing catabolism increases blood phenylalanine levels. It is recommended that the dietary phenylalanine be continued along with a source of easily digested calories such as sugary drinks if the infection continues for more than two or three days, though the Aminogran Food Supplement can be temporarily omitted.

Because of the preponderance of synthetic foods in the diet adequate vitamin supplementation is essential. Rashes, failure to thrive, and even death can result from a deficiency of phenylalanine or vitamins such as choline chloride, calcium pantothenate, inositol, biotin, α -tocopherol, vitamin B₁₂ and folic acid. A complete vitamin supplement is provided by 3 Ketovite Tablets (Paines & Byrne Ltd) plus 5 ml of Ketovite Liquid each day. For young children Ketovite Tablets should be crushed, suspended in the Ketovite Liquid and given once daily as a medicine.

The aim of dietary management in children with Aminogran is to maintain the blood phenylalanine concentration between 0.2 and 0.5 mmols/litre (3 and 8 mg/100 ml). For this the blood phenylalanine levels should be monitored at regular intervals and the phenylalanine (natural protein) allowance adjusted as necessary.

Women with phenylketonuria in pregnancy: The children of mothers with untreated phenylketonuria have a very high incidence of congenital abnormalities, including mental retardation, intrauterine and postnatal retardation of growth, microcephaly, skeletal, cardiac and ocular manifestations. Patients treated from early life are now reaching reproductive age and it is suggested that all their pregnancies should be planned and dietary restriction together with Aminogran Food Supplement and Mineral Mixture should commence before stopping the contraceptive method and prior to conception. Even then it is impossible to guarantee that the child will be normal at birth.

the onset of pregnancy but when this has not been planned the diet with Aminogran preparations should be instituted as soon as pregnancy is suspected. It should be then continued until the onset of labour. More frequent monitoring of the blood phenylalanine level during pregnancy is mandatory because of the increasing demand for phenylalanine by the growing foetus. This is of particular importance during the third trimester of pregnancy.

Initially a protein plus amino acid intake of 1 g/kg body weight using Aminogran Food Supplement is the suggested dose provided that the total intake of protein is not less than 50 g per day. Phenylalanine from natural foods should be given as indicated by previous tolerance. Initially 15 mg/kg is suggested, adjusted according to tolerance and increasing with foetal growth. The total diet should provide the energy requirement to maintain satisfactory weight gain and any weight loss should be avoided as it causes blood phenylalanine levels to rise.

Contra-indications, warnings, etc

Contra-indications: Aminogran Food Supplement is prepared solely for the dietary management of phenylketonuria and is unsuitable for the dietary management of any other disorder or to form part of the nutrition of normal persons.

Precautions: Aminogran Food Supplement when mixed with Aminogran Mineral Mixture presents a high osmolar load that requires an adequate fluid intake, especially in infants and young children.

Care should be taken to ensure all patients taking the Aminogran diet consume the full calculated diet which must contain adequate energy foods. If the diet is insufficient in energy the blood phenylalanine concentration will show an increase due to catabolism of body protein. The existence of an infection will also cause a rise in blood phenylalanine but under these circumstances appetite should be the guide to nutritional intake.

The priority will be for high-energy protein-free drinks and the phenylalanine allowance, in foods such as milk, is only a secondary consideration. Only if milk is acceptable should the mixture of Aminogran Food Supplement and Aminogran Mineral Mixture be administered. A temporary period without Aminogran, as in any child not eating during an infection, does no harm and blood level control of phenylalanine returns when the infection is over.

Side-effects: No side-effects arise from administration of Aminogran Food Supplement so long as there is correct dietary management to avoid too high or too low a blood level of phenylalanine. The high osmolality may give rise to vomiting and/or diarrhoea but can be overcome by additional fluid. Parental or patient anxiety over the dietary regime and/or diagnosis may cause similar effects so careful frequent supervision and monitoring of the diet is essential.

Overdosage: Not applicable.

Pharmaceutical precautions Store in a cool dry place and ensure that the container lid is always replaced securely.

Legal category P.

Package quantities Aminogran Food Supplement is supplied in containers of 500 g.

Further information A booklet describing the use of Aminogran preparations is available on request. It is advisable that this be consulted before Aminogran Food Supplement is prescribed.

Product licence number 0045/0114.

AMINOGRAN[®] MINERAL MIXTURE

Presentation Aminogran Mineral Mixture contains all the necessary minerals for balanced nutrition in the correct proportions for human needs and is intended for use with Aminogran Food Supplement (see separate Data Sheet for Aminogran Food Supplement). Aminogran Mineral Mixture is packed as 250 g in a yellow polythene bag in a cylindrical plastic container with cardboard carton. The mixture is a mottled white powder. A yellow measuring scoop is provided which contains 2.7 g when levelled with a knife edge. Three scoops provide the usual daily dose of 8 g.

Uses Aminogran Mineral Mixture is indicated in conjunction with Aminogran Food Supplement for the dietary management of phenylketonuria. Aminogran Mineral Mixture is also indicated as an adjuvant in the treatment of the following conditions:

1. Other disorders of amino-acid metabolism such as maple syrup urine disease and homocystinuria.
2. Urea cycle defects. These include carbamyl phosphate synthetase deficiency, ornithine carbamyl transferase deficiency, argininosuccinate synthetase deficiency (citrullinaemia), argininosuccinase deficiency (argininosuccinaciduria), arginase deficiency (hyperargininaemia), hyperlysinaemia and other urea cycle defects as they are recognised.
3. Organicacidurias. These include hypervalinaemia, isovalericaciduria, beta-methylcrotonylglycinuria, alpha-methylacetoaceticaciduria and propionicaciduria.
4. In conjunction with artificial diets used in the treatment of food intolerance with malabsorption.

5. In any diet in infants and children where there is severe restriction of natural food, such as in some ketogenic diets for the treatment of epilepsy.

Content per 100 g and per 8 g dose

	per 100 g		per 8 g dose	
Potassium	8.3 g	0.21 mol	0.66 g	17 mmol
Calcium	8.1 g	0.20 mol	0.65 g	16 mmol
Phosphorus	6.0 g	0.19 mol	0.48 g	15 mmol
Sodium	4.0 g	0.17 mol	0.32 g	14 mmol
Magnesium	0.97 g	40 mmol	77 mg	3.2 mmol
Iron	63 mg	1 mmol	5 mg	90 micromol
Zinc	48 mg	0.7 mmol	4 mg	59 micromol
Copper	13 mg	0.2 mmol	1 mg	16 micromol
Manganese	4 mg	81 micromol	0.4 mg	6 micromol
Iodine				
Aluminium				
Cobalt				
Molybdenum				
Trace quantities				

Dosage and administration Used for the dietary management of phenylketonuria, with Aminogran Food Supplement, it is recommended that the total daily intake of Aminogran Mineral Mixture is 8 g per day, provided that the patient's body weight is not less than 5.5 kg. For infants under 5.5 kg body weight the dosage is calculated on the basis of 1.5 g/kg/day. Solutions with a high osmolality may cause vomiting, abdominal pain and diarrhoea in young infants so that it is advised that each gram of Aminogran Mineral Mixture should be diluted for infants with at least 100 ml of fluid. The usual method of administration is to prepare a drink or paste of Aminogran Food Supplement, in the required daily quantity (see separate Data Sheet for this product), together with three level, unpacked scoops (8 g) of Aminogran Mineral Mixture. The drink or paste may be prepared with water and/or a vegetable oil or emulsion (Prosparol; Duncan, Flockhart & Co. Ltd) sugar and/or protein-free flavouring such as fruit, milk-shake, syrup or concentrate. If the oil is included then sugar should be added. The drink or paste is divided into three equal portions and one portion taken with each of the three main meals of the day like a dose of medicine and washed down with water or fruit juice. For older children the preparation may be divided into two portions with each portion taken with a convenient main meal. Some food containing natural protein must be consumed at the time of administration to supply the phenylalanine necessary for utilisation of the amino acids for growth. Aminogran Mineral Mixture may be similarly used in the other conditions for which it is indicated.

Contra-indications, warnings, etc

Contra-indications: Aminogran Mineral Mixture is unsuitable for use where trace element supplementation only is required. If used for infants of less than 5.5 kg body weight the total daily dose should not exceed 1.5 g per kg body weight.

Precautions: When used in infants under the age of six months each 1 g of Aminogran Mineral Mixture must be diluted with at least 100 ml of fluid. For older children a drink to follow is satisfactory.

Side-effects: Mineral solutions with high osmolality may cause vomiting, abdominal pain and diarrhoea. This may be avoided by dilution as advised under 'Precautions'.

Overdosage: If Aminogran Mineral Mixture is inadvertently given to infants in excess of the recommended

dose of 1.5 g/kg/day or inadequately diluted to at least 1 g per 100 ml, symptoms of hyperosmolarity may occur and the serum electrolytes should be checked. Treatment is administration of fluids by the oral or, if necessary, parenteral routes.

Pharmaceutical precautions Store below 25°C in a dry place and ensure that the container lid is always replaced securely.

Legal category P.

Package quantities Aminogran Mineral Mixture is supplied in containers of 250 g.

Further information It is essential that the Data Sheet for Aminogran Food Supplement is consulted for a full understanding of the use of Aminogran preparations in the dietary management of phenylketonuria. A booklet describing the use of Aminogran preparations in phenylketonuria is available on request and it is advisable that it should be read before the products are prescribed.

Product licence number 0045/0115.

BECONASE* NASAL SPRAY

Presentation Beconase Nasal Spray is a metered-dose aerosol which delivers 50 mcg Beclomethasone Dipropionate BP per actuation into a specially designed nasal applicator.

Uses Beconase is indicated for the prophylaxis and treatment of perennial and seasonal allergic rhinitis, including hay fever and vasomotor rhinitis. Beclomethasone Dipropionate BP has a potent anti-inflammatory effect within the respiratory tract at doses which are not systemically active.

Dosage and administration Beconase is for administration by the intranasal route only. The recommended dosage is two applications into each nostril twice daily (400 mcg/day).

For some patients, a dosage regimen of a single application into each nostril three or four times daily may be preferred. Total daily administration should not normally exceed 8 puffs.

For full therapeutic benefit regular usage is essential. The co-operation of the patient should be sought to comply with the regular dosage schedule and it should be explained that maximum relief may not be obtained with the first few applications. Not for use in children under six years of age.

Contra-indications, warnings, etc

Contra-indications: There are no specific contra-indications to the use of Beconase.

Precautions: Infections of the nasal passages and paranasal sinuses should be appropriately treated but do not constitute a specific contra-indication to treatment with Beconase.

Care must be taken while transferring patients from systemic steroid treatment to Beconase if there is any reason to suppose that their adrenal function is impaired.

Although Beconase Nasal Spray will control seasonal allergic rhinitis in most cases, an abnormally heavy challenge of summer allergens may in certain instances necessitate appropriate additional therapy.

Unnecessary administration of drugs during the first trimester of pregnancy is undesirable.

Side-effects: No major side-effects attributable to Beconase have been reported, but occasionally sneezing attacks have followed immediately after the use of the aerosol.

Overdosage: The only harmful effect that follows inhalation of large amounts of the drug over a short time period is suppression of hypothalamic-pituitary-adrenal (HPA) function. No special emergency action need be taken. Treatment with Beconase Nasal Spray should be continued at the recommended dose. HPA function recovers in a day or two.

Pharmaceutical precautions Beconase should be stored at a temperature below 30°C. Exposure to direct sunlight or heat should be avoided. The canister should not be punctured, broken or burnt even if it is apparently empty.

Legal category POM.

Package quantities Beconase Nasal Spray is a metered-dose aerosol with a specially designed nasal applicator. Each canister provides 200 sprays.

Further information When Beconase is administered as two applications into each nostril the first puff should be directed at the upper and the second at the lower part of the nasal cavity.

Product licence number 0045/0093.

BECOTIDE* INHALER

Presentation Becotide Inhaler is a metered-dose aerosol which delivers 50 mcg Beclomethasone Dipropionate BP per actuation into the mouthpiece of a specially designed actuator.

Uses Beclomethasone Dipropionate BP given by inhalation has a potent glucocorticoid anti-inflammatory action within the lungs but does not cause adverse systemic glucocorticoid effects at therapeutic doses. Becotide Inhaler therefore is indicated for a wide range of patients with bronchial asthma.

These patients include: those whose asthma is becoming worse and the relief provided by bronchodilators is less effective; those who are inadequately controlled by sodium cromoglycate in addition to bronchodilators; those with severe asthma who are dependent on systemic corticosteroids, or adrenocorticotrophic hormone (ACTH) or its synthetic equivalent.

Becotide Inhaler is particularly important for managing severe asthma in children because good control can be achieved without retardation of growth.

Dosage and administration *Adults:* 2 inhalations (100 mcg) three or four times a day is the usual maintenance dose. Alternatively, the total daily dose may be administered as two divided doses. In severe cases dosage may be started at 600–800 mcg per day and subsequently reduced when the patient begins to respond.

Children: 1 or 2 inhalations (50–100 mcg) should be given two, three or four times daily, according to the response.

Contra-indications, warnings, etc

Contra-indications: No specific contra-indications to Becotide Inhaler are known, but special care is necessary in patients with active or quiescent pulmonary tuberculosis.

Precautions: Patients should be instructed on the proper use of the inhaler to ensure that the drug reaches the target areas within the lungs. They should also be made aware that Becotide Inhaler has to be used regularly for optimum benefit.

The maximum daily intake of Becotide Inhaler should not exceed 20 inhalations (1 mg); significant reduction of plasma cortisol levels has been reported in patients who received twice this amount.

Unnecessary administration of drugs during the first trimester of pregnancy is undesirable.

Patients inadequately controlled by bronchodilator therapy: The use of Becotide Inhaler in patients who have never taken steroids or taken only occasional courses of steroids is straightforward. An improvement in respiratory function is obvious within a week. The few patients who do not respond during this period usually have excessive mucus in their bronchi so that the drug is unable to penetrate to its site of action. In such cases a short course of systemic steroid in relatively high dosage should be given to control secretion of mucus and other inflammatory changes in the lungs. Continuation of treatment with Becotide Inhaler usually maintains the improvement achieved, the oral steroid being gradually withdrawn. Exacerbation of asthma caused by infection is usually controlled by appropriate antibiotic treatment, by increasing the dose of Becotide Inhaler and if necessary by giving systemic steroid.

Steroid-dependent patients: The transfer of steroid-dependent patients to Becotide Inhaler and their subsequent management needs special care mainly because recovery from impaired adrenocortical function, caused by prolonged systemic steroid therapy, is slow. The patient should be in a reasonably stable state before being given Becotide Inhaler in addition to his usual maintenance dose of systemic steroid. After about a week, gradual withdrawal of the systemic steroid is started by reducing the daily dose by 1 mg prednisolone, or its equivalent of other corticosteroid, at not less than weekly intervals. Patients treated with systemic steroids for long periods of time or who have received high doses may have adrenocortical suppression. With these patients adrenocortical function should be monitored regularly and their dose of systemic steroid reduced cautiously. Some patients feel unwell during the withdrawal phase despite maintenance or even improvement of respiratory function. They should be encouraged to persevere with the inhaler and withdrawal of systemic steroids continued, unless there are objective signs of adrenal insufficiency. Most patients can be successfully transferred to Becotide Inhaler with maintenance of good respiratory function, but special care is necessary for the first months after the transfer until the pituitary-adrenal system has sufficiently recovered to enable the patient to cope with emergencies such as trauma, surgery or infections. Transferred patients whose adrenocortical function is impaired should carry a warning card indicating that they need supplementary systemic steroid during periods of stress. They should also be given a supply of oral steroid to use in emergency, for example when the asthma worsens as a result of a chest infection. The dose of Becotide Inhaler should be increased at this time and then reduced to the maintenance level after the systemic steroid has been discontinued.

Replacement of systemic steroid treatment with Becotide Inhaler sometimes unmasks allergies such as allergic rhinitis or eczema previously controlled by the

systemic drug. These allergies should be symptomatically treated with antihistamine and/or topical preparations.

Side-effects: No major side-effects attributable to the use of recommended doses of Becotide Inhaler have been reported. Candidiasis of the mouth and throat (thrush) occurs in some patients; patients with high blood levels of Candida precipitins, indicating a previous infection, are more likely to develop this complication. The incidence of candidiasis is increased with doses greater than 400 mcg beclomethasone dipropionate per day. The condition usually responds to topical antifungal therapy without discontinuing treatment with Becotide Inhaler.

Overdosage: The acute toxicity of beclomethasone dipropionate is low. The only harmful effect that follows inhalation of large amounts of the drug over a short time period is suppression of hypothalamic-pituitary-adrenal (HPA) function. No special emergency action need be taken. Treatment with Becotide Inhaler should be continued at the recommended dose to control the asthma; HPA function recovers in a day or two.

Reduction of plasma cortisol levels has been reported in patients who received twice the recommended maximum dose of Becotide Inhaler. In the unlikely event of grossly excessive intake of beclomethasone dipropionate for weeks or months on end a degree of adrenocortical atrophy could occur in addition to suppression of HPA function. The patient should be treated as steroid-dependent and transferred to a suitable maintenance dose of a systemic steroid such as prednisolone. Once the patient's condition is stabilised he should be transferred to Becotide Inhaler by the method recommended in this Data Sheet.

Pharmaceutical precautions *Storage:* Becotide Inhaler should be stored at a temperature below 30°C. Direct sunlight and heat should be avoided.

The canister should not be punctured, broken or burnt even if it is apparently empty.

Legal category POM.

Package quantities Becotide Inhaler is a metered-dose aerosol with a specially designed actuator. Each canister provides 200 inhalations.

Further information Nil.

Product licence number 0045/0089.

BECOTIDE* ROTACAPS*

Presentation Becotide Rotacaps, an alternative inhalation form of beclomethasone dipropionate to Becotide Inhaler, are especially valuable for treating patients who are unable to use pressurised inhalers effectively or who might use them incorrectly.

Becotide Rotacaps contain a mixture of microfine beclomethasone dipropionate and larger particle lactose in buff or chocolate-brown/colourless hard gelatine cartridges. Each Rotacap contains 100 mcg (buff) or 200 mcg (chocolate-brown) of beclomethasone dipropionate and is marked Becotide 100 or Becotide 200. The contents of a Rotacap are inhaled using a specially developed device called a Rotahaler*, which separates the cartridge into halves that rotate and release the drug when the patient inhales. This breath actuation is very sensitive and so the drug is fully available even at the lowest inspiratory flow rates. The Rotahaler is therefore a more reliable drug delivery system for many patients

but a rather larger unit dose relative to Becotide Inhaler is necessary for the same therapeutic effect.

Uses Beclomethasone Dipropionate BP given by inhalation has a potent glucocorticoid anti-inflammatory action within the lungs but does not cause adverse systemic glucocorticoid effects at therapeutic doses. Becotide Rotacaps therefore are indicated for a wide range of patients with bronchial asthma. These patients include: those whose asthma is becoming worse and the relief provided by bronchodilators is less effective; those who are inadequately controlled by sodium cromoglycate in addition to bronchodilators; those with severe asthma who are dependent on systemic corticosteroids, or adrenocorticotrophic hormone (ACTH) or its synthetic equivalent.

Becotide Rotacaps are particularly important for managing severe asthma in children because good control can be achieved without retardation of growth.

Dosage and administration Becotide Rotacaps are for inhalation use only, using a Becotide Rotahaler. For optimum results Becotide Rotacaps should be used regularly.

Adults: One 200 mcg Rotacap three or four times a day is the usual maintenance dose. Alternatively, the total daily dose may be administered as two divided doses.

Children: One 100 mcg Rotacap two, three or four times a day, according to the response.

Contra-indications, warnings, etc

Contra-indications: No specific contra-indications to Becotide Rotacaps are known, but special care is necessary in patients with active or quiescent pulmonary tuberculosis.

Precautions: Patients should be instructed in the proper use of the Rotahaler to ensure that the drug reaches the target areas within the lungs. They should also be made aware that Becotide Rotacaps have to be used regularly for optimum benefit.

The maximum daily intake of beclomethasone dipropionate should not exceed 1 mg; significant reduction of plasma cortisol levels has been reported in patients who received twice this amount.

Unnecessary administration of drugs during the first trimester of pregnancy is undesirable.

Patients inadequately controlled by bronchodilator therapy: The use of Becotide Rotacaps in patients who have never taken steroids or taken only occasional courses of steroids is straightforward. An improvement in respiratory function is obvious within a week. The few patients who do not respond during this period usually have excessive mucus in their bronchi so that the drug is unable to penetrate to its site of action. In such cases a short course of systemic steroid in relatively high dosage should be given to control secretion of mucus and other inflammatory changes in the lungs. Continuation of treatment with Becotide Rotacaps usually maintains the improvement achieved, the oral steroid being gradually withdrawn. Exacerbation of asthma caused by infection is usually controlled by appropriate antibiotic treatment, by increasing the dose of Becotide Rotacaps and if necessary by giving systemic steroid.

Steroid-dependent patients: The transfer of steroid-dependent patients to Becotide Rotacaps and their subsequent management needs special care mainly because recovery from impaired adrenocortical function, caused by prolonged systemic steroid therapy, is slow. The patient should be in a reasonably stable state before

being given Becotide Rotacaps in addition to his usual maintenance dose of systemic steroid. After about a week, gradual withdrawal of the systemic steroid is started by reducing the daily dose by 1 mg prednisolone, or its equivalent of other corticosteroid, at not less than weekly intervals. Patients treated with systemic steroids for long periods of time or who have received high doses may have adrenocortical suppression. With these patients adrenocortical function should be monitored regularly and their dose of systemic steroid reduced cautiously. Some patients feel unwell during the withdrawal phase despite maintenance or even improvement of respiratory function. They should be encouraged to persevere with the Rotacaps and withdrawal of systemic steroid continued unless there are objective signs of adrenal insufficiency. Most patients can be successfully transferred to Becotide Rotacaps with maintenance of good respiratory function, but special care is necessary for the first months after the transfer until the pituitary-adrenal system has sufficiently recovered to enable the patient to cope with emergencies such as trauma, surgery or infections. Transferred patients whose adrenocortical function is impaired should carry a warning card indicating that they need supplementary systemic steroid during periods of stress. They should also be given a supply of oral steroid to use in emergency, for example when the asthma worsens as a result of a chest infection. The dose of Becotide Rotacaps should be increased at this time and then reduced to the maintenance level after the systemic steroid has been discontinued.

Replacement of systemic steroid treatment with Becotide Rotacaps sometimes unmasks allergies such as allergic rhinitis or eczema previously controlled by the systemic drug. These allergies should be symptomatically treated with antihistamine and/or topical preparations.

Side-effects: No major side-effects attributable to the use of recommended doses of Becotide Rotacaps have been reported. Candidiasis of the mouth and throat (thrush) occurs in some patients; patients with high blood levels of Candida precipitins, indicating a previous infection, are more likely to develop this complication. The condition usually responds to topical anti-fungal therapy, without discontinuing treatment with Becotide Rotacaps.

Overdosage: The acute toxicity of beclomethasone dipropionate is low. The only harmful effect that follows inhalation of large amounts of the drug over a short time period is suppression of hypothalamic-pituitary-adrenal (HPA) function. No special emergency action need be taken. Treatment with Becotide Rotacaps should be continued at the recommended dose to control the asthma; HPA function recovers in a day or two.

Reduction of plasma cortisol levels has been reported in patients who received twice the recommended maximum dose of beclomethasone dipropionate. In the unlikely event of grossly excessive intake of beclomethasone dipropionate for weeks or months on end a degree of adrenocortical atrophy could occur in addition to suppression of HPA function. The patient should be treated as steroid-dependent and transferred to a suitable maintenance dose of a systemic steroid such as prednisolone. Once the patient's condition is stabilised he should be transferred to Becotide Rotacaps by the method recommended in this Data Sheet.

Pharmaceutical precautions To keep the Rotacaps in good condition it is important that they are stored in a dry place where they will not be exposed to extremes

of temperature. A convenient supply may be carried in the special container for the Rotahaler. The Rotacaps should only be inserted in the Rotahaler immediately prior to use. Failure to observe this instruction may affect the operation of the Rotahaler.

Legal category POM.

Package quantities Becotide Rotacaps 100 mcg and 200 mcg are supplied in containers of 100.

Further information Nil.

Product licence numbers

Becotide Rotacaps 100 micrograms 0045/0119

Becotide Rotacaps 200 micrograms 0045/0120

EUDEMINE* TABLETS 50 mg

EUDEMINE* INJECTION

Presentation Eudemine Tablets 50 mg are white, sugar-coated tablets each containing Diazoxide BP 50 mg. Identification code AH/8D.

Eudemine Injection. Ampoules of 20 ml containing Diazoxide BP 300 mg in an aqueous, colourless solution with sodium hydroxide at pH 11.6.

Uses Diazoxide is a benzothiadiazine analogue which has two main therapeutic actions. Clinically it is used in the treatment of intractable hypoglycaemia, and for the treatment of severe hypertension associated with renal disease and for patients resistant to conventional hypotensive agents. Diazoxide also causes salt and water retention.

Hypoglycaemia: Eudemine administered orally is indicated for the treatment of intractable hypoglycaemia with severe symptoms from a variety of cases including: idiopathic hypoglycaemia of infancy, leucine-sensitive or unclassified; functional islet-cell tumours both malignant and benign if inoperable, extra-pancreatic neoplasms producing hypoglycaemia; glycogen storage disease; hypoglycaemia of unknown origin.

Hypertensive emergencies: Eudemine Injection is used particularly for the emergency treatment of acute hypertensive crises, especially those occurring in association with acute hypertensive encephalopathy, congestive heart failure, acute glomerular nephritis, eclampsia or pre-eclampsia.

Severe hypertension: It is also indicated for the control of severe hypertension associated with renal disease.

In hypertensive patients requiring such diagnostic procedures as renal biopsy, arteriography or cardiac catheterisation, Eudemine Injection may be given to facilitate the procedure and reduce the danger of haemorrhage due to hypertension. Eudemine injection is also indicated in patients who have failed to respond to other hypotensive agents.

Eudemine Tablets may be used to treat patients with severe hypertension associated with renal disease or where the conventional hypotensive agents have failed. It is also possible that Eudemine Tablets may be used as maintenance therapy in patients who have had their hypertension controlled initially with Eudemine Injection.

Dosage and administration *Hypoglycaemia:* In hypoglycaemia the dosage schedule of Eudemine Tablets is determined according to the clinical needs and the response of the individual patient. For both adults and children a starting oral dose of 5 mg/kg body weight divided into 2 or 3 equal doses per 24 hours will establish the patient's response and thereafter the dose can be

increased until the symptoms and blood glucose level respond satisfactorily. Regular determinations of the blood glucose in the initial days of treatment are essential. In children with leucine-sensitive hypoglycaemia, a dosage range of 15–20 mg/kg/day is suggested.

In adults with benign or malignant islet-cell tumours producing large quantities of insulin, high dosages of up to 1,000 mg per day have been used.

Hypertensive emergencies and severe hypertension: In the treatment of hypertension, Eudemine Injection is administered by the intravenous route only and it should never be given intramuscularly or subcutaneously.

Adults: A full dose of 300 mg in 20 ml will be required by most patients. However, an adequate fall in blood pressure in some patients may be obtained with as little as 150 mg. Patients must be recumbent during the injection which must be rapid and not exceed 30 seconds.

Children: On the rare occasions that Eudemine Injection is indicated for hypertension in children the dosage should be based on a level of 5 mg per kg body weight by injection.

A response occurs within five minutes and usually persists for at least four hours. One injection is usually effective, but further injections may be required, particularly in hypertensive crises or in accelerating disease refractory to other hypotensive agents. Up to four ampoules of 300 mg may be given in 24 hours. An initial dose of 600 mg is recommended only in life-threatening situations. Once the blood pressure is controlled by Eudemine Injection, treatment with anti-hypertensive agents designed for maintenance therapy can be initiated. It appears that if hypertensive patients treated with Eudemine Injection are allowed an unrestricted sodium intake then the subsequent response to oral hypotensive agents will be improved.

When Eudemine Tablets are used in the treatment of hypertension the dosage ranges from 400 mg to 1,000 mg daily, given in 2 or 3 divided doses. Apart from obtaining control over hypertension, dosage adjustment may also be occasioned by the development of side-effects.

Contra-indications, warnings, etc

Contra-indications: In the treatment of hypoglycaemia, Eudemine is contra-indicated in all cases which are amenable to surgery or other specific therapy.

There are no absolute contra-indications to Eudemine for the relief of hypertension but it should be used with discretion. Agents which can be given by infusion, such as hydralazine or labetalol, should have been shown to be ineffective before a bolus injection of diazoxide is given.

Precautions: Each of the two main therapeutic actions of Eudemine tend to be unwanted effects when the product is used for the alternative main indication. Thus in the treatment of hypoglycaemia it is necessary that the blood pressure be monitored regularly, whilst in the treatment of hypertension long-term therapy with Eudemine necessitates regular monitoring of the blood glucose levels.

In either indication, retention of sodium and water is likely to necessitate therapy with an oral diuretic such as frusemide or ethacrynic acid. The dosage of either of the diuretics mentioned may be up to 1 g daily. It must be appreciated that if diuretics are employed then both the hypotensive and the hyperglycaemic activities of diazoxide will be potentiated and it is likely that the dosage

of diazoxide will require adjustment downwards. In patients with severe renal failure it is desirable to maintain, with diuretic therapy, urinary volumes in excess of 1 litre daily. Hypokalaemia should be avoided by adequate potassium replacement.

In the long-term treatment of hypertension with oral diazoxide it is advisable to employ four-hourly diabetic urine testing in the initial stages. Explosive forms of hyperglycaemia will occur early, if at all, so that with maintenance therapy diabetic urine testing will only be required twice daily. Control of hyperglycaemia is usually effected with tolbutamide, of which the dosage should be regulated by the results of regular monitoring of the blood sugar.

Whenever Eudemine is given over a prolonged period regular haematological examinations are indicated to exclude changes in white blood cell and platelet counts. Also in children, there should be regular assessment of growth, bone and psychological maturation.

Eudemine Tablets are only to be used in pregnant women when the indicated condition is deemed to put the mother's life at risk.

With Eudemine Injection the high alkalinity of the solution necessitates that great care is taken to ensure that the injection is given directly into a vein without leakage into surrounding tissues.

The very rapid, almost complete protein binding of diazoxide requires cautious dosage to be used in patients whose plasma proteins may be lower than normal.

Side-effects: In the treatment of hypertension the hyperglycaemia induced by diazoxide is generally inevitable. Each injection of diazoxide usually means a transient rise in blood sugar of about 10%. Fortunately the hyperglycaemia in hypertensive patients can be readily controlled with tolbutamide, or exceptionally with insulin. A hypotensive effect in normotensive patients is of minor importance and rarely requires any specific therapy. An oral diuretic may be indicated to control sodium and water retention.

With Eudemine Injection reflex tachycardia is not uncommon in the first few minutes after injection and is more frequent in digitalised patients. Orthostatic hypotension is unlikely but it may occur in those recently treated with adrenergic blocking agents. When it is used during labour for the treatment of toxæmia, the smooth muscle relaxant effect can cause delay in the second stage. This should be counteracted with oxytocic agents.

With oral therapy nausea is common in the first two or three weeks and may require relief with an anti-nauseant. Prolonged therapy has given rise to reports of hypertrichosis lanuginosa, anorexia and hyperuricaemia. In the treatment of hypertension with oral Eudemine a recent report has confirmed the extrapyramidal side-effects which have been reported with oral diazoxide in the treatment of hypoglycaemia. In oral hypotensive therapy, it was found that extra-pyramidal effects, such as Parkinsonian tremor, cogwheel rigidity and oculogyric crises, could be easily suppressed by intravenous injection of an anti-Parkinsonian drug such as procyclidine and that they could be prevented by maintenance therapy with such a drug given orally.

Prolonged oral therapy of Eudemine during pregnancy has been reported to cause alopecia in the newborn.

Other adverse effects of Eudemine which have been reported are hyperosmolar non-ketotic coma, cardiomegaly, leucopenia and thrombocytopenia.

Drugs potentiated by diazoxide therapy include: oral diuretics, antihypertensive agents and anticoagulants.

Overdosage: Excessive dosage of Eudemine can result in hyperglycaemia which will respond to insulin; or to hypotension which will necessitate maintenance of blood volume with intravenous fluids.

Pharmaceutical precautions No special storage conditions are needed for Eudemine Tablets.

It is particularly important that Eudemine Injection is protected from light.

Eudemine Injection should never be mixed with other drugs and it should not be diluted.

Legal category POM.

Package quantities Eudemine Tablets 50 mg are packed in containers of 100.

Eudemine Injection is in ampoules individually boxed in packs of five.

Further information Nil.

Product licence numbers

Eudemine Tablets 50 mg 0045/5081

Eudemine Injection 0045/0084

FENTAZIN* TABLETS FENTAZIN* INJECTION FENTAZIN* CONCENTRATE

Presentation Fentazin Tablets 2 mg each contain Perphenazine BP 2 mg. Identification code is AH/1C.

Fentazin Tablets 4 mg each contain Perphenazine BP 4 mg. Identification code is AH/2C.

Fentazin Tablets 8 mg each contain Perphenazine BP 8 mg. Identification code is AH/4C.

All are white, sugar-coated tablets.

Fentazin Injection contains 5 mg Perphenazine BP in each ampoule of 1 ml. It is colourless.

Fentazin Concentrate contains 8 mg Perphenazine BP in 4 ml. Available to hospitals only.

Uses Fentazin is a potent tranquilliser and anti-emetic of the phenothiazine group. It is indicated in the following: severe anxiety and tension states, particularly where agitation is present; anxiety associated with psychosomatic disorders; severe anxiety associated with obsessive and compulsive disorders; psychotic states characterised by CNS hyperactivity, including schizophrenia of various types and senile psychoses; control of behaviour disorders; nausea and vomiting; adjunctive therapy to analgesics in the management of severe pain, e.g. terminal carcinoma.

Fentazin Injection is indicated in cases where rapid control of symptoms is essential or when oral administration is impracticable.

Fentazin Injection can also be used as pre-medication and for the control of post-operative vomiting.

It may be of value in the control of intractable hiccough.

Dosage and administration Fentazin Tablets are administered orally in a usual dosage of 4 mg perphenazine three times daily. This may be adjusted upwards or downwards according to response, but the total daily dosage should not exceed 24 mg.

Fentazin Injection is administered intramuscularly. The usual initial dose is 5–10 mg, which may be followed by further 5 mg doses at six-hourly intervals.

Children: Fentazin should not be given to children under the age of 14 years.

Contra-indications, warnings, etc

Contra-indications: Fentazin should not be administered to patients with leucopenia or in association with drugs liable to cause bone-marrow depression.

Precautions: Fentazin should be used with caution in patients with congestive heart failure or coronary artery disease. Unnecessary administration of drugs during the first trimester of pregnancy is undesirable.

Side-effects: Extrapyramidal symptoms such as dystonia, torsion spasm and pseudo-Parkinsonism may occur. These reactions can be controlled by withdrawal of the drug or reduction of the dosage. Concurrent administration of an anti-Parkinson agent may be used to advantage. Persistent oral dyskinesia has been reported occasionally, particularly in elderly female patients, after long-term treatment with potent phenothiazine drugs including perphenazine.

Overdosage: With oral preparations of Fentazin gastric lavage is recommended. Emetics are likely to be of little value because of the potent anti-emetic activity of the drug. Hypotension is not usually a problem, especially if the patient is passing urine satisfactorily. Severe hypotension may require fluid infusion therapy. Central nervous system depression is best treated conservatively, anaesthetics should not be used. Rewarming measures should not be employed unless the body temperature falls below 30°C. Convulsions may be controlled with standard methods, but the use of barbiturates should be avoided.

Pharmaceutical precautions *Storage:* Fentazin liquid preparations, including Fentazin Injection, should be protected from light.

Dilution: Fentazin Injection should not be mixed with other agents as this may affect the stability of the solution.

Fentazin Concentrate is supplied to hospitals only and must be diluted to the required concentration with unpreserved Syrup BP.

Legal category POM.

Package quantities Fentazin Tablets 2 mg, 4 mg and 8 mg are issued in cartons each containing 100 tablets in 10 foil strips of 10 (5 × 2) tablets.

Fentazin Concentrate is available in bottles of 1 litre to hospitals only, for dilution.

Fentazin injection is available in boxes of 5 and 100 ampoules of 1 ml each containing 5 mg.

Further information Nil.**Product licence numbers**

Fentazin Tablets 2 mg	0045/5082
Fentazin Tablets 4 mg	0045/5083
Fentazin Tablets 8 mg	0045/5084
Fentazin Injection	0045/5055
Fentazin Concentrate	0045/5060

GUANIMYCIN* SUSPENSION FORTE

Presentation Each bottle of Guanimycin Suspension Forte contains:

Dihydrostreptomycin Sulphate BP 1958	2.5 g
(equivalent to 1.975 g of base)	
Sulphaguanidine BPC	19.85 g
Light Kaolin BP	42.5 g

Guanimycin Suspension Forte is issued in the form of a pleasantly flavoured, orange-coloured suspension ready for immediate use. Each 15 ml dose contains:

Dihydrostreptomycin Sulphate BP 1958	0.25 g
(equivalent to 0.1975 g of base)	
Sulphaguanidine BPC	1.985 g
Light Kaolin BP	4.25 g

Uses The treatment of acute gastro-enteritis and acute diarrhoeal illnesses of bacterial origin including salmonella infections and Sonne dysentery.

Dosage and administration Administration is oral and should start as early as possible. Concomitant with Guanimycin Suspension Forte therapy, the patient, especially the dehydrated patient, must maintain an adequate fluid intake.

Adults: One 15 ml dose four times daily at approximately four-hour intervals, before rather than after food.

Children and infants: The dosage should be based on the patient's age, weight and the severity of the disease. For the average child dosage may be prescribed according to age – the following scale being adequate for all but the more severe infections:

1–4 years: 5 ml every four hours.

5–9 years: 5–10 ml four-hourly.

10–15 years: 10 ml every four hours.

Contra-indications, warnings, etc

Contra-indications: Patients known to be hypersensitive to sulphonamides or derivatives of streptomycin.

Precautions: In infants and children the necessity for maintaining the fluid volume is of paramount importance.

Unnecessary administration of drugs during the first trimester of pregnancy is undesirable.

Side-effects: A single case of hypersensitivity to Guanimycin Suspension Forte has been reported. Apart from this no other side effects are known to have occurred.

Overdosage: Dihydrostreptomycin is very poorly absorbed after oral administration and light kaolin is not absorbed. Sulphaguanidine may be absorbed to a slight extent so that systemic effects, including crystalluria, are possible.

Treatment would consist of the immediate withdrawal of the mixture; the administration of alkalis such as sodium bicarbonate and the maintenance of fluid intake, if necessary by the parenteral route.

Pharmaceutical precautions *Storage:* Store in a cool place.

Dilution: No attempt to dilute Guanimycin Suspension Forte should be made.

Legal category POM.

Package quantities Guanimycin Suspension Forte is supplied in bottles of 150 ml.

Further information The combination of sulphaguanidine and dihydrostreptomycin reduces the likelihood of the emergence of strains of bacteria resistant to dihydrostreptomycin.

Product licence number 0045/5059.

ISOGEL*

Presentation Isogel is a preparation of Ispaghula Husk BP, which consists of the epidermis and collapsed

adjacent layers removed from the dried ripe seeds of *Plantago ovata* Forssk.

Isogel is supplied as small, reddish-pink granules in containers of 200 g.

Uses Isogel is not absorbed from the gastrointestinal tract, but it adsorbs water to form a mucilaginous mass. This results in a purely mechanical stimulus to mass peristalsis without any purgative effect. It is for this reason that Isogel is not only an effective remedy for constipation but is also of value in the treatment of diarrhoea, the irritable bowel syndrome and the management of patients with a colostomy. Isogel is indicated in habitual constipation, including cases due to spastic colon, dietary insufficiencies and in patients with haemorrhoids or diabetes. It can be used to normalise the bowel movement in patients with mucous or ulcerative colitis.

Isogel is a help to patients with colostomy as the formation of a well-formed, easily passed stool assists in the maintenance of cleanliness and the establishment of control.

Dosage and administration The required quantity of Isogel should be stirred briskly into half a glass of water and swallowed at once. An aerated water is frequently preferred and may be easier to swallow.

Adults: 2 teaspoonfuls once or twice daily, preferably at mealtimes.

Children: 1 teaspoonful once or twice daily, preferably at mealtimes.

The above dosage is only a general guide and it should be adjusted to suit the needs of each individual patient.

In diarrhoea the dose, usually 1 teaspoonful, is taken three times daily until symptoms abate.

Contra-indications, warnings, etc

Contra-indications: Nil.

Precautions: A few cases of inhalation of the mucilaginous mass which forms on allowing an Isogel/water mixture to stand have been reported. In consequence, it is important that Isogel should be swallowed immediately after mixing, and elderly or debilitated patients should be supervised whilst taking it.

Unnecessary administration of drugs during the first trimester of pregnancy is undesirable.

Side-effects: Nil.

Overdosage: As Isogel is not absorbed and it has no purgative action the problem of overdosage does not arise.

Pharmaceutical precautions *Storage:* Store in a cool dry place.

Legal category GSL.

Package quantities Isogel is supplied in containers of 200 g.

Further information Nil.

Product licence number 0045/5028.

PIRITON* TABLETS PIRITON* SPANDETS* PIRITON* DUOLETS* PIRITON* SYRUP PIRITON* INJECTION

Presentation Piriton is a potent antihistamine (Chlor-

pheniramine Maleate BP) presented as tablets, sustained-action tablets, syrup and injection.

Piriton Tablets: Round, biconvex, yellow tablets each containing Chlorpheniramine Maleate BP 4 mg. Identification engraved Piriton AH.

Piriton Spandets*: Yellow and white, round, layered tablets each containing Chlorpheniramine Maleate BP 12 mg. After swallowing 4 mg Chlorpheniramine Maleate BP is released immediately from the yellow layer and then a further 8 mg chlorpheniramine maleate is gradually released from the special porous matrix comprising the white layer. Identification engraved Piriton AH Spandet.

Piriton Duolets*: Round, yellow, sugar-coated tablets each containing Chlorpheniramine Maleate BP 8 mg. The outer layer contains 4 mg for immediate release and the inner core contains 4 mg for delayed release. Printed in black on each tablet PIRITON AH DUOLET.

Piriton Syrup: Each 10 ml of Piriton Syrup contains Chlorpheniramine Maleate BP 4 mg. It is colourless.

Piriton Injection: Each 1 ml of Piriton Injection contains Chlorpheniramine Maleate BP 10 mg. It is colourless.

Uses The oral preparations of Piriton are indicated for symptomatic control of all allergic conditions responsive to antihistamines, including hay fever, vasomotor rhinitis, urticaria, angioneurotic oedema, food allergy, drug and serum reactions, pruritus ani et vulvae, insect bites.

Piriton Injection is indicated for acute urticaria, insect bites and stings, angioneurotic oedema, drug and serum reactions, desensitisation reactions, hay fever, vasomotor rhinitis, severe pruritus of non-specific origin.

Dosage and administration *Piriton Tablets:*

Adults: 1 tablet three or four times a day.

Children (aged 6–12 years): $\frac{1}{2}$ –1 tablet three or four times a day.

Piriton Spandets: **Adults:** 1 Spandet every 8–12 hours.

Children (over 12 years of age): 1 Spandet daily.

Piriton Spandets must be swallowed whole and not chewed.

Piriton Duolets: **Adults:** 1 Duolet should be taken every 8–10 hours.

Children (over 12 years of age): 1 Duolet daily.

Piriton Syrup: **Adults:** Two 5 ml spoonfuls three or four times a day.

Children (up to 1 year): $\frac{1}{2}$ spoonful (2.5 ml) twice daily.

Children (1–5 years): $\frac{1}{2}$ –1 spoonful (2.5–5 ml) three times daily.

When Piriton Syrup is dispensed to meet prescriptions involving doses of 2.5 ml it should be diluted with an equal quantity of unpreserved Syrup BP. The resultant mixture should be used within 14 days.

Piriton Injection: The injection may be subcutaneous, intramuscular or intravenous. The latter is recommended when a rapid effect is desired as in anaphylactic reactions. For the intravenous route Piriton should be diluted in the syringe with 5–10 ml of blood and then injected slowly over a period of one minute. Any drowsiness, giddiness or hypotension which may follow is usually transitory.

The usual dose of Piriton Injection for adults is 10–20 mg, but not more than 40 mg should be given per 24 hours.

In the event of a blood transfusion reaction a dose of 10–20 mg of Piriton should be given by the subcutaneous

route. This can be repeated to a total of 40 mg per 24 hours or oral forms of Piriton may be given until the symptoms subside. Though Piriton may be helpful in the prevention of delayed reactions to penicillin and other drugs it cannot be relied on to prevent anaphylactic reactions in patients known to be allergic to a particular drug. Piriton Injection 10 mg should be mixed, where practicable, with the drug to be injected, or injected separately by the intramuscular route immediately prior to injection of the other drug.

In the event of an anaphylactic reaction Piriton Injection 10–20 mg may be given by slow intravenous injection in addition to the emergency therapy of adrenaline, corticoids, oxygen and supportive therapy.

Contra-indications, warnings, etc

Contra-indications: There are no known definite contra-indications to therapy with Piriton.

Precautions: All antihistamines, given in effective dosage, may cause dizziness or drowsiness. In consequence, until the effect of the treatment is known, patients treated with Piriton should be warned not to take charge of vehicles or machinery. The sedative action of alcohol may be potentiated by antihistamines so that drowsiness can occur in patients not otherwise subject to it if alcohol is taken.

Unnecessary administration of drugs during the first trimester of pregnancy is undesirable.

Side-effects: Drowsiness and dizziness may occur. Some patients have reported a stinging or burning sensation at the site of injection. Rapid intravenous injection may cause transitory hypotension or CNS stimulation.

Overdosage: The estimated lethal dose of Piriton is 25–50 mg per kg body weight. Treatment should include gastric lavage if massive overdosage has been by the oral route. In the event of convulsions sedate with intramuscular paraldehyde. Severe respiratory depression may necessitate mechanical ventilation. Severe hypotension may require fluid replacement.

Pharmaceutical precautions *Storage:* There are no special storage conditions needed for Piriton Tablets. Piriton Spandets and Piriton Duolets require a cool dry place and Piriton Syrup a cool dark place. Piriton Injection should be protected from light.

Dilution: If it is necessary to dilute Piriton Syrup then the suitable diluent is unpreserved Syrup BP. The resulting mixture will keep for 14 days at room temperature.

Legal category Tablets P.
Spandets P.
Duolets P.
Syrup P.
Injection POM.

Package quantities Piriton Tablets are supplied in containers of 50 and 500.

Piriton Spandets are supplied in containers of 100.

Piriton Duolets are supplied in containers of 250.

Piriton Syrup is supplied in bottles of 150 ml.

Piriton Injection is supplied in boxes of 5 and 100 ampoules.

Further information No Piriton preparation contains tartrazine.

Product licence numbers

Piriton Tablets 0045/5077
Piriton Spandets 0045/5078
Piriton Duolets 0045/5086

Piriton Syrup 0045/5019
Piriton Injection 0045/5056

PROPADERM* CREAM PROPADERM* OINTMENT PROPADERM*-FORTE CREAM

Presentation Propaderm Cream, Ointment and Propaderm-Forte Cream are topical preparations of Beclomethasone Dipropionate BP. Beclomethasone Dipropionate BP is a potent anti-inflammatory steroid when applied topically to the skin.

Propaderm Cream: Beclomethasone Dipropionate BP 0.025% in a cream base.

Propaderm Ointment: Beclomethasone Dipropionate BP 0.025% in an ointment base.

Propaderm-Forte Cream: Beclomethasone Dipropionate BP 0.5% in a cream base.

Propaderm Cream and Propaderm-Forte Cream are all white in colour; Propaderm Ointment is yellowish.

Uses Propaderm Cream and Ointment are indicated for the local treatment of the various forms of eczema and dermatitis; the various forms of psoriasis; neurodermatoses including lichen simplex; intertrigo; discoid lupus erythematosus.

Propaderm Cream is preferred for weeping conditions or where the skin is usually moist or hairy.

Propaderm Ointment is suitable for dry, lichenified or scaly conditions or for use under occlusive dressings.

Propaderm-Forte Cream is used for resistant dermatoses, including pustular psoriasis of palms and soles, discoid lupus erythematosus, pemphigus erythematosus, mycosis fungoides, and some unusual conditions such as pretibial myxoedema, necrobiosis lipoidica, granuloma annulare.

Dosage and administration Propaderm preparations should be applied thinly over the whole of the affected area and gently rubbed in. Initial application is made twice daily, but when improvement is seen the intervals between applications may be extended and treatment eventually stopped. If the condition recurs, treatment should be re-instituted. Subsequent re-appearance of the condition is likely to be avoided by application of Propaderm every third or fourth day. Propaderm-Forte Cream may have to be applied three times daily in the initial stages until improvement is observed. The beneficial effect may be enhanced by preliminary use of hot soaks, or by intermittent applications of occlusive dressings.

Contra-indications, warnings, etc

Contra-indications: Propaderm should not be applied to the eyes. Infections of the skin should receive specific therapy, and the steroid withdrawn if the response is delayed. Propaderm is contra-indicated in the presence of tuberculosis of the skin, chickenpox, vaccinia, herpes virus infections and, also, for the treatment of varicose ulcers or any other stasis ulcers.

Precautions: When Propaderm, and in particular Propaderm-Forte Cream, is used under occlusive dressings over extensive areas there is the possibility of systemic absorption which could lead to side-effects and adrenal suppression. For this reason it is inadvisable to use more than 2 g of Propaderm-Forte Cream under occlusive dressings per application.

In infants there is the possibility of adrenal suppression with long-term application of Propaderm even without occlusion.

Topical administration of steroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Side-effects: A single case of skin atrophy has been reported in a patient who had continuous therapy with Propaderm Ointment for 700 days. In the event of adverse effects occurring the preparation should be withdrawn.

Overdosage: Should systemic corticosteroid effects arise from excessive application of Propaderm preparations topical treatment should be discontinued. If adrenal function is impaired the patient will need to be protected from any harmful effects of stress with oral corticosteroid preparations until normal adrenal function is established.

Pharmaceutical precautions *Storage:* All Propaderm preparations should be stored at a temperature below 25°C and protected from light.

Dilution: Propaderm Cream may be diluted, if necessary, with Cetomacrogol Cream Formula A BPC. For Propaderm Ointment dilution can be effected with white soft paraffin.

Legal category POM.

Package quantities Propaderm Cream is available in tubes of 15 g and 50 g; Propaderm Ointment in tubes of 15 g and 50 g; and Propaderm-Forte Cream in tubes of 5 g.

Further information No Propaderm preparation contains lanolin or parabens.

Product licence numbers

Propaderm Cream	0045/5000
Propaderm Ointment	0045/5005
Propaderm-Forte Cream	0045/5001

PROPADERM*-A OINTMENT

Presentation Propaderm-A Ointment contains Beclomethasone Dipropionate BP 0.025% and Chlortetracycline Hydrochloride BP 3.0%. It is pale yellow in colour.

Beclomethasone Dipropionate BP is a potent anti-inflammatory steroid when applied topically to the skin. Chlortetracycline BP is a broad-spectrum antibiotic unlikely to cause skin sensitisation reactions.

Uses Propaderm-A Ointment is indicated for skin conditions which respond to therapy with an anti-inflammatory steroid where infection is present or is likely to occur, e.g. infective eczema of various types, seborrhoeic dermatitis and infective intertrigo. The combination of an anti-inflammatory steroid with an antibacterial is frequently preferred when occlusive dressings are used in conjunction with topical steroid therapy.

Occlusive dressings of an impermeable material such as polythene film can enhance the effect of Propaderm-A Ointment in certain resistant conditions such as fissured and lichenified eczema and neurodermatoses, hypertrophic lichen planus, chronic discoid lupus erythematosus, and psoriasis on the elbows and knees.

Dosage and administration Propaderm-A Ointment should be applied thinly over the whole of the affected area and gently rubbed in. Initially application should be twice daily, but when improvement is seen the intervals between applications may be extended and treatment eventually stopped. If the condition recurs, treatment should be re-instituted. Subsequent re-appearance of the condition can usually be avoided by application of Propaderm-A Ointment every third or fourth day.

Contra-indications, warnings, etc

Contra-indications: Propaderm-A Ointment should not be applied to the eyes. Infections of the skin failing to respond necessitate withdrawal of Propaderm-A and use of specific therapy. Propaderm is contra-indicated in the presence of tuberculosis of the skin, chickenpox, vaccinia, herpes virus infections, fungal infections and, also, for the treatment of varicose ulcers or any other stasis ulcers.

Precautions: When Propaderm-A Ointment is used under occlusive dressings over extensive areas there is the possibility that this could lead to side-effects and adrenal suppression. In infants long-term continuous topical steroid therapy could cause adrenal suppression even without occlusion. Topical administration of steroids to pregnant animals can cause foetal abnormalities. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Side-effects: Chlortetracycline very occasionally causes sensitisation. A single case of skin atrophy has been reported in a patient who had continuous therapy with Propaderm Ointment for 700 days. If adverse effects occur the preparation should be withdrawn.

Overdosage: Should systemic corticosteroid effects arise from excessive application of Propaderm preparations topical treatment should be discontinued. If adrenal function is impaired the patient will need to be protected from any harmful effects of stress with oral corticosteroid preparations until normal adrenal function is established.

Pharmaceutical precautions *Storage:* Store at a temperature not exceeding 25°C and protect from light.

Dilution: Propaderm-A Ointment may be diluted, if necessary, with white soft paraffin.

Legal category POM.

Package quantities Propaderm-A Ointment is available in tubes of 15 g and 50 g.

Further information No lanolin or parabens included in the formula of Propaderm-A Ointment.

Product licence number 0045/5006.

PROPADERM*-C CREAM PROPADERM*-C OINTMENT

Presentation Propaderm-C Cream and Ointment are topical preparations of Beclomethasone Dipropionate BP and Clotrimazole BP.

Propaderm-C Cream contains Beclomethasone Dipropionate BP 0.025% and Clotrimazole BP 3.0%. Propaderm-C Ointment contains Beclomethasone Dipropionate BP 0.025% and Clotrimazole BP 3.0%. Both Propaderm-C Cream and Ointment are pale yellow in colour.

Beclomethasone Dipropionate BP is a potent anti-inflammatory steroid when applied topically to the skin. Clioquinol BP has a wide range of antibacterial and antifungal activity.

Uses Propaderm -C Cream and Ointment are indicated for skin conditions which respond to topical steroid therapy where infection is present or is likely to occur, particularly where the infection is fungal.

Propaderm-C Cream is preferred for weeping conditions or where the skin is usually moist or hairy. Propaderm-C Ointment is suitable for dry, lichenified or scaly conditions or for use under occlusive dressings.

Dosage and administration Propaderm-C should be applied thinly over the whole of the affected area and gently rubbed in. Initial application is made twice daily, but when improvement is seen the intervals between the applications may be extended and treatment eventually stopped.

If the condition recurs, treatment should be reinstated. Subsequent re-appearance of the condition can usually be avoided by application of Propaderm-C every third or fourth day.

Contra-indications, warnings, etc

Contra-indications: Propaderm-C should not be applied to the eyes. Infections of the skin failing to respond necessitate withdrawal of Propaderm-C and use of specific therapy. Propaderm is contra-indicated in the presence of tuberculosis of the skin, chickenpox, vaccinia, herpes virus infections and, also, for the treatment of varicose ulcers or any other stasis ulcers.

Precautions: When Propaderm-C is used under occlusive dressings over extensive areas there is the possibility of systemic absorption which could lead to side-effects and adrenal suppression.

In infants there is the possibility of adrenal suppression with long-term application of Propaderm-C even without occlusion.

Topical administration of steroids to pregnant animals can cause foetal abnormalities. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Side-effects: Sensitisation reactions to clioquinol have been reported. Where there is unexplained relapse with continued treatment this possibility may be responsible.

A single case of skin atrophy has been reported in a patient who had continuous therapy with Propaderm Ointment for 700 days. If adverse effects occur the preparation should be withdrawn.

Overdosage: Should systemic corticosteroid effects arise from excessive application of Propaderm preparations topical treatment should be discontinued. If adrenal function is impaired the patient will need to be protected from any harmful effects of stress with oral corticosteroid preparations until normal adrenal function is established.

Pharmaceutical precautions *Storage:* Store at a temperature below 25°C and protect from light.

Dilution: Propaderm-C Cream may be diluted, if necessary, with Cetomacrogol Cream Formula A BPC and Propaderm-C Ointment with white soft paraffin.

Legal category POM.

Package quantities Propaderm-C Cream and Ointment are available in tubes of 15 g.

Further information Propaderm-C Cream and Ointment do not contain lanolin or parabens.

Product licence numbers

Propaderm-C Cream 0045/5002

Propaderm-C Ointment 0045/5007

STERISPON*

Presentation Sterispon is Absorbable Gelatin Sponge BP and an effective haemostatic. It is not friable and may be cut into any desired shape or size or moulded with the fingers. Sterispon is prepared sterile and specially packed ready for use in the operating theatre. It is white in colour.

Uses For control of capillary oozing and venous bleeding in most forms of surgery (for exceptions, see **Contra-indications**). Sterispon may be used as a material for the obliteration of surgical 'dead spaces'.

Dosage and administration The sponge should be removed from the packings with sterile forceps and, if necessary, cut into pieces of the desired size and shape. It may be used in the dry state or moistened with normal saline. If the latter state is required, place the sponge in normal saline and remove the air by gentle squeezing before use. Sterispon is applied to the site of bleeding with sufficient pressure to enable adherence of the sponge and control of bleeding. Since Sterispon is completely absorbed by normal phagocytosis it is usually left *in situ* and the wound closed.

Contra-indications, warnings, etc

Contra-indications: Sterispon is contra-indicated for use in stapedectomy or other aural surgery where it could come into contact with fluid from the internal ear. In ophthalmic surgery it is inadvisable to use Sterispon in operations where the aqueous or vitreous humours are exposed.

Precautions: It is not advisable to apply Sterispon in the usual manner in the presence of infection, but it may be used to control haemorrhage if treated as a removable pack.

Side-effects: None.

Overdosage: Not applicable.

Pharmaceutical precautions Sterispon cannot be re-sterilised once the container has been opened without alteration to the properties of the sponge.

Storage: Store at a temperature not exceeding 25°C.

Legal category P.

Package quantities Sterispon is supplied sterile in the following sizes:

- | | |
|------------|--|
| Size No. 1 | Strips, 6 × 2 × 0.7 cm, in glass tubes each containing one piece. |
| Size No. 2 | Strips, 20 × 10 × 0.1 cm, in glass tubes each containing one piece. |
| Size No. 3 | Thin wafers, 2 × 2 × 0.1 cm, in glass tubes each containing six pieces. |
| Size No. 4 | Strips, 10 × 10 × 0.5 cm, in envelopes containing one piece. |
| Size No. 5 | For dental use. Pieces, 2 × 2 × 1 cm, in glass tubes each containing six pieces. |

Further information Nil.

Product licence number 0045/5063.

TRANDATE* TABLETS 100 mg
TRANDATE* TABLETS 200 mg
TRANDATE* TABLETS 400 mg

Presentation 1. *Trandate Tablets 100 mg*: Circular, orange coloured, film-coated biconvex tablets, each containing labetalol hydrochloride 100 mg, marked TRANDATE 100AH on one face.

2. *Trandate Tablets 200 mg*: Circular, orange coloured, film-coated biconvex tablets, each containing labetalol hydrochloride 200 mg, marked TRANDATE 200AH on one face.

3. *Trandate Tablets 400 mg*: Circular, orange coloured, film-coated biconvex tablets, each containing labetalol hydrochloride 400 mg, marked TRANDATE 400AH on one face.

Labetalol hydrochloride is 2-hydroxy-5-[1-hydroxy-2-(1-methyl-3-phenylpropylamino) ethyl] benzamide hydrochloride.

Uses *Indications*: Trandate Tablets are indicated for the treatment of all forms of hypertension, including the hypertensions of pregnancy, and all grades of hypertension (mild, moderate and severe) when oral antihypertensive therapy is desirable.

Mode of action: Trandate lowers the blood pressure primarily by blocking alpha-adrenoceptors in peripheral arterioles and thereby reducing the peripheral resistance. Concurrent beta-blockade protects the heart from the reflex sympathetic drive normally induced by peripheral vasodilatation. Cardiac output is not significantly reduced at rest or after moderate exercise. Increases in systolic pressure during exercise are, however, reduced after Trandate; corresponding changes in the diastolic pressure are essentially normal. All these effects would be expected to benefit hypertensive patients.

Dosage and administration *Adults*: Treatment may start with one 200 mg tablet twice daily but in some patients, including those already being treated with antihypertensive drugs, the elderly and those of low bodyweight, one 100 mg tablet twice daily is more appropriate. If the blood pressure is not controlled by the initial dosage, increases should be made at intervals of about 14 days. By prescribing tablets of increasing strength, the dose can be maintained at one tablet twice daily until a total daily dose of 800 mg is reached. Daily doses of up to 2,400 mg have been given in the treatment of severe and refractory hypertension. In such patients it is preferable to administer Trandate three or four times daily.

Satisfactory control of blood pressure will be obtained in many patients at a total daily dosage of 400 mg (one 200 mg tablet twice daily).

In severe hypertension, particularly that of pregnancy, the dosage may be increased on a daily basis until adequate control of blood pressure is obtained.

Tablets should be taken with food.

For hospital in-patients daily increases in dosage may be made if the need to reduce blood pressure is urgent. If it is necessary to reduce the blood pressure rapidly in very severe hypertension, Trandate Injection is indicated (see Data Sheet for Trandate Injection).

Children: Not applicable.

Use with other agents: Hypertension is usually controlled by Trandate alone. Diuretic therapy is not usually necessary in patients receiving Trandate Tablets, but may be introduced or continued if required. Diuretics

usually increase the antihypertensive action of Trandate.

If Trandate Tablets are prescribed together with another antihypertensive drug, such as methyldopa or clonidine, an additive effect may be expected in patients who are responsive to both drugs. When transferring patients from other drugs, Trandate Tablets should be introduced as recommended above and the dosage of the existing therapy progressively decreased.

Abrupt withdrawal of clonidine or beta-adrenoceptor blockers is undesirable.

Contra-indications, warnings, etc

Contra-indications: There are no known absolute contra-indications to the use of Trandate Tablets.

Warning: There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenoceptor blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when the treatment was withdrawn. Discontinuance of the drug should be considered if any such reaction is not otherwise explicable.

Precautions: Heart failure should be controlled with digitalis and diuretic therapy before treatment is initiated. Trandate should not normally be given to patients with digitalis-resistant heart failure or atrio-ventricular block.

Patients with severe liver damage may have higher than normal plasma concentrations of labetalol due to reduced metabolism. Consequently, patients with liver disease may require lower than the usual doses of Trandate to control their blood pressure.

Caution must be observed if Trandate is used to treat asthmatic patients or individuals prone to bronchospasm. Any resultant bronchospasm may be controlled by an inhaled selectively-acting bronchodilator such as salbutamol; the required dose may be greater than the normal anti-asthmatic dose. If further treatment is required, intravenous atropine 1 mg should be given.

It is not necessary to discontinue Trandate Tablets in patients requiring anaesthesia but they should be given intravenous atropine prior to induction; the effect of halothane on blood pressure may be enhanced by Trandate.

Although no teratogenic effects have been demonstrated in animals the unnecessary use of Trandate during the first trimester of pregnancy is undesirable.

Trandate crosses the placental barrier and the possibility of the consequences of alpha- and beta-adrenoceptor blockade in the foetus and neonate (e.g., bradycardia and hypoglycaemia) should be borne in mind. Experience has shown this to have been an exceptionally rare occurrence.

Trandate is excreted in breast milk. No adverse effects in breast feeding infants have been reported.

Side-effects: Where side effects to Trandate have occurred they have usually done so during the first weeks of treatment and have been transient. Symptoms tend to have been similar in nature to those often observed in untreated hypertensive patients and have included headache, tiredness, dizziness, depressed mood and lethargy.

If the initial dosage is too high, or the dose increased too rapidly, symptoms of postural hypotension may occur. These are uncommon, except at very high doses, if the drug is used as recommended.

In a few patients certain other side-effects have occurred which appear to be more directly related to Trandate treatment. These include difficulty in micturition, epigastric pain, nausea and vomiting.

Again, in a few patients a tingling sensation in the scalp associated with Trandate treatment has been reported. It usually occurs early in the treatment and tends to be transient in nature.

In a very small number of patients a lichenoid rash has appeared during Trandate treatment but has disappeared on withdrawing treatment. Other skin rashes not necessarily induced by Trandate treatment have been reported. Blurring of vision, eye irritation and cramps have also been reported but have been difficult to relate directly to Trandate treatment.

Overdosage: Overdosage with Trandate causes excessive hypotension, which is posture sensitive and sometimes, excessive bradycardia. Patients should be laid supine and their legs raised if necessary to improve the blood supply to the brain. Atropine 3 mg should be given intravenously to relieve bradycardia.

Massive overdosage with Trandate in man has not been reported but profound cardiovascular effects are to be expected. Atropine at least 3 mg intravenously should always be given. Gastric lavage or induced emesis is warranted for a few hours after oral ingestion of the drug. If further measures are required to obtain adequate circulatory function, intravenous noradrenaline may be preferable to isoprenaline, the established pharmacological treatment for excessive cardiac beta-blockade. The recommended starting dose of noradrenaline in patients is 5–10 mcg by intravenous injection repeated as required according to the response. Alternatively, noradrenaline may be infused at a rate of 5 mcg per minute until a satisfactory response is achieved.

Pharmaceutical precautions No special storage precautions are required.

Legal category POM.

Package quantities

Trandate Tablets 100 mg: Containers of 50 and 250.

Trandate Tablets 200 mg: Containers of 50 and 250.

Trandate Tablets 400 mg: Containers of 50 and 250.

Further information Trandate does not adversely affect renal function and is a particularly suitable drug for use in hypertensive patients with renal disease. The metabolites of Trandate are excreted in the faeces as well as the urine and so the drug is unlikely to accumulate in the body even in renal failure.

In non-pregnant patients the half-life of Trandate in plasma is about four hours and somewhat less in pregnancy. Only about 50% of Trandate in the blood is protein bound.

Trandate fluoresces in alkaline solution at an excitation wavelength of 334 nm and a fluorescence wavelength of 412 nm and may therefore interfere with the assays of certain fluorescent substances.

Product licence numbers

Trandate Tablets 100 mg 0045/0106

Trandate Tablets 200 mg 0045/0107

Trandate Tablets 400 mg 0045/0109

TRANDATE* INJECTION

Presentation *Trandate Injection:* 20 ml ampoules each containing 100 mg (5 mg/ml) labetalol hydrochloride in an aqueous colourless solution.

Labetalol hydrochloride is 2-hydroxy-5-[1-hydroxy-2-(1-methyl-3-phenylpropylamino) ethyl] benzamide hydrochloride.

Uses *Indications:* Trandate Injection is indicated when rapid control of blood pressure is essential in severely hypertensive patients including severe hypertension of pregnancy and for use in anaesthesia where a hypotensive technique is indicated.

Mode of action: Trandate lowers the blood pressure primarily by blocking alpha-adrenoceptors in peripheral arterioles and thereby reducing the peripheral resistance.

Concurrent beta-blockade protects the heart from reflex sympathetic drive normally induced by peripheral vasodilatation. Cardiac output is not significantly reduced at rest or after moderate exercise. Increases in systolic pressure during exercise are, however, reduced after Trandate; corresponding changes in diastolic pressure are essentially normal. All these effects would be expected to benefit hypertensive patients.

Dosage and administration *Adults:* Trandate Injection is intended for intravenous use in hospitalised patients. The plasma concentrations achieved after intravenous doses of Trandate in severe hypertension are substantially greater than those following oral administration of the drug and provide the greater degree of blockade of alpha-adrenoceptors necessary to control the more severe disease. Patients should, therefore, always receive the drug whilst in the supine or left lateral position.

Raising the patient into the upright position, within three hours of intravenous Trandate administration, should be avoided since excessive postural hypotension may occur.

If it is essential to reduce the blood pressure quickly, as, for example, in hypertensive encephalopathy, a dose of 50 mg of Trandate should be given by intravenous injection over a period of at least one minute. If necessary, doses of 50 mg may be repeated at five minute intervals until a satisfactory response occurs. The total dose should not exceed 200 mg. After bolus injection, the maximum effect usually occurs within five minutes and the effective duration of action is usually about six hours but may be as long as eighteen hours.

An alternative method for administering Trandate is intravenous infusion of a solution made by diluting the contents of two ampoules (200 mg) to 200 ml with Sodium Chloride and Dextrose Injection BP or 5% Dextrose Intravenous Infusion BP. The resultant infusion solution contains 1 mg/ml of Trandate. It should be administered using a paediatric giving set fitted with a 50 ml graduated burette to facilitate dosage.

In the hypertensions of pregnancy, the infusion can be started at the rate of 20 mg per hour and this dose may be doubled every thirty minutes until a satisfactory reduction in blood pressure has been obtained or a dosage of 160 mg per hour is reached. Occasionally, higher doses may be necessary.

In hypertension due to other causes the rate of infusion of Trandate should be about 2 mg (2 ml of infusion solution) per minute, until a satisfactory response is obtained; the infusion should then be stopped. The effective dose is usually in the range of 50–200 mg, depending on the severity of the hypertension. For most patients it is unnecessary to administer more than 200 mg but larger doses may be required especially in patients with phaeochromocytoma. The rate of infusion may be adjusted according to the response, at the discretion of the physician. The blood pressure and pulse rate should be monitored throughout the infusion.

It is desirable to monitor the heart rate after injection and during infusion. In most patients, there is a small

decrease in the heart rate; severe bradycardia is unusual but may be controlled by injecting atropine 1–2 mg intravenously. Respiratory function should be observed particularly in patients with any known impairment.

Once the blood pressure has been adequately reduced, maintenance therapy with Trandate Tablets should be instituted with a starting dose of one 200 mg tablet twice daily. (See Trandate Tablets Data Sheet for further details.) Trandate Injection has been administered to patients with uncontrolled hypertension already receiving other hypotensive agents, including beta-blocking drugs, without adverse effects.

In hypotensive anaesthesia induction should be with standard agents (e.g., sodium thiopentone) and anaesthesia maintained with nitrous oxide and oxygen with or without halothane. The recommended starting dose of Trandate Injection is 10–20 mg intravenously depending on the age and condition of the patient. Patients for whom halothane is contra-indicated usually require a higher initial dose of Trandate (25–30 mg). If satisfactory hypotension is not achieved after five minutes, increments of 5–10 mg should be given until the desired level of blood pressure is attained.

Halothane and Trandate act synergistically therefore the halothane concentration should not exceed 1–1.5% as profound falls in blood pressure may be precipitated.

Following Trandate Injection the blood pressure can be quickly and easily adjusted by altering the halothane concentration and/or adjusting table tilt. The mean duration of hypotension following 20–25 mg of Trandate is fifty minutes.

Hypotension induced by Trandate Injection is readily reversed by atropine 0.6 mg and discontinuation of halothane.

Tubocurarine and pancuronium may be used when assisted or controlled ventilation is required. IPPV may further increase the hypotension resulting from Trandate Injection and/or halothane.

Children: Not applicable.

Contra-indications, warnings, etc

Contra-indications: There are no known absolute contra-indications to the use of Trandate Injection.

Precautions: Trandate Injection should not normally be given to patients with digitalis-resistant heart failure or atrio-ventricular block.

Caution must be observed if Trandate is used to treat asthmatic patients or individuals prone to bronchospasm. Any resultant bronchospasm may be controlled by an inhaled selectively-acting bronchodilator such as salbutamol; the required dose may be greater than the normal anti-asthmatic dose. If further treatment is required, intravenous atropine 1 mg should be given.

It is not necessary to discontinue Trandate therapy in patients requiring anaesthesia but they should be given intravenous atropine prior to induction; the effect of halothane on blood pressure may be enhanced by Trandate.

During anaesthesia Trandate may mask the compensatory physiological responses to sudden haemorrhage (tachycardia and vasoconstriction). Close attention must therefore be paid to blood loss and the blood volume maintained.

Although no teratogenic effects have been demonstrated in animals the unnecessary use of Trandate during the first trimester of pregnancy is undesirable. Trandate crosses the placental barrier and the possibility of the consequences of alpha- and beta-adrenoceptor

blockade in the foetus and neonate (e.g., bradycardia and hypoglycaemia) should be borne in mind. Experience has shown this to have been an exceptionally rare occurrence. Trandate is excreted in breast milk. No adverse effects in breast feeding infants have been reported.

Side-effects: Trandate Injection is usually well tolerated. Excessive postural hypotension may occur if patients are allowed to assume the upright position within three hours of receiving Trandate Injection.

Overdosage: Overdosage with Trandate causes excessive hypotension, which is posture sensitive, and sometimes excessive bradycardia. Patients should be laid supine and their legs raised if necessary to improve the blood supply to the brain. Atropine 3 mg should be given intravenously to relieve bradycardia.

Massive overdosage with Trandate in man has not been reported, but profound cardiovascular effects are to be expected. Atropine at least 3 mg intravenously should always be given. If further measures are required to obtain adequate circulatory function, intravenous noradrenaline may be preferable to isoprenaline, the established pharmacological treatment for excessive cardiac beta-blockade. The recommended starting dose of noradrenaline in patients is 5–10 mcg by intravenous injection repeated as required according to the response. Alternatively noradrenaline may be infused at a rate of 5 mcg per minute until a satisfactory response is achieved.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities *Trandate Injection 20 ml ampoules:* Boxes of 5.

Further information Trandate does not adversely affect renal function and is a particularly suitable drug for use in hypertensive patients with renal disease. The metabolites of Trandate are excreted in the faeces as well as in the urine and so the drug is unlikely to accumulate in the body even in renal failure.

In non-pregnant patients the half-life of Trandate in plasma is about four hours and somewhat less in pregnancy. Only about 50% of Trandate in the blood is protein bound.

Trandate fluoresces in alkaline solution at an excitation wavelength of 334 nm and a fluorescence wavelength of 412 nm and may therefore interfere with the assays of certain fluorescent substances.

Product licence number 0045/0104.

TRIPTAFEN*-MINOR TRIPTAFEN*-DA

Presentation These are combined preparations of Amitriptyline Hydrochloride BP and Perphenazine BP.

Triptafen-Minor Tablets each contain Amitriptyline Hydrochloride BP 10 mg and Perphenazine BP 2 mg. Sugar-coated red tablets coded AH/2D.

Triptafen-DA Tablets each contain Amitriptyline Hydrochloride BP 25 mg and Perphenazine BP 2 mg. Sugar-coated, pink tablets coded AH/1D.

Uses Amitriptyline Hydrochloride BP is a tricyclic compound with antidepressive activity. Perphenazine is a piperazine derivative of phenothiazine which has potent tranquillising activity. Both Triptafen preparations are primarily indicated for combined depression with anxiety.

Triptafen-Minor: Anxiety states where depression may be a factor; psychosomatic disorders; the initiation of Triptafen treatment of depression, and continuation treatment of depressed patients requiring lower doses of amitriptyline.

Triptafen-DA: Depression, psychoneurosis, anxiety, psychosomatic illness, climacteric disorders associated with anxiety and depression, withdrawal syndrome in chronic alcoholism.

Dosage and administration Both Triptafen preparations are administered orally.

Adults: Triptafen-Minor: 1 tablet three times daily with a further tablet at night if necessary.

Triptafen-DA: 1 tablet three times daily with a fourth dose at night, if necessary.

With both Triptafen preparations the dosage may be adjusted to suit the needs of the individual patient with interchange of the preparation according to the requirements of tranquilliser or antidepressive medication.

Children: Triptafen preparations are not suitable for administration to children under 14 years of age.

Contra-indications, warnings, etc

Contra-indications: Glaucoma; urinary retention; congestive heart failure; coronary artery disease; epilepsy; severely impaired liver function; concurrent administration of other antidepressive drugs, particularly monoamine oxidase inhibitors (MAOIs). No Triptafen preparation should be given to patients with leucopenia or in association with drugs liable to cause bone-marrow depression.

Precautions: The Triptafen range of preparations should not be given in conjunction with MAOIs and, because of the persistent action of the latter, an interval of at least 14 days should be allowed to elapse between withdrawal of an MAOI and introduction of a Triptafen. Unnecessary administration of drugs during the first trimester of pregnancy is undesirable.

Side-effects: The side-effects of the Triptafen range are those of the drugs which they contain. Amitriptyline has atropine-like and sedative actions and may therefore give rise to drowsiness, dry mouth, blurred vision, tachycardia and, more rarely, insomnia. Perphenazine may cause mild drowsiness and a slight fall in blood pressure; in higher dosage, tremor and extrapyramidal effects may occur. Idiosyncratic side-effects, such as pruritus, nausea, diarrhoea and indigestion, may occur.

Persistent oral dyskinesia has been reported occasionally, particularly in elderly female patients, after long-term treatment with potent phenothiazine drugs including perphenazine.

Overdosage: Gastric lavage should be performed as soon as possible. If convulsions occur or threaten they should be controlled with standard methods, but barbiturates should be avoided. In severe cases haemodialysis may be performed if practicable. It is recommended that patients who have taken an overdose of Triptafen should

be observed for at least 48 hours even if symptoms are not severe.

Pharmaceutical precautions *Storage:* No special storage conditions are necessary for either of the Triptafen preparations.

Legal category POM.

Package quantities Triptafen-Minor Tablets and Triptafen-DA Tablets are issued in cartons each containing 100 tablets in 10 foil strips of 10 (5 × 2) tablets.

Further information Nil.

Product licence numbers

Triptafen-Minor Tablets	0045/5089
Triptafen-DA Tablets	0045/5087

VENTOLIN* INHALER

Presentation Metered-dose aerosol delivering 100 mcg Salbutamol BP per actuation, with a specially designed actuator.

Uses Salbutamol BP is a beta-adrenergic stimulant which has a highly selective action on the receptors in bronchial muscle and, in therapeutic dosage, little or no action on the cardiac receptors.

Salbutamol is also highly active in preventing antigen-induced release of histamine and slow-reacting substance of anaphylaxis, SRS(A), from mast cells in human lung sensitised with IgE antibody. Such Type I hypersensitivity reactions are generally considered to be the primary triggers of the allergic asthma syndrome.

Ventolin Inhaler is, therefore, indicated both for the treatment and prophylaxis of bronchial asthma, and also for the treatment of other conditions, such as bronchitis and emphysema, with associated reversible airways obstruction. Because Ventolin Inhaler is long-acting it is ideally suited for routine maintenance therapy in chronic asthma and chronic bronchitis. The inhaler drug-delivery system, using salbutamol in microgram dosage, avoids the skeletal muscle tremor sometimes associated with oral therapy.

Ventolin Inhaler acts rapidly and may be used when necessary to relieve attacks of acute dyspnoea. Doses may be taken prophylactically before exertion or to prevent exercise-induced asthma.

Because of its selective action on the bronchi and its lack of effects on the cardiovascular system, Ventolin Inhaler is suitable for treating bronchospasm in patients with co-existing heart disease or hypertension, including those taking beta-blocking drugs which often impair respiratory function.

Dosage and administration **Adults:** For the relief of acute bronchospasm and for managing intermittent episodes of asthma, one or two inhalations may be administered as a single dose. The recommended dose for chronic maintenance or prophylactic therapy is two inhalations three or four times a day.

To prevent exercise-induced bronchospasm, two inhalations should be taken before exertion.

Children: One inhalation is the recommended dose for the relief of acute bronchospasm, in the management of episodic asthma or before exercise.

One inhalation should be administered three or four times a day for routine maintenance or prophylactic therapy. These doses may be increased to two inhalations, if necessary.

For optimum results, in most patients, Ventolin Inhaler should be used regularly.

The bronchodilator effect of each administration of inhaled Ventolin lasts at least four hours except in patients whose asthma is worsening. Such patients should be warned not to increase their usage of inhaler but should seek medical advice in case treatment with a glucocorticoid is indicated.

Contra-indications, warnings, etc

Contra-indications: Although intravenous salbutamol and occasionally salbutamol tablets are used to prevent premature labour Ventolin preparations should not be used for threatened abortion during the first or second trimesters.

Precautions: In the event of a previously effective dose of Ventolin Inhaler failing to give relief for at least three hours, the patient should be advised to seek medical advice in order that any necessary additional steps may be taken. Ventolin should be administered cautiously to patients suffering from thyrotoxicosis.

Unnecessary administration of drugs during the first trimester of pregnancy is undesirable.

Side-effects: No important side-effects have been reported following Ventolin Inhaler therapy.

Overdosage: The preferred antidote for overdosage with Ventolin Inhaler is a cardioselective beta-blocking agent, but beta-blocking drugs should be used with caution in patients with a history of bronchospasm.

Pharmaceutical precautions *Storage:* Ventolin Inhaler should be stored in a cool place, protected from frost and direct sunlight. The canister should not be broken, punctured or burnt, even when apparently empty.

Legal category POM.

Package quantities Ventolin Inhaler is a metered-dose aerosol with a specially designed actuator. Each canister provides 200 inhalations.

Further information Ventolin does not cause difficulty in micturition because, unlike sympathomimetic drugs such as ephedrine, it does not stimulate alpha-adrenoceptors. Ventolin is not contra-indicated in patients under treatment with monoamine oxidase inhibitors (MAOIs).

Product licence number 0045/5022.

VENTOLIN® PARENTERAL PREPARATIONS

VENTOLIN® INJECTION 0.5 mg in 1 ml

(500 mcg/ml)

VENTOLIN® INJECTION 0.25 mg in 5 ml

(50 mcg/ml)

VENTOLIN® SOLUTION FOR INTRAVENOUS INFUSION 5 mg in 5 ml (1,000 mcg/ml)

Presentation Ventolin Injection 0.5 mg in 1 ml (500 mcg/ml) is presented in ampoules of 1 ml each containing 0.5 mg Salbutamol BP as Salbutamol Sul-

phate BP, in a sterile isotonic solution adjusted to pH 3.5 with sulphuric acid.

Ventolin Injection 0.25 mg in 5 ml (50 mcg/ml) is presented as ampoules of 5 ml each containing 0.25 mg Salbutamol BP as Salbutamol Sulphate BP, in a sterile isotonic solution adjusted to pH 3.5 with sulphuric acid.

Ventolin Solution For Intravenous Infusion 5 mg in 5 ml (1,000 mcg/ml) is presented as ampoules of 5 ml each containing 5 mg Salbutamol BP as Salbutamol Sulphate BP, in a sterile isotonic solution adjusted to pH 3.5 with sulphuric acid.

The ampoules are of clear, neutral glass and the solution is colourless or faintly straw coloured.

Uses Salbutamol BP is a beta-adrenergic stimulant that has a selective action on the beta₂-adrenoceptors in the bronchi and uterus and much less action on the beta₁-adrenoceptors in the heart.

Ventolin parenteral preparations are indicated for two distinct clinical situations:

1. For the relief of severe bronchospasm associated with asthma or bronchitis and for the treatment of status asthmaticus.
2. For the management of uncomplicated premature labour in the last trimester of pregnancy.

Dosage and administration 1. *In severe bronchospasm and status asthmaticus*

Subcutaneous route: Adults: 500 mcg (8 mcg/kg body weight) and repeated every four hours as required.

Intramuscular route: Adults: 500 mcg (8 mcg/kg body weight) and repeated every four hours as required.

Intravenous route: Adults: 250 mcg (4 mcg/kg body weight) injected slowly. If necessary the dose may be repeated. Ventolin Injection 0.25 mg in 5 ml (50 mcg/ml) is a suitably dilute preparation for slow intravenous injection, but if Ventolin Injection 0.5 mg in 1 ml (500 mcg/ml) is used the injection may be facilitated by dilution with Water for Injections BP.

Infusion: In status asthmaticus, infusion rates of 3–20 mcg per minute are generally adequate, but in patients with respiratory failure higher dosage has been used with success. A starting dose of 5 mcg per minute is recommended with appropriate adjustments in dosage according to patient response.

A suitable solution for infusion may be prepared by diluting 5 ml of Ventolin Solution. For Intravenous Infusion in 500 ml of an infusion solution such as Sodium Chloride and Dextrose Injection BP to provide a salbutamol dose of 10 mcg/ml of solution.

Children: At present there is insufficient evidence to recommend a dosage regimen for routine use in children.

2. In the management of premature labour

For this indication Ventolin Solution for Intravenous Infusion is recommended using a solution prepared as in 1. above.

Infusion rates of 10–45 mcg per minute are generally adequate to control uterine contractions, but greater or lesser infusion rates may be required according to the strength and frequency of contractions. A starting rate of 10 mcg per minute is recommended, increasing the rate at 10-minute intervals until there is evidence of patient response shown by diminution in strength, frequency or duration of contractions. Thereafter the infusion rate may be increased slowly until contractions cease. The maternal pulse rate should be monitored and

the infusion rate adjusted to avoid excessive maternal heart rates (above 140 beats per minute). Once uterine contractions have ceased the infusion rate should be maintained at the same level for one hour and then reduced by 50% decrements at six-hourly intervals. Treatment may be continued orally with Ventolin Tablets 4 mg given three or four times daily.

As an alternative procedure or to counteract inadvertent overdosage with oxytocic drugs Ventolin Injection may be administered as a single injection by the intravenous or intramuscular routes. The usual recommended dose is 100–250 mcg of salbutamol. The dose may be repeated according to the response of the patient.

Note. The contents of the ampoules of Ventolin Solution For Intravenous Infusion must not be injected undiluted.

Ventolin parenteral preparations should not be administered in the same syringe or infusion as any other medication.

Contra-indications, warnings, etc

Contra-indications: Though Ventolin parenteral preparations are recommended for the prevention of uncomplicated premature labour their use in premature labour associated with toxæmia of pregnancy or ante-partum haemorrhage from whatever cause is contra-indicated. Ventolin preparations should not be used for threatened abortion during the first or second trimesters of pregnancy.

Precautions: The use of Ventolin parenteral preparations in the treatment of severe bronchospasm or status asthmaticus does not obviate the requirement for glucocorticoid steroid therapy as appropriate. When practicable, administration of oxygen concurrently with parenteral Ventolin is recommended, particularly when it is given by intravenous infusion to hypoxic patients. In common with other beta-adrenoceptor agonists, Ventolin can induce reversible metabolic changes. These are most pronounced during infusions of the drug when an increase in blood glucose is likely. The diabetic patient may be unable to compensate for this and the development of ketoacidosis has been reported. Concurrent administration of corticosteroids can exaggerate this effect. Therefore diabetic patients and those concurrently receiving corticosteroids should be monitored frequently during intravenous infusion of Ventolin so that remedial steps (e.g. an increase in insulin dosage) can be taken to counter any metabolic change occurring. For these patients it may be preferable to dilute Ventolin Solution For Intravenous Infusion in Sodium Chloride Injection BP rather than Sodium Chloride and Dextrose Injection BP.

Ventolin should be administered cautiously to patients suffering from thyrotoxicosis. In patients being treated to inhibit uterine contractions in premature labour by intravenous infusion of salbutamol, increases in maternal heart rate of the order of 20–50 beats per minute usually accompany the infusion. The maternal pulse rate should be monitored and not normally allowed to exceed a steady rate of 140 beats per minute. Maternal blood pressure may fall slightly during the infusion, the effect being greater on diastolic than on systolic pressure. Falls in diastolic pressure are usually within the range of 10–20 mmHg. The effect of infusion on foetal heart rate is less marked, but increases of up to 20 beats per minute may occur. In the treatment of premature labour before Ventolin parenteral preparations are given to any patient with known heart disease, an adequate assessment of the patient's cardiovascular status should be made by a

physician experienced in cardiology. Unnecessary administration of drugs during the first trimester of pregnancy is undesirable.

Side-effects: Intramuscular use of the undiluted injection may produce slight pain or stinging. Enhancement of physiological tremor may occur with Ventolin. This effect is caused by a direct action on skeletal muscle and is common to all beta-adrenergic stimulants.

Ventolin parenteral preparations may dilate some peripheral arterioles leading to a small reduction in arterial pressure and a compensatory increase in cardiac rate. Increases in heart rate are more likely to occur in patients with normal heart rates and these increases are dose-dependent. In patients with pre-existing sinus tachycardia, especially those in status asthmaticus, the heart rate tends to fall as the condition of the patient improves.

In the management of premature labour, intravenous infusion of Ventolin has occasionally been associated with nausea, vomiting and headaches.

Overdosage: The preferred antidote for overdosage with Ventolin is a cardioselective beta-blocking agent. Beta-blocking drugs should be used with caution in patients with a history of bronchospasm.

Pharmaceutical precautions Ventolin parenteral preparations may be diluted with Water for Injections BP, Sodium Chloride Injection BP, Sodium Chloride and Dextrose Injection BP or Dextrose Injection BP. These are the only recommended diluents.

Ventolin parenteral preparations should not be administered in the same syringe or infusion as any other medication.

The contents of the ampoule of Ventolin Solution For Intravenous Infusion must not be injected in the undiluted form; the concentration should be reduced by at least 50% before administration.

Storage: Ventolin parenteral preparations should be protected from light and stored at a temperature below 30°C.

Legal category POM.

Package quantities Ventolin Injection 0.5 mg in 1 ml (500 mcg/ml) is available in boxes of 5 ampoules.

Ventolin Injection 0.25 mg in 5 ml (50 mcg/ml) is available in boxes of 10 ampoules.

Ventolin Solution For Intravenous Infusion 5 mg in 5 ml (1,000 mcg/ml) is available in boxes of 10 ampoules.

Further information Ventolin does not cause difficulty in micturition because, unlike sympathomimetic drugs such as ephedrine, it does not stimulate alpha-adrenoceptors. Ventolin is not contra-indicated in patients under treatment with monoamine oxidase inhibitors (MAOIs).

Product licence numbers

Ventolin Injection 0.5 mg in 1 ml (500 mcg/ml)	0045/0102
Ventolin Injection 0.25 mg in 5 ml (50 mcg/ml)	0045/0108
Ventolin Solution for Intravenous Infusion 5 mg in 5 ml (1,000 mcg/ml)	0045/0103

VENTOLIN® RESPIRATOR SOLUTION

Presentation Ventolin Respirator Solution is an aqueous colourless solution of Salbutamol Sulphate BP

adjusted with acid to pH 3.5. The concentration, which is expressed in terms of Salbutamol BP, is 0.5% or 5 mg per ml of solution.

Uses Ventolin Respirator Solution is indicated for the treatment of severe acute asthma (status asthmaticus) and other forms of bronchospasm.

Dosage and administration 1. *By intermittent administration. Adults:* Ventolin Respirator Solution 0.5–1.0 ml (2.5–5.0 mg of salbutamol) should be diluted to a final volume of 2.0 or 2.5 ml with sterile distilled water or normal saline for injection. The resulting solution is inhaled from a suitably driven nebuliser until aerosol generation ceases. Using a correctly matched nebuliser and driving source this should take about ten minutes.

Ventolin Respirator Solution may be used undiluted for intermittent administration. For this, 2.0 ml of Ventolin Respirator Solution (10.0 mg salbutamol) is placed in the nebuliser and the patient allowed to inhale the nebulised solution until bronchodilatation is achieved. This usually takes 3–5 minutes.

Some adult patients may require higher doses of salbutamol, up to 10 mg, in which case nebulisation of the undiluted solution may continue until aerosol generation ceases.

Children: The same mode of administration for intermittent administration is also applicable to children. The usual dosage for children under the age of twelve years is 0.5 ml (2.5 mg salbutamol) diluted to 2.0 or 2.5 ml with sterile distilled water or normal saline. Some children may however require higher doses of salbutamol up to 5.0 mg.

Intermittent treatment may be repeated four times daily.

2. *By continuous administration:* Ventolin Respirator Solution is diluted with sterile distilled water or normal saline for injection to contain 50–100 mcg of salbutamol per ml, (1–2 ml solution made up to 100 ml with diluent). The diluted solution is administered as an aerosol by a suitably driven nebuliser. The usual rate of administration is 1–2 mg per hour.

Delivery of the aerosol may be by facemask, 'T' piece or via an endotracheal tube. Intermittent positive pressure ventilation may be used but is rarely necessary. When there is a risk of anoxia through hypoventilation, oxygen should be added to the inspired air.

Contra-indications, warnings, etc

Contra-indications: Nil.

Precautions: Ventolin Respirator Solution should be used with care in patients known to have received large doses of other sympathomimetic drugs.

It should be administered cautiously to patients suffering from thyrotoxicosis.

Ventolin Respirator Solution is to be used with a respirator or nebuliser only, under the direction of a physician. It is not to be injected or administered orally.

Patients receiving treatment at home with Ventolin Respirator Solution must be warned that if either the usual relief is diminished or the usual duration of action reduced, they should not increase the dose or its frequency of administration, but should seek medical advice.

Unnecessary administration of drugs during the first trimester of pregnancy is undesirable.

Side-effects: A small increase in heart rate may occur in patients who inhale large doses of Ventolin. This is not usually accompanied by any changes in the electrocar-

diogram. Other side-effects which may occur with very high doses of Ventolin by inhalation are peripheral vasodilatation and fine tremor of skeletal muscle.

Overdosage: During continuous administration of Ventolin Respirator Solution any signs of overdosage can usually be counteracted by withdrawal of the drug.

The preferred antidote for overdosage with Ventolin Respirator Solution is a cardioselective beta-blocking agent, but β -blocking drugs should be used with caution in patients with a history of bronchospasm.

Pharmaceutical precautions *Storage:* Ventolin Respirator Solution should be stored at a temperature below 25°C and protected from light. Once a bottle has been opened the contents should be discarded after one month.

Dilution: Ventolin Respirator Solution may be diluted with Water for Injections BP or Sodium Chloride Injection BP (normal saline).

Solutions in nebulisers should be replaced daily.

Legal category POM.

Package quantities Ventolin Respirator Solution is supplied in screw-capped bottles of 20 ml.

Further information Ventolin does not cause difficulties in micturition because, unlike sympathomimetic drugs such as ephedrine, it does not stimulate alpha-adrenoceptors. Ventolin is not contra-indicated in patients under treatment with monoamine oxidase inhibitors (MAOIs).

Ventolin Respirator Solution is suitable for treating bronchospasm in patients with co-existing heart disease or hypertension.

Product licence number 0045/5023.

VENTOLIN® ROTACAPS*

Presentation Ventolin Rotacaps, an alternative inhalation form of salbutamol to Ventolin Inhaler, are especially valuable for treating patients who are unable to use pressurised inhalers effectively or who might use them unwisely.

Ventolin Rotacaps contain a mixture of microfine salbutamol sulphate and larger particle lactose in blue/colourless hard gelatine cartridges. Each Rotacap contains 200 mcg (light blue) or 400 mcg (dark blue) of salbutamol (as sulphate) and is marked Ventolin 200 or Ventolin 400. The contents of a Rotacap are inhaled using a specially developed device called a Rotahaler* which separates the cartridge into halves that rotate and release the drug when the patient inhales. This breath actuation is very sensitive and so the drug is fully available even at the lowest inspiratory flow rates. The Rotahaler is, therefore, a more reliable drug delivery system for many patients, but a rather larger unit dose relative to Ventolin Inhaler is necessary for the same therapeutic effect.

Uses Salbutamol BP is a beta-adrenergic stimulant which has a highly selective action on bronchial beta-adrenoceptors and little or no effect on cardiac beta-receptors at therapeutic doses.

Salbutamol is also highly active in preventing antigen-induced release of histamine and slow-reacting substance of anaphylaxis, SRS(A), from mast cells in human lung sensitised with IgE antibody. Such Type I hyper-

sensitivity reactions are generally considered to be the primary triggers of the allergic asthma syndrome.

Ventolin Rotacaps are therefore indicated both for the treatment and prevention of bronchial asthma, and also for the treatment of other conditions, such as bronchitis and emphysema, with associated reversible airway obstruction. Inhaled salbutamol has a long duration of action and Ventolin Rotacaps are ideally suited for routine maintenance therapy and prophylaxis in chronic asthma, both to relieve persistent bronchospasm and to suppress the allergic response within the lungs. Their regular use is also indicated for controlling persistent bronchospasm in chronic bronchitis.

Ventolin Rotacaps act rapidly and may be used when necessary to relieve attacks of acute dyspnoea. Rotacaps may also be used before exertion to prevent exercise-induced asthma or before exposure to a known unavoidable allergen challenge.

The effective dose of salbutamol from Rotacaps is only one tenth of the usual oral dose and so the skeletal muscle tremor sometimes associated with oral therapy does not occur.

The selective action of salbutamol on the bronchi and its lack of effects on the cardiovascular system make Ventolin Rotacaps particularly suitable for treating patients with co-existing heart disease or hypertension, including those taking beta-blocking drugs which often impair respiratory function.

Dosage and administration Ventolin Rotacaps for inhalation use only, using a Ventolin Rotahaler.

Adults: For the relief of acute bronchospasm and for managing intermittent episodes of asthma, 200 mcg or 400 mcg may be administered as a single dose.

The recommended dose for chronic maintenance or prophylactic therapy is 400 mcg three or four times a day.

To prevent exercise-induced bronchospasm, 400 mcg should be taken before exertion.

Children: 200mcg is the recommended dose for the relief of acute bronchospasm, in the management of episodic asthma or before exercise.

200 mcg should be administered three or four times a day for routine maintenance or prophylactic therapy.

For optimum results, in most patients Ventolin Rotacaps should be used regularly.

The bronchodilator effect of these doses of inhaled salbutamol should last for at least four hours, except in patients with relatively severe asthma who require additional treatment with an inhaled and/or systemic glucocorticosteroid.

Contra-indications, warnings, etc

Contra-indications: Although intravenous salbutamol and salbutamol tablets are used in the management of premature labour, Ventolin preparations should not be used for threatened abortion during the first or second trimesters.

Precautions: In the event of a previously effective dose of inhaled Ventolin failing to give relief lasting at least three hours, the patient should be advised to seek medical advice in order that any necessary additional steps may be taken. Ventolin should be administered cautiously to patients suffering from thyrotoxicosis. Unnecessary administration of drugs during the first trimester of pregnancy is undesirable.

Side-effects: No important side effects have been reported following treatment with Ventolin Rotacaps.

Overdosage: The preferred antidote for overdosage with salbutamol is a cardioselective beta-blocking agent, but beta-blocking drugs should be used with caution in patients with a history of bronchospasm.

Pharmaceutical precautions To keep the Rotacaps in good condition it is important that they are stored in a dry place where they will not be exposed to extremes of temperature. A convenient supply may be carried in the special container for the Rotahaler. The Rotacaps should only be inserted in the Rotahaler immediately prior to use. Failure to observe this instruction may affect the operation of the Rotahaler.

Legal category POM.

Package quantities Ventolin Rotacaps 200 mcg and 400 mcg are supplied in containers of 100.

Further information Ventolin does not cause difficulty in micturition because, unlike sympathomimetic drugs such as ephedrine, it does not stimulate alpha-adrenoceptors. Ventolin is not contra-indicated in patients under treatment with monoamine oxidase inhibitors (MAOIs).

Product licence numbers

Ventolin Rotacaps 200 mcg 0045/0116
Ventolin Rotacaps 400 mcg 0045/0117

VENTOLIN* TABLETS VENTOLIN* SYRUP VENTOLIN* SPANDETS*

Presentation *Ventolin Tablets 2 mg:* Pink tablets each containing Salbutamol BP 2 mg as sulphate. Engraved VENTOLIN AH around the perimeter of one side and the number 2 in the centre.

Ventolin Tablets 4 mg: Pink tablets each containing Salbutamol BP 4 mg as sulphate. Engraved VENTOLIN AH around the perimeter of one side and the number 4 in the centre.

Ventolin Syrup: Salbutamol BP 2 mg as sulphate in each 5 ml of a fruit-flavoured, red syrup.

Ventolin Spandets: Salbutamol BP 8 mg as sulphate in a specially designed, two-layered pink and white tablet. Salbutamol is released immediately from the pink layer and gradually from the porous matrix in the white layer. Engraved VENTOLIN SPANDET around the perimeter of one side and AH in the centre.

Uses Salbutamol BP is a beta-adrenergic stimulant which has a highly selective action on the receptors in bronchial muscle and, in therapeutic dosage, little or no action on the cardiac receptors.

Ventolin Tablets 2 mg and 4 mg, Syrup and Spandets are indicated for the relief of bronchospasm in bronchial asthma of all types, chronic bronchitis and emphysema.

Ventolin Syrup is suitable oral therapy for children or for those adults who prefer liquid medicines.

Ventolin Spandets are sustained-action tablets, particularly suitable when nocturnal bronchospasm is a problem.

Because of their selective action on the bronchi and their lack of effects on the cardiovascular system, Ventolin oral preparations are suitable for treating bronchospasm in patients with co-existing heart disease or hypertension.

The selective action of salbutamol on the β_2 -adrenoceptors has led to the use of parenteral Ventolin, usually

as a continuous intravenous infusion, for the management of premature labour during the third trimester of pregnancy. Once the uterine contractions have ceased and the infusion of Ventolin has been gradually withdrawn, maintenance therapy can be effected with Ventolin Tablets.

Dosage and administration *Ventolin Tablets 2 mg and 4 mg and Syrup*: *Adults*: The usual effective dose is 4 mg (one tablet 4 mg or 10 ml of syrup) three or four times per day. If adequate bronchodilatation is not obtained each single dose may be gradually increased to as much as 8 mg.

However, it has been established that some patients obtain adequate relief with 2 mg three or four times daily. In elderly patients or in those known to be unusually sensitive to beta-adrenergic stimulant drugs, it is advisable to initiate treatment with 2 mg three or four times per day.

Children: The following doses should be administered three or four times daily:

2-6 years: 1-2 mg as 2.5-5 ml of syrup or $\frac{1}{2}$ -1 tablet 2 mg.

6-12 years: 2 mg as 5 ml of syrup or 1 tablet 2 mg.

Over 12 years: 2-4 mg as 1 tablet 2 mg or 1 tablet 4 mg.

The drug is well tolerated by children so that, if necessary, these doses can be cautiously increased.

In the management of premature labour, after uterine contractions have been controlled by intravenous infusion of Ventolin and the infusion has been withdrawn, maintenance therapy can be continued with oral Ventolin. The usual dosage is 4 mg three or four times daily.

Ventolin Spandets: *Adults*: 1 Spandet night and morning. In severe cases the dose may be increased to 4 Spandets per 24 hours.

Children over 12 years: 1 Spandet every 12 hours.

Ventolin Spandets must be swallowed whole and not chewed.

Contra-indications, warnings, etc

Contra-indications: Although intravenous salbutamol and salbutamol tablets are used in the management of premature labour Ventolin preparations should not be used for threatened abortion during the first or second trimesters.

Ventolin oral preparations and beta-blocking drugs such as propranolol, should not usually be prescribed together.

Precautions: Ventolin should be administered cautiously to patients suffering from thyrotoxicosis.

Long-term treatment with Ventolin Syrup increases the risk of dental caries and it is essential that adequate dental hygiene is maintained.

Unnecessary administration of drugs during the first trimester of pregnancy is undesirable.

Side-effects: The only side-effect of significance with oral Ventolin is a fine tremor of skeletal muscle which occurs in some patients, usually the hands are most obviously affected. This effect is dose related and is common to all beta-adrenergic stimulants. A few patients feel tense; this is also due to the effects on skeletal muscle and not to direct CNS stimulation. With doses of Ventolin higher than those recommended or in patients who are unusually sensitive to beta-adrenergic stimulants peripheral vasodilatation and a compensatory small increase in heart rate may occur. Occasionally headaches have been reported.

Overdosage: The preferred antidote for overdosage with Ventolin is a cardioselective beta-blocking agent, but beta-blocking drugs should be used with caution in patients with a history of bronchospasm.

Pharmaceutical precautions *Storage*: Ventolin Tablets 2 mg and 4 mg and Ventolin Spandets should be stored at a temperature not exceeding 30°C. Ventolin Syrup should be stored at a temperature below 25°C and protected from light.

Dilution: Ventolin Syrup may be diluted with unpreserved Syrup BP. The resulting mixture should be protected from light and it will keep for 14 days.

Legal category POM.

Package quantities Ventolin Tablets 2 mg are supplied in containers of 100 and 500.

Ventolin Tablets 4 mg are supplied in containers of 100 and 500.

Ventolin Syrup is supplied in bottles of 150 ml and 2 litres.

Ventolin Spandets are supplied in containers of 50.

Further information Ventolin does not cause difficulty in micturition because, unlike sympathomimetic drugs such as ephedrine, it does not stimulate alpha-adrenoceptors. Ventolin is not contra-indicated in patients under treatment with monoamine oxidase inhibitors (MAOIs).

Product licence numbers

Ventolin Tablets 2 mg	0045/5079
Ventolin Tablets 4 mg	0045/0088
Ventolin Syrup	0045/5024
Ventolin Spandets	0045/0083

* *Trade Mark.*

Allergan Ltd
Fennels Lodge
St Peters Close
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BLEPH* - 10 OPHTHALMIC SOLUTION

Presentation Clear, colourless to slightly straw colour, sterile, ophthalmic solution containing 10.0% sodium sulphacetamide, and 0.005% thimerosal as preservative.

Uses For the treatment of conjunctivitis, corneal ulcer, and other superficial ocular infections from susceptible micro-organisms, and as an adjunct to systemic sulphonamide therapy of trachoma.

Dosage and administration 1 to 2 drops into lower conjunctival sac every two to three hours during the day, less often at night.

Contra-indications, warnings, etc The product should not be used when there is known to be hypersensitivity to sulphonamide preparations. The solution is incompatible with silver preparations. Non-susceptible organisms, including fungi, may proliferate with the use of this preparation. Sulphonamides are inactivated by the aminobenzoic acid present in purulent exudates.

Pharmaceutical precautions Protect from excessive light and heat. Do not use if the solution is discoloured (dark brown).

Legal category POM.

Package quantities Bleph-10 is available in 5 ml and 10 ml plastic dropper bottles.

Further information Nil (sulphonamides exert a bacteriostatic effect against a wide range of gram-positive and gram-negative micro-organisms by restricting, through competition with para-aminobenzoic acid, the synthesis of folic acid which bacteria require for growth).

Product licence number 0426/0003.

EPIFRIN* 1% OPHTHALMIC SOLUTION

Presentation Clear, colourless to very slightly straw coloured, sterile, aqueous ophthalmic solution containing 1.0% Adrenaline, present as the hydrochloride, and 0.004% benzalkonium chloride as preservative.

Uses Chronic simple glaucoma. In many cases control of intraocular pressure can be obtained when miotics have failed, and is most useful in combination with miotics to obtain better control.

Dosage and administration The usual dosage is one drop in affected eye(s) once daily. However the dosage should be adjusted to meet the needs of the individual patient.

Contra-indications, warnings, etc Should not be used in closed-angle glaucoma, since the dilation of the pupil may precipitate an acute attack. Undesirable side reactions may include eye pain or ache, brow ache, headache, conjunctival hyperemia and allergic lid reactions. Adrenochrome deposits in the conjunctiva and cornea after prolonged epinephrine therapy have been reported. Adrenaline has been reported to produce macular oedema in some aphakic patients and should be used with caution in these patients.

Pharmaceutical precautions Protect from excessive light. If the solution discolours or a precipitate forms it should be discarded.

Legal category P.

Package quantities Epifrin 1% is available in a 10 ml plastic dropper bottle.

Further information Nil.

Product licence number 0426/0018.

EPIFRIN* 2% OPHTHALMIC SOLUTION

Presentation Clear, colourless to very slightly yellow, sterile, aqueous ophthalmic solution containing 2.0% Adrenaline, present as the hydrochloride, and 0.004% benzalkonium chloride as preservative.

Uses Chronic simple glaucoma. In many cases control of intraocular pressure can be obtained when miotics have failed, and is most useful in combination with miotics to obtain better control.

Dosage and administration The usual dosage is one drop in affected eye(s) once daily. However the dosage should be adjusted to meet the needs of the individual patient.

Contra-indications, warnings, etc Should not be used in closed-angle glaucoma, since the dilation of the pupil may precipitate an acute attack. Undesirable side reactions may include eye pain or ache, brow ache, headache, conjunctival hyperemia and allergic lid reactions. Adrenochrome deposits in the conjunctiva and cornea after prolonged epinephrine therapy have been reported. Adrenaline has been reported to produce macular oedema in some aphakic patients and should be used with caution in these patients.

Pharmaceutical precautions Protect from excessive light. If the solution discolours or a precipitate forms, it should be discarded.

Legal category P.

Package quantities Epifrin 2% is available in a 10 ml plastic dropper bottle.

Further information Nil.

Product licence number 0426/0008.

FML* STERILE OPHTHALMIC SUSPENSION ▼

Presentation White microfine sterile ophthalmic suspension containing 0.1% fluoromethalone and 0.004% benzalkonium chloride as preservative.

Uses Topical ophthalmic suspension for steroid responsive inflammation of the palpebral and bulbar conjunctiva, cornea and anterior segment of the globe.

Dosage and administration 1 to 2 drops instilled into the conjunctival sac two to four times daily. During the initial 24 to 48 hours the dosage may be safely increased to 2 drops every hour. Care should be taken not to discontinue therapy prematurely.

Contra-indications, warnings, etc

Contra-indications: Acute superficial herpes simplex keratitis. Fungal diseases of ocular structures. Vaccinia, varicella and most other viral diseases of the cornea and conjunctiva. Tuberculosis of the eye. Hypersensitivity to the constituents of this medication.

Warnings: Steroid medication in the treatment of herpes simplex keratitis (involving the stroma) requires great caution: frequent slit-lamp microscopy is mandatory. Prolonged use may result in glaucoma, damage to the optic nerve, defects in visual acuity and fields of vision, posterior subcapsular cataract formation, or may aid in the establishment of secondary ocular infections from fungi or viruses liberated from ocular tissue.

In those diseases causing thinning of the cornea or sclera, perforation has been known to occur with use of topical steroids.

Safety and effectiveness have not been demonstrated in children of the age group two years or below.

This preparation contains benzalkonium chloride and should be used with caution in association with hydrophilic contact lenses.

Use in pregnancy: Safety of the use of topical steroids during pregnancy has not been established.

Precautions: As fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid applications, fungus invasion must be suspected in any persistent corneal ulceration where a steroid has been used or is in use.

Intraocular pressure should be checked frequently.

Adverse reactions: Glaucoma with optic nerve damage, visual acuity or field defects, posterior subcapsular cataract formation, secondary ocular infection from pathogens liberated from ocular tissues, perforation of the globe.

Local side-effects of steroid therapy, i.e. skin atrophy, striae and telangiectasia, are especially likely to affect facial skin.

Pharmaceutical precautions Protect from freezing.

Legal category POM.

Package quantities Supplied in plastic dropper bottles of 5 ml and 10 ml.

Further information Nil.

Product licence number 0426/0028.

LACRI-LUBE*

Presentation Sterile, bland, non-medicated ophthalmic ointment, for topical administration to humans, containing white petrolatum mineral oil, non-ionic lanolin derivatives with chlorobutanol 0.5% as a preservative.

Uses Useful as adjunctive therapy to lubricate and protect the eye in conditions characterized by exposure keratitis, decreased corneal sensitivity, recurrent corneal erosions, keratitis sicca, ophthalmic surgeries and non-ophthalmic surgeries.

Dosage and administration For topical administration. Pull lower lid down to form pocket. Apply small amount as needed.

Contra-indications, warnings, etc No known contra-indications.

Pharmaceutical precautions Store away from heat. To avoid contamination during use, do not touch tip to any surface.

Legal category P.

Package quantities Available in 3.5 g ophthalmic ointment tubes.

Further information Nil.

Product licence number 0426/0041.

LIQUIFILM* TEARS

Presentation Clear, colourless to slightly straw coloured, sterile, aqueous ophthalmic solution, containing 1.4% polyvinyl alcohol and 0.5% chlorobutanol as preservative.

Uses For dry eyes, especially where natural mucus is absent, or deficient, also as an ocular lubricant.

Dosage and administration 1 drop in the eye as needed, or as directed.

Contra-indications, warnings, etc Not for use with soft contact lenses. If irritation increases or persists, discontinue use.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Liquifilm Tears is available in plastic dropper bottles containing 15 ml.

Further information Nil.

Product licence number 0426/0009.

PREFRIN* EYE DROPS

Presentation Clear, colourless, sterile, aqueous ophthalmic solution containing 0.12% phenylephrine hydrochloride, and 0.004% benzalkonium chloride as preservative.

Uses For treatment of non-infectious, mild ocular irritations and redness of non specific aetiology.

Dosage and administration 1 or 2 drops in each eye every three or four hours.

Contra-indications, warnings, etc The product should not be used in the presence of narrow-angle glaucoma. If irritation persists or increases the treatment should be discontinued.

Pharmaceutical precautions The product should not be used later than two weeks after opening the container.

Legal category P.

Package quantities Prefrin is available in plastic dropper bottles of 15 ml.

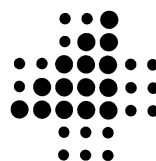
Further information Nil.

Product licence number 0426/0014.

**Trade Mark*

American Hospital Supply (UK) Limited

Station Road Didcot Oxfordshire OX11 7NP



INTROPIN®

Presentation Intropin 800 mg/5 ml ampoules; each ml contains 160 mg dopamine hydrochloride and 1% sodium bisulphite. Intropin 200 mg/5 ml ampoules and prefilled syringes; each ml contains 40 mg dopamine hydrochloride and 1% sodium bisulphite. The solutions are clear and practically colourless.

Uses Actions: Intropin exerts its beneficial haemodynamic effects by its action on different receptors; at 1–5 mcg/kg/min Intropin dilates the renal and mesenteric vascular beds by its unique action on 'dopaminergic' receptors, causing increases in glomerular filtration rate, renal blood flow, sodium excretion, and urine output.

At 5–20 mcg/kg/min Intropin exerts a direct inotropic effect on the myocardium causing dose related increases in cardiac output with minimal effect on heart rate. Blood pressure usually rises and further increases in the urine output are seen.

At 20 mcg/kg/min and above there are further increases in cardiac output and Intropin raises blood pressure by its alpha adrenergic action on peripheral blood vessels, however, even at these doses, renal blood flow is higher than prior to therapy.

Preparation: Transfer 800 mg Intropin by aseptic technique to 500 ml of one of the following sterile intravenous solutions:

1. Sodium Chloride Injection
2. 5% Dextrose Injection
3. 5% Dextrose and 0.9% Sodium Chloride Injection
4. 5% Dextrose in 0.45% Sodium Chloride Solution
5. 5% Dextrose in Lactated Ringer Solution
6. Sodium Lactate (1/6 Molar) Injection
7. Lactated Ringer's Injection.

This gives a concentration of 1,600 micrograms/ml of Intropin.

Intropin is stable for a minimum of 24 hours after dilution in the above solutions, however dilution should be made just before administration.

Do NOT add Intropin to 5% sodium bicarbonate or other alkaline solution since the drug is inactivated.

Administration: Intropin, after dilution, is administered intravenously through an intravenous catheter or needle in as large a vein as possible. An I.V. drip chamber or infusion pump is essential for controlling the infusion rate in drops/minute. The infusion rate should be titrated to the optimum patient response and constantly evaluated in terms of patient's changing condition.

Indications: Intropin is indicated for the correction of poor perfusion, low cardiac output, impending renal failure and shock associated with: Myocardial infarction, Trauma, Endotoxic septicaemia, Open heart surgery, Heart failure.

Dosage and administration Warning: This is a potent drug. It must be diluted before administration.

Dosage: Where appropriate, restoration of blood volume with a suitable plasma expander should be started or completed before Intropin therapy. Begin infusion of Intropin therapy at 2 mcg/kg/min in patients who are likely to respond to modest increments in heart force and renal perfusion. In more seriously ill patients begin infusion of Intropin at 5 mcg/kg/min, and in both cases the infusion rate should be titrated upwards in 5–10 mcg/kg/min increments until the optimum dose for the patient is achieved as judged by increases in blood pressure, urine flow, and perfusion generally. Doses of 50 mcg/kg/min and above have been successfully used, although urine output should be checked frequently, and should it fall, dosage reduction of Intropin should be considered.

Contra-indications, warnings, etc

Contra-indications: Intropin should not be used in patients with phaeochromocytoma.

Warnings: Intropin should not be used in the presence of uncorrected tachyarrhythmias or ventricular fibrillation.

Patients who have been treated with monoamine oxidase (MAO) inhibitors prior to Intropin should be given reduced doses; the starting dose should be one tenth ($\frac{1}{10}$) of the usual dose.

Usage in Pregnancy: Animal studies have shown no evidence of teratogenic effects with Intropin. The drug may be used in pregnant women when the expected benefits outweigh the potential risk to the foetus.

Usage in children: The safety and efficacy of Intropin use in children has not been established.

Precautions: Hypovolaemia should be corrected where necessary prior to Intropin infusion. Vasoconstriction can occur due to the alpha adrenergic actions of Intropin, especially in patients with a history of occlusive vascular disease. If desired, this condition can be rapidly reversed by dose reduction or discontinuing the infusion, since Intropin has a half-life of less than 2 minutes in the body. Intropin at the infusion site can cause local vasoconstriction, hence the desirability of infusing into a large vein. The resulting ischaemia can be reversed by infiltration of the affected area with 10–15 ml of saline containing 5 to 10 mg phentolamine mesylate. A syringe with a fine hypodermic needle should be used to liberally infiltrate the ischaemic area as soon as extravasation is noted.

Adverse reactions: Adverse reactions to Intropin are entirely related to its pharmacological action; immune mediated reactions are not seen since dopamine is a normal body product. The most frequently reported reactions to Intropin have been ectopic beats, tachycardia, anginal pain, palpitations, dyspnoea, nausea, vomiting, hypotension and vasoconstriction. Very rarely reported reactions include aberrant conduction, bradycardia, piloerection, widened QRS complex, azotaemia and hypertension. Vomiting is rare with Intropin, but should it occur, electrolyte replacement should be given.

Overdosage: Accidental overdosage as evidenced by excessive blood pressure elevation can be controlled by dose reduction or discontinuing the Intropin infusion for a short period, since the duration of action of Intropin is short.

Should these measures fail, an infusion of phentolamine mesylate should be considered.

Pharmaceutical precautions Do not add Intropin to 5% sodium bicarbonate or other alkaline solution since the drug is inactivated. Protect from light, do not use if discoloured. Avoid contact with solutions of alkalis.

Legal category POM.

Package quantities Ampoules containing 200 mg dopamine hydrochloride, 20 ampoules per outer carton. Ampoules containing 800 mg dopamine hydrochloride 20 ampoules per outer carton. Pre-filled syringes containing 200 mg dopamine hydrochloride, 5 syringes per outer carton.

Further information Nil.

Product licence numbers

Intropin 200 mg 3295/0001
Intropin 800 mg 3295/0004

TRIDIL*

Presentation Tridil 50 mg is supplied as a sterile, non-pyrogenic, practically colourless solution containing 5 mg/ml nitroglycerin in 30% alcohol and 30% propylene glycol and water for injection. Each 10 ml ampoule contains 50 mg nitroglycerin for intravenous infusion.

Tridil 5 mg is supplied as a sterile, non-pyrogenic solution containing 0.5 mg/ml nitroglycerin stabilized by alcohol BP 10% v/v, lactose and monobasic potassium phosphate. Each 10 ml glass ampoule contains 5 mg nitroglycerin for intravenous use.

Actions: Nitroglycerin causes relaxation of vascular smooth muscle. In a dose related manner nitroglycerin produces dilatation of both the arterial and venous vascular beds, however, the venous effects predominate. Dilatation of the post capillary vessels including large veins results in peripheral pooling and a reduction in venous return. Therapeutic doses of Tridil given intravenously produce a reduction in left ventricular end diastolic volume, left ventricular end diastolic pressure and myocardial wall tension. Myocardial oxygen consumption, as measured by the rate pressure product and tension time index is decreased.

Pulmonary vascular resistance, systemic vascular resistance and arterial pressure are all reduced by Tridil administration. Although the predominant clinical benefits result from the peripheral venodilating effects and the resultant reduction in myocardial oxygen demand, some effect on oxygen supply may occur by direct coronary vasodilatation. A re-distribution of blood from normal to ischaemic areas of the myocardium has been demonstrated.

Uses *Surgery:* Tridil may be used for the prompt control of hypertension encountered during cardiac surgery.

Tridil may be used to reduce blood pressure and maintain controlled hypotension during surgical procedures.

Tridil may be used to control myocardial ischaemia during and after cardiovascular surgery.

Unresponsive Congestive Cardiac Failure Secondary to

Acute Myocardial Infarction: Tridil may be used to reduce elevated left ventricular filling pressure in patients with unresponsive congestive cardiac failure secondary to acute myocardial infarction.

Unstable Angina: Tridil infusion can reduce myocardial oxygen demand in proportion to the reduction in pre-load and after-load. Tridil may be indicated for the control of anginal episodes in patients with unstable angina who are refractory to treatment with standard therapy.

Patients with recurrent myocardial ischaemia not responsive to beta-blockers or sublingual nitrates may benefit from the intravenous Tridil infusion prior to surgery or angiography.

Frequent monitoring of blood pressure and pulse rate are recommended during the infusion.

Dosage and administration Tridil is a concentrated pharmacological drug which should be diluted in 5% Dextrose in Water or 0.9% Sodium Chloride prior to its infusion.

It is recommended that the drug is diluted to give a final concentration of 400 mcg/ml or less according to the dosage requirements of the patient. Most patients respond to doses between 10–200 mcg/min, although doses up to 400 mcg/min may be required during some surgical procedures.

Compatibility: (See also Pharmaceutical Precautions) Tridil is compatible with glass infusion bottles. Tridil has also been shown to be compatible with certain rigid infusion packs made of polyethylene; these include the Boots polyfusor and the bottlepack distributed by Dylade, Cheshire U.K. (bottlepack; flatpak) or Antigen Ltd., Roscrea, S. Ireland (Braun). Tridil can be administered as an infusion using one of these recommended infusion bottles/packs.

Tridil is not compatible with infusion bags made from PVC and loss of activity in excess of 40% may occur if contact between nitroglycerin and polyvinylchloride is prolonged. It is therefore recommended that contact with PVC bags is avoided. Some loss of activity can also occur through the infusion sets but the clinical response should be used to determine the rate of infusion and thus the dosage of the drug required by the patient.

An alternative method of administration is via a syringe pump. Tridil can be infused slowly via a syringe pump using a glass syringe or rigid plastic syringe (Gillette Sabre syringe, Brunswick Disposable, B.D. plastipak syringes). A high pressure polyethylene tubing known to be compatible with nitroglycerin is the Lectrocath tubing, Vygon Gloucester.

The chosen method of administration should ensure that the drug is given at a constant infusion rate.

Dosage: The recommended dosage range is 10–200 mcg/min. Doses in excess of these have been used and up to 400 mcg/min may be required during some surgical procedures.

Clinical assessment and frequent monitoring of blood pressure are essential to maintain the appropriate infusion rate. Where available, measurement of pulmonary capillary wedge pressure and cardiac output can be used to titrate dosage to response.

Surgery: For the control of hypertensive episodes the recommended starting dose is 25 mcg/min increasing in steps of 25 mcg/min at 5 minute intervals until the desired drop in B.P. is achieved. Although most patients respond to doses between 10–200 mcg/min, doses up to 400 mcg/min have been required during some surgical

procedures. In the treatment of perioperative myocardial ischaemia, the recommended starting dose is 15–20 mcg/min increasing in steps of 10–15 mcg/min until the desired effect is achieved.

Unresponsive Congestive Cardiac Failure Secondary to Acute Myocardial Infarction: The recommended starting dose is 20–25 mcg/min which can be decreased to 10 mcg/min or increased in steps of 20–25 mcg/min at 15–30 minute intervals until the desired effect is achieved.

Unstable angina: The recommended starting dose is 10 mcg/min increasing in steps of 5–10 mcg/min at approximately 30 minute intervals.

Children: The safety and efficacy of Tridil has not been established in children.

Contra-indications, warnings, etc Tridil should not be given to patients with known hypersensitivity to nitrates.

Tridil should not be used in patients with marked anaemia, severe cerebral haemorrhage, uncorrected hypovolaemia or severe hypotension.

Tridil should be used with caution in patients suffering from hypothyroidism, malnutrition, severe liver or renal disease or hypothermia.

As with all vasodilators, Tridil should be used with caution in patients predisposed to closed angle glaucoma.

As the safety of Tridil during pregnancy and lactation has not been established, it should not be used unless considered essential by the physician.

Adverse reactions to nitrates may include hypotension, tachycardia, nausea, retching, diaphoresis, apprehension, headache, restlessness, muscle twitching, retrosternal discomfort, palpitations, dizziness, and abdominal pain. Paradoxical bradycardia has occasionally been observed.

Mild overdosage usually resulting in hypotension and tachycardia can be reversed by elevating the legs or decreasing or terminating the infusion. If severe, intravenous administration of methoxamine or phenylephrine is recommended.

Pharmaceutical precautions Opened ampoules should be used immediately and any unused diluted drug should be discarded.

Tridil solution is stable for at least 24 hours at room temperature in glass or recommended plastic containers (see compatibility). Considerable losses of nitroglycerin will occur if Tridil is in contact with polyvinylchloride (PVC) plastic infusion bags and therefore contact with PVC should be avoided. Tridil should therefore be administered in the recommended infusion bottles/packs or via a syringe pump.

Protect from strong light. Do not use if discoloured.

Legal category POM.

Package quantities Tridil 50 mg is available as either a Tridilkit (incorporating one 10 ml ampoule and a compatible infusion set—Tridilset) or in a box containing four 10 ml ampoules.

Tridil 5 mg is available in a box containing five 10 ml ampoules.

Further information Experience so far has shown that when given by slow infusion, the onset of action occurs within approximately 3–5 minutes.

Nitroglycerin is also known as glyceryl trinitrate, trinitroglycerin and trinitrin.

Product licence numbers

Tridil 5 mg 3295/0002.

Tridil 50 mg 3295/0007

**Trade Mark*

Approved Prescription Services Limited

Whitcliffe House

Whitcliffe Road, Cleckheaton

West Yorkshire BD19 3BZ



APSIFEN® **APSIFEN®-F**

Presentation Apsifen is available in two presentations:
Apsifen: Plain round biconvex pink sugar-coated tablets.
Apsifen-F: Round biconvex pink film-coated tablets marked 'APS' on one side and plain on the other side.

Both presentations contain the same active ingredient, Ibuprofen BP, and both are available in two strengths, 200 mg and 400 mg. They comply with the monograph for Ibuprofen Tablets BP.

Uses Ibuprofen is a non-steroidal anti-inflammatory agent with analgesic and anti-pyretic activity. Its principal effects are to relieve pain and stiffness and to reduce swelling.

Apsifen and Apsifen-F may therefore be used in the management of:

- (a) Rheumatoid Arthritis including Still's disease;
- (b) Osteoarthritis and seronegative (non rheumatoid) arthropathies;
- (c) Ankylosing Spondylitis.

Like other similar agents, Ibuprofen has also been used in non-articular rheumatic conditions and in soft-tissue injuries.

Dosage and administration (Oral)

Adults: Initially 1200 mg per day in divided doses. In severe conditions up to 1600 mg per day may be given until the acute phase of the condition has been brought under control. Some patients may be maintained on doses in the range 600–1200 mg per day.

Children: 20 mg/kg of body weight given daily in divided doses. The tablets are not suitable for children weighing less than 20 kg and no more than two 200 mg tablets should be given in 24 hours to those weighing less than 30 kg.

Contra-indications, warnings, etc

Contra-indications: Ibuprofen should not be used in patients with:

- (a) active peptic ulceration;
- (b) a history of severe peptic ulceration.

Precautions: Special care must be taken when using Ibuprofen in the following situations:

- (a) In patients with asthma;
- (b) In allergic patients or in patients who have developed bronchospasm with other non-steroidal anti-inflammatory agents;
- (c) Pregnancy: As with other agents the use of Ibuprofen during pregnancy should be avoided if possible.

Adverse reactions: As with other non-steroidal anti-inflammatory agents, the most common unwanted effects with Ibuprofen include dyspepsia, gastro-intestinal intolerance and bleeding. Other unwanted effects include a variety of skin rashes and, less commonly, thrombocytopenia. A few cases of toxic amblyopia which recovered on withdrawal of treatment have been reported.

Overdosage: There is no specific antidote to Ibuprofen. Management usually includes gastric lavage associated with special care of plasma electrolytes and any other appropriate symptomatic relief.

Pharmaceutical precautions Apsifen and Apsifen-F Tablets should be stored at room temperature in a dry place and protected from light.

Legal category POM.

Package quantities Polypropylene tubes of 100 and 500 tablets.

Further information Nil.

Product licence numbers

Apsifen and Apsifen-F Tablets 200 mg 0289/0029

Apsifen and Apsifen-F Tablets 400 mg 0289/0037

APSIN® VK

Presentation Apsin VK is available in two presentations, tablets and granules for syrup.

Apsin VK Tablets are round, white, biconvex tablets, scored on one surface, available in two strengths containing the equivalent of 125 mg and 250 mg Penicillin V (as the potassium salt). The products comply with the specification for Phenoxymethylpenicillin Tablets BP.

Apsin VK Syrups are prepared by adding water to the granules to produce an orange coloured and flavoured clear syrup. Each 5 ml syrup contains the equivalent of 125 mg or 250 mg Penicillin V (as the potassium salt). The products comply with the specification for Penicillin V Elixir BPC.

Uses Phenoxymethylpenicillin is a bactericidal agent active against penicillin-sensitive Gram-positive bacteria.

Apsin VK may therefore be used in the management of infections due to penicillin-sensitive organisms, in particular streptococci and staphylococci.

As with other similar agents Phenoxymethylpenicillin has occasionally been used prophylactically, when appropriate before and after surgery or dental treatment in patients at risk from bacterial endocarditis owing to congenital or acquired cardiac valvular disease – eg. rheumatic heart disease.

Dosage and administration (Oral).

Adults: 250 mg every 4 hours, or for prophylaxis 125 mg every 12 hours.

Children: aged 6 to 12 years, 250 mg every six hours; aged 1 to 5 years, 125 mg every six hours.

Infants: under 12 months old should receive 62.5 mg every six hours.

It is recommended that doses are taken 30 minutes before food.

In patients with beta-haemolytic streptococcal infection, it is usual to continue treatment at the full dosage for 10 days in order to minimise the occurrence of secondary complications such as acute nephritis and rheumatic fever.

Contra-indications, warnings, etc

Contra-indications: Phenoxymethylpenicillin should not be used in patients with:

- (a) chronic or deep-seated infections such as subacute bacterial endocarditis, meningitis or syphilis.
- (b) hypersensitivity to penicillins.

Precautions: Special care must be taken when using Phenoxymethylpenicillin in patients with a history of allergy, as they are more likely to develop hypersensitivity reactions. For this reason, penicillin should not be used for trivial infections.

Adverse reactions: Occasionally patients suffer from transient diarrhoea. Hypersensitivity reactions such as urticaria are less common and usually milder than those associated with penicillins given by injection. However, as with all penicillins, anaphylaxis can occur in susceptible hypersensitive individuals and is an acute emergency. Normally, sensitivity reactions may be controlled with antihistamines or, if these fail, with systemic corticosteroids or pressor amines such as adrenaline.

Overdosage: There are no serious sequelae reported, and management should be symptomatic.

Pharmaceutical precautions

Storage: Apstin VK Tablets and granules for Syrup should be stored below 20°C in a dry place, not in a refrigerator. The tablets should be dispensed in airtight containers.

Apstin VK Syrups, when reconstituted, should be used within seven days. They will retain potency for this period if stored below 15°C.

Dilution: Apstin VK Syrups can be diluted with Syrup BP if required. Such dilutions must be freshly prepared.

Legal category POM.

Package quantities

Apstin VK Tablets: Polypropylene tubes of 500 and 1000.

Apstin VK Syrups: Granules to produce 100 ml of Syrup when reconstituted with 60 ml water for 250 mg/5 ml Syrup or 65 ml water for 125 mg/5 ml Syrup.

Further information Nil.

Product licence numbers

Apstin VK Tablets 125 mg	0289/5129
Apstin VK Tablets 250 mg	0289/5130
Apstin VK Syrup 125 mg/5 ml	0289/5278
Apstin VK Syrup 250 mg/5 ml	0289/5279

APSOLOL*

Presentation Apsolol is presented as pink, round, biconvex, film-coated tablets scored on one side and marked 'APS' on the other side. The tablets are also marked with the strength and code number on the scored side. They contain Propranolol Hydrochloride BP and comply with the monograph for Propranolol Tablets BP. Four strengths are available:

Apsolol 10 mg (of Propranolol Hydrochloride BP) marked '10/0212'
Apsolol 40 mg (of Propranolol Hydrochloride BP) marked '40/0213'

Apsolol 80 mg (of Propranolol Hydrochloride BP) marked '80/0214'

Apsolol 160 mg (of Propranolol Hydrochloride BP) marked '160/0215'

Uses Propranolol is a beta adrenergic receptor blocking agent. Its principal effects are on the cardiovascular system.

Apsolol may therefore be used in the management of:

- (a) Angina Pectoris;
- (b) Hypertension;
- (c) Some forms of Cardiac Dysrhythmias;
- (d) Anxiety and Anxiety-induced Tachycardia;
- (e) Hypertrophic Obstructive Cardiomyopathy;
- (f) Essential Tremor.

Beta adrenergic blocking agents, including propranolol, are also used in the prophylaxis of migraine and as an adjunct to the management of Thyrotoxicosis and Cardiac Dysrhythmias associated with anaesthesia.

Dosage and administration (Oral)

Adults: Angina Pectoris, Anxiety, Migraine and Essential Tremor: Initially 40 mg two to three times per day increased at weekly intervals to suit the patient's requirements. The usual dose for angina is in the range 120–240 mg per day and for anxiety, migraine and essential tremor in the range 80–160 mg per day.

Adults: Hypertension: The usual initial dose is 80 mg twice daily and may be increased at weekly intervals as necessary. Most patients will be managed with a dose in the range 160–320 mg per day. It is usual to add a suitable diuretic to the management of most hypertensives who require the higher doses of a beta-blocker.

Adults: Dysrhythmias, Anxiety-induced Tachycardia, Hypertrophic Obstructive Cardiomyopathy and Thyrotoxicosis: Initially 10–40 mg three to four times per day. This dose may be increased to achieve the desired effect.

Children: Occasionally beta-blockers have been given to children for the management of dysrhythmias. There is no accepted dosage scheme, but a useful guide is 0.25–0.50 mg/kg body weight three to four times per day.

Contra-indications, warnings, etc

Contra-indications: Propranolol should not be used:

- (a) In patients with 2nd or 3rd degree heart-block.
- (b) In patients with a history of bronchospasm (Asthma).
- (c) In patients with marked bradycardia (less than 55 b/minute).
- (d) In patients with cardiogenic shock or uncontrolled heart failure.
- (e) In patients receiving VERAPAMIL or other calcium antagonists. Several days should be allowed for complete elimination of one agent before administering the other.

Precautions: Special care must be taken when using beta-blockers such as propranolol in the following situations:

- (a) **Cardiac failure:** If there is evidence of cardiac failure this must be controlled before initiating and during treatment with propranolol.
- (b) **Pulse Rate:** If the pulse rate falls below 50 b/min, treatment should be withdrawn temporarily and resumed at a lower dose.
- (c) **Metabolic Disorders:** In patients with metabolic disorders including alcoholism and diabetic acidosis, great care should be taken in the administration.

tion of propranolol. Treatment with beta-blockers is liable to mask symptoms and deepen the underlying abnormality in hypoglycaemia and other disorders of carbohydrate metabolism. In patients with labile or insulin-dependent diabetes in whom it is proposed to initiate beta-blocker treatment, it may prove necessary to adjust the dosage of the antidiabetic therapy.

- (d) **High Doses:** When high doses of a beta-blocker such as propranolol are used, excessive reduction in blood pressure or pulse rate may occur, particularly when used in conjunction with other hypotensive agents such as neurone blocking agents, vasodilators, reserpine or diuretics.
- (e) **Pregnancy:** Many beta-blockers such as propranolol have been known to cause bradycardia in the foetus, and this may persist after birth. As with all treatment during pregnancy, labour and lactation, extra care should be taken, and as far as possible treatment should be avoided during these periods, to protect the foetus or the suckling new-born child.
- (f) **Other Anti-arrhythmic agents:** Care should be exercised during co-administration or sequential administration, because serious interactions have been reported between some beta-blocking agents and other anti-arrhythmics/cardiac depressants besides verapamil.
- (g) **Anaesthesia:** Should treatment with propranolol be continued over the period of anaesthesia, then atropine (1–2 mg intravenously) should be included in the pre-medication and special care taken to avoid anaesthetics with negative inotropic activity or that encourage vagal dominance, such as ether, cyclopropane, halothane and trichloroethylene. Otherwise withdrawal should be gradual and completed 24 hours before anaesthesia.
- (h) **Renal Failure:** An increased interval between doses may be required to avoid accumulation of propranolol.

Adverse Reactions: Like other beta-blockers, propranolol is well tolerated in normal use. In general untoward effects are minor and include dizziness, headache, insomnia, drowsiness, excitability, gastrointestinal disturbances and rarely bradycardia. Like other beta-blockers, propranolol may precipitate bronchospasm, heart failure, or be associated with cold extremities, and occasionally paraesthesia of the hands, skin rashes and/or dry eyes. The occurrence of these latter symptoms is a reason for discontinuing treatment. (See next paragraph about stopping treatment).

Cessation of treatment: Withdrawal should be gradual, as several beta-blockers, including propranolol, have been associated with a significant increase in symptoms of angina or increase in blood pressure following abrupt withdrawal. If clonidine is co-prescribed, then clonidine should not be withdrawn until several days after Apsolol withdrawal has been completed. (Please refer to prescribing information on clonidine for further information).

Overdosage: Excessive bradycardia and hypotension may be treated with atropine 1–2 mg intravenously and, if necessary, this may be followed by a beta-receptor stimulant such as isoprenaline hydrochloride 25 micrograms intravenously. Where cardiogenic shock has supervened, glucagon 5–10 mg intravenously has been reported to be useful. Bronchospasm may be countered by appropriate beta₂ receptor stimulants such as salbutamol, either by inhalation or 4 micrograms/kg body weight by slow intravenous injection.

Pharmaceutical precautions Apsolol Tablets should be stored at room temperature in a dry place and protected from light.

Legal category POM.

Package quantities

Dispensary packs:

Apsolol 10, 40 and 80 mg: polypropylene tubes of 500 tablets
Apsolol 160 mg: polypropylene tubes of 100 tablets

Patient packs:

Apsolol 10 and 40 mg: white high density polythene bottles of 100 tablets with child resistant screw cap closures.
Apsolol 80 and 160 mg: white high density polythene bottles of 60 tablets with child resistant screw cap closures.

Further information Hypertension is a condition which can benefit from the use of both a beta-blocking agent as contained in Apsolol and a thiazide diuretic such as bendrofluazide. This is because their separate pharmacological actions are complementary in hypertension and may allow adequate treatment with smaller doses of each than would be required if either were to be used alone.

The time-to-peak plasma level in fasted healthy young human volunteers following a single dose of Apsolol is approximately 2 hours, and the excretion half-life of propranolol in plasma is about 2½ hours. However, as with most other beta-blocking agents the onset of biological activity is delayed and the duration is prolonged relative to the plasma concentration. The decay half-life of the biological effect following a single-dose in normal volunteers has been reported to be 11 hours for propranolol, the measure of 'effect' being the reduction in exercise-induced double product (maximum heart rate × systolic blood pressure).†

Product licence numbers

Apsolol Tablets 10 mg 0289/0034
Apsolol Tablets 40 mg 0289/0035
Apsolol Tablets 80 mg 0289/0036
Apsolol Tablets 160 mg 0289/0044

†Vukovich R. A. et al. *Br. J. Clin. Pharmacol.* 1979; 7 Supp 2: 167S–172S.

APSOLOX®

Presentation Apsolex is presented as round, biconvex, film-coated tablets marked 'APS' on one side, while the strength and code number are marked on the other side. The tablets contain Oxprenolol Hydrochloride BP and comply with the monograph for Oxprenolol Tablets BP. Four strengths are available:

Apsolex 20 mg (of Oxprenolol Hydrochloride BP) marked '20/0220' and coloured white.
Apsolex 40 mg (of Oxprenolol Hydrochloride BP) marked '40/0221' and coloured white.
Apsolex 80 mg (of Oxprenolol Hydrochloride BP) marked '80/0222' and coloured yellow.
Apsolex 160 mg (of Oxprenolol Hydrochloride BP) marked '160/0223' and coloured orange.

Uses Oxprenolol is a beta adrenergic receptor blocking agent. As with propranolol its principal effects are on the cardiovascular system. However, oxprenolol is dissimilar

in having partial agonist activity (sometimes termed intrinsic sympathomimetic activity).

Apsolox may therefore be used in the management of:

- (a) Angina Pectoris
- (b) Hypertension
- (c) Some forms of Cardiac Dysrhythmias
- (d) Anxiety-induced Tachycardia
- (e) Hypertrophic Obstructive Cardiomyopathy

Beta adrenergic blocking agents, including oxprenolol, are also used as an adjunct to the management of Thyrotoxicosis and Cardiac Dysrhythmias associated with anaesthesia.

Dosage and administration (Oral)

Adults: Angina Pectoris: The usual dose range is 120–480 mg per day in divided doses to suit the patient's requirements.

Adults: Hypertension: The usual initial dose is 80 mg twice daily and may be increased at weekly intervals as necessary. Most patients will be managed with a dose in the range 160–320 mg per day. It is usual to add a suitable diuretic to the management of most hypertensives who require the higher doses of a beta-blocker.

Adults: Dysrhythmias, Anxiety-induced Tachycardia, Hypertrophic Obstructive Cardiomyopathy and Thyrotoxicosis: Initially 20–40 mg three times per day. This dose may be increased up to 480 mg per day (in divided doses) to achieve the desired effect.

Children: Occasionally beta-blockers have been given to children for the management of dysrhythmias. There is no accepted dosage scheme, but it has been found useful to start with a dose based on 1 mg/kg body weight per day.

Contra-indications, warnings, etc

Contra-indications: Oxprenolol should not be used:

- (a) In patients with 2nd or 3rd degree heart-block.
- (b) In patients with a history of bronchospasm (Asthma).
- (c) In patients with marked bradycardia (less than 55 b/minute).
- (d) In patients with cardiogenic shock or uncontrolled heart failure.
- (e) In patients receiving verapamil or other calcium antagonists. Several days should be allowed for complete elimination of one agent before administering the other.

Precautions: Special care must be taken when using beta-blockers such as oxprenolol in the following situations:

- (a) **Cardiac failure:** If there is evidence of cardiac failure this must be controlled before initiating and during treatment with oxprenolol.
- (b) **Pulse Rate:** If the pulse rate falls below 50 b/min, treatment should be withdrawn temporarily and resumed at a lower dose.
- (c) **Metabolic Disorders:** In patients with metabolic disorders including alcoholism and diabetic acidosis, great care should be taken in the administration of oxprenolol. Treatment with beta-blockers is liable to mask symptoms and deepen the underlying abnormality in hypoglycaemia and other disorders of carbohydrate metabolism. In patients with labile or insulin-dependent diabetes in whom it is proposed to initiate beta-blocker treatment, it may prove necessary to adjust the dosage of the antidiabetic therapy.

(d) **High Doses:** When high doses of a beta-blocker such as oxprenolol are used, excessive reduction in blood pressure or pulse rate may occur, particularly when used in conjunction with other hypotensive agents such as neurone blocking agents, vasodilators, reserpine or diuretics.

(e) **Pregnancy:** Many beta-blockers such as oxprenolol have been known to cause bradycardia in the foetus, and this may persist after birth. As with all treatment during pregnancy, labour and lactation, extra care should be taken, and as far as possible treatment should be avoided during these periods, to protect the foetus or the suckling new-born child.

(f) **Other Anti-arrhythmic agents:** Care should be exercised during co-administration or sequential administration, because serious interactions have been reported between some beta-blocking agents and other antiarrhythmics/cardiac depressants besides verapamil.

(g) **Anaesthesia:** Should treatment with oxprenolol be continued over the period of anaesthesia, then atropine (1–2 mg intravenously) should be included in the pre-medication and special care taken to avoid anaesthetics with negative inotropic activity or that encourage vagal dominance, such as ether, cyclopropane, halothane and trichloroethylene. Similarly, some muscle relaxants – for example suxamethonium – may also increase bradycardia. Otherwise withdrawal should be gradual and completed 24 hours before anaesthesia.

(h) **Renal Failure:** An increased interval between doses may be required to avoid accumulation of oxprenolol.

Adverse Reactions: Like other beta-blockers, oxprenolol is well tolerated in normal use. In general untoward effects are minor and include dizziness, headache, insomnia, drowsiness, excitability, gastrointestinal disturbances and rarely bradycardia. Like other beta-blockers, oxprenolol may precipitate bronchospasm, heart failure, or be associated with cold extremities, skin rashes and/or dry eyes. The occurrence of any of these latter symptoms is a reason for discontinuing treatment. (See next paragraph about stopping treatment).

Cessation of treatment: Withdrawal should be gradual, as several beta-blockers, including oxprenolol, have been associated with a significant increase in symptoms of angina or increase in blood pressure following abrupt withdrawal. If clonidine is co-prescribed, then clonidine should not be withdrawn until several days after Apsolox withdrawal has been completed. (Please refer to prescribing information on clonidine for further information).

Overdosage: Excessive bradycardia and hypotension may be treated with atropine 1–2 mg intravenously and, if necessary, this may be followed by a beta receptor stimulant such as isoprenaline hydrochloride 25 micrograms intravenously. Where cardiogenic shock has supervened, glucagon 5–10 mg intravenously has been reported to be useful. Bronchospasm may be countered by appropriate beta₂ receptor stimulants such as salbutamol, either by inhalation or 4 micrograms/kg body weight by slow intravenous injection.

Pharmaceutical precautions Apsolox Tablets should be stored at room temperature in a dry place. The 80 mg and 160 mg strengths should be protected from light.

Legal category POM.

Package quantities

Dispensary packs:

Apsolox 20, 40 and 80 mg: polypropylene tubes of 500 tablets.

Apsolox 160 mg: polypropylene tubes of 100 tablets

Patient packs:

Apsolox 20 and 40 mg: white high density polythene bottles of 100 tablets with child resistant screw cap closures.

Apsolox 80 and 160 mg: white high density polythene bottles of 60 tablets with child resistant screw cap closures.

Further information Hypertension is a condition which can benefit from the use of both a beta-blocking agent as contained in Apsolox and a thiazide diuretic such as bendrofluazide. This is because their separate pharmacological actions are complementary in hypertension and may allow adequate treatment with smaller

doses of each than would be required if either were to be used alone.

The time-to-peak plasma level in fasted healthy young human volunteers following a single dose of Apsolox is approximately 1½–2 hours, and the excretion half-life of oxprenolol in plasma is about 1½ hours. However, as with most other beta-blocking agents the onset of biological activity is delayed and the duration is prolonged relative to the plasma concentration. The decay half-life of the biological effect following a single-dose in normal volunteers has been reported to be 13 hours for oxprenolol, the measure of 'effect' being the reduction in exercise-induced double product (maximum heart rate × systolic blood pressure).†

Product licence numbers

Apsolox Tablets 20 mg 0289/0050

Apsolox Tablets 40 mg 0289/0051

Apsolox Tablets 80 mg 0289/0052

Apsolox Tablets 160 mg 0289/0053

†Vukovich R. A. et al. *Br. J. Clin. Pharmacol.* 1979; 7 Supp 2: 167S–172S.

* *Trade Mark*

Armour Pharmaceutical Company Limited

St. Leonards House
St. Leonards Road
Eastbourne
East Sussex BN21 3YG



AAA* MOUTH AND THROAT SPRAY

Presentation The can contains 7.5 g with a valve providing 60 × 100 mg metered doses.

Each metered dose contains:

Benzocaine PhEur 1.5 mg
Cetalkonium Chloride 0.0413 mg.
in an inert flavoured propellant.

Uses Treatment of sore throats caused by cold, post-nasal drip and other irritants, and minor infections of the mouth and throat.

Dosage and administration Shake can before use.

Adults: 2 shots every two to three hours if required (not more than 16 shots in 24 hours or as directed by the physician).

Children aged 6–12: 1 shot every two to three hours if required (not more than 8 shots in 24 hours or as directed by the physician).

Contra-indications, warnings, etc

Side-effects: Hypersensitivity reactions to benzocaine have been reported.

Precautions: Avoid spraying into eyes.

Contents under pressure – do not puncture.

Keep away from heat and flames – do not throw finished container into fire.

Contra-indications: Known hypersensitivity to Benzocaine.

Pharmaceutical precautions Store in a cool place. Shelf-life 5 years. Shake can before use.

Legal category P.

Package quantities Single can containing 7.5 g with a valve providing 60 × 100 mg metered doses (shots).

Further information Published clinical studies have demonstrated antibacterial activity by the reduction in the population of pathogenic organisms of the buccal mucosa. Together with the spray's local anaesthetic activity, this has been found of value in the treatment of pain and infection following tonsillectomy.

Product licence number 0231/5026.

ACTHAR* GEL

Presentation Corticotrophin Gelatin Injection BP in vials containing 20, 40 and 80 i.u./ml for subcutaneous or intramuscular use only.

Uses Rheumatic and Collagen diseases. Asthma. Diseases of the GI tract (e.g. ulcerative colitis). Nephrotic syndrome. Diseases of the CNS (e.g. Bell's Palsy, Retrobulbar Neuritis and Multiple Sclerosis). Adrenal function tests. Chronic skin and allergic conditions responsive to corticosteroids (e.g. psoriasis and certain eczemas and refractory hay fever unresponsive to conventional treatment).

Dosage and administration General information on dosage for therapeutic use. The aim of treatment with Acthar Gel is to obtain a satisfactory therapeutic effect with minimal dosage, the clinical response being the sole measure of adequate dosage. Therapeutic effects may appear within hours, although with some chronic diseases improvement may not show for several days.

Because patients' adrenal glands vary in their sensitivity to ACTH and because disease conditions vary in their response to corticosteroids, no specific uniform dose can be equally effective for all individuals. Some conditions, e.g. acute exacerbations of asthma and multiple sclerosis may require high doses initially to obtain a remission. Once the disease is under control the total daily dosage should be decreased as rapidly as possible. Dosage reduction should be consistent with maintaining clinical improvement. Some conditions, e.g. rheumatoid arthritis, nephrotic syndrome and chronic asthma may need long-term maintenance therapy. Again, the aim is to obtain satisfactory therapeutic effect with minimal dosage. If the treatment regimen is started on a daily basis when the smallest daily maintenance dose has been established (say 20 i.u.), attempts should be made to lengthen the dosage intervals. If at any step of dosage reduction symptoms reappear, a return to the previous effective schedule is necessary before a further attempt at dosage reduction is made. On occasions Acthar Gel can be completely withdrawn as the patient experiences a remission.

Instead of starting with daily injections, it may be more convenient to commence with an initial higher fixed unit dosage (say 40 i.u. per injection) twice or thrice weekly.

Suggested practical regimens for specific conditions are given below. These are guidelines only, the dosage should be titrated to the patient's response.

Conditions needing maintenance therapy

Rheumatoid arthritis: Initially a dose of 40 i.u. should be given daily. Review the dosage at intervals of three days and adjust according to the clinical response. The dosage should be increased or decreased bearing in mind that the ideal dosage is the minimum necessary to relieve symptoms.

Chronic asthma: Initially a dose of 40–80 i.u. should be given daily for a period of five days. Reduce by steps of 10 i.u. until symptoms are satisfactorily controlled. On remission of symptoms, treatment may be withdrawn completely. In some patients, however, continued therapy may be necessary.

Still's disease: 40 i.u. Acthar Gel daily for three days reducing to 20 i.u. on alternate days. Suppression of symptomatology without the appearance of 'cushingoid signs' is the aim of therapy.

The administration of ACTH to children should be confined to early morning (approximately 10 a.m.) to reduce the incidence of 'growth interference'.

Conditions requiring short – medium term therapy *Acute exacerbation of asthma:* 200 i.u. Acthar

Gel repeated at a 72-hour interval gives remission in the majority of cases. Upon remission the dosage should be reduced to maintenance levels (see chronic asthma).

Very high levels of corticosteroids may be needed rapidly in cases of status asthmaticus, and the delay in achieving this by corticotrophin treatment may render this form of therapy inappropriate here, at least initially.

Hay fever: Acthar Gel should be reserved for patients with refractory hay fever unresponsive to conventional treatment, e.g. antihistamines and topical medication, who may benefit from treatment with ACTH Gel. The dosage and duration of treatment will depend upon the severity of the condition. In adults, dosages of up to 40–80 i.u. once or twice weekly during the pollen season can be given. In children under the age of seven, the use of ACTH treatment for hay fever is not recommended unless absolutely necessary. In children over the age of seven, the dosage should not exceed 40–80 i.u. Acthar Gel given in the early morning once or twice weekly during the pollen season. The child should be carefully monitored during the course of therapy for side-effects including diminution of growth velocity and hypothalamic pituitary suppression.

Bell's Palsy: Treatment should commence as soon as possible after the onset of paralysis.

Acthar Gel 80 i.u. daily for five days, reducing to 60 i.u. on day 6, 40 i.u. on day 7, 20 i.u. on day 8 and 10 i.u. on days 9 and 10.

Alternatively a simplified regimen of 40 i.u. daily for 10 days, or until signs of improvement occur, can be employed.

Retrobulbar neuritis: Acthar Gel 40 i.u. daily for a period of 30 days.

Ulcerative colitis and Crohn's disease: For the treatment of acute exacerbations of Crohn's disease and Ulcerative Colitis, a short course of treatment is generally used. The starting dose should be 80–120 units daily and should be rapidly reduced consistent with maintaining clinical remission. Maintenance therapy with other agents may then be necessary.

Multiple Sclerosis: For the treatment of exacerbations of Multiple Sclerosis a diminishing dosage regimen is generally used. The initial dosage should be between 80–120 i.u. daily for the first week. Subsequently daily dosages should be reduced on a weekly basis over three-six weeks to 10–20 i.u. and then stopped.

Nephrotic Syndrome: For the treatment of nephrotic syndrome, a short course of treatment is generally used. Administer Acthar Gel 60–80 i.u. daily for 10–12 days and then stop treatment abruptly to allow spontaneous diuresis. If diuresis is inadequate repeat treatment after 5 days.

Adrenal function tests: Withdraw 5–8 ml venous blood into a heparinised tube, then inject intramuscularly 40 i.u. Acthar Gel. A further sample should be taken after approximately 4 hours and the rise in plasma hydroxy-corticosteroids measured.

Contra-indications, warnings, etc

Precautions and contra-indications: The contra-indications to ACTH are those of corticosteroids but are rarely absolute. Only after careful consideration should ACTH be given to patients suffering from: active tuberculosis, peptic ulcer, acute psychosis, hypertension, diabetes mellitus, congestive heart failure. Cushing's syndrome, osteoporosis or pregnancy.

As with corticosteroids, ACTH may increase susceptibility to infections.

Side-effects: Side-effects such as hyperglycaemia, psychological disturbances, hypertension, sodium retention, potassium loss, peptic ulcer formation and osteoporosis may occur. The occurrence of these side effects may be a sign of overdosage and may be reversed either by reducing the dosage or withdrawing therapy. Some side-effects, such as peptic ulceration and osteoporosis are thought to be less common with ACTH than with corticosteroid therapy.

Warnings: Hypersensitivity reactions may occur.

Pharmaceutical precautions *Acthar Gel:* Should be stored between 2–10°C and protected from light. Shelf-life 18 months.

Legal category POM.

Package quantities For intramuscular and subcutaneous use.

Acthar Gel:

5 ml vial 20 i.u. per ml

2 ml vial 40 i.u. per ml

5 ml vial 40 i.u. per ml

5 ml vial 80 i.u. per ml

Further information

To replace corticosteroids with Acthar Gel:

1. To establish adrenal responsiveness: Administer 80–120 i.u. daily together with current steroid dosage until therapeutic or biochemical response or overdosage effects occur.

Clinical: Increased weight, sense of well-being and increased appetite, flushing of the face, and major reduction of disease symptoms.

Biochemical: Raised plasma cortisol levels or raised urinary excretion of 17-hydroxycorticosteroids.

2. As soon as adrenal response is established, reduce steroids by 25% of the original dose each day, maintaining the above dosage pattern of Acthar Gel.

3. When steroids are safely withdrawn, reduce Acthar Gel dosage to maintenance level.

To replace tetracosactrin depot with Acthar Gel: Substitute 40 units of Acthar Gel for each 0.5 mg of the tetracosactrin depot preparation. There should be no necessity to increase the frequency of injections.

Unduly large or small injection volumes are obviated by the comprehensive range of Acthar Gel strengths which are available.

Product licence numbers

Acthar Gel 0231/5000, 0231/5051, 0231/5052

ALBUMINAR[®]-5

Presentation Albuminar-5 is a sterile aqueous solution of Normal Serum Albumin (Human) 5% obtained from large pools of adult human venous plasma. Each 100 ml of Albuminar-5 contains 5 g of human serum albumin which is osmotically equivalent to normal human plasma.

The product conforms to the monograph for Normal Serum Albumin (Human) USP.

Indications Albuminar-5 is indicated in: The emergency treatment of shock and in other conditions where the restoration of blood volume is urgent.

Serious burns to prevent haemoconcentration and to combat fluid and sodium losses.

Clinical situations associated with low plasma protein (Hypoproteinaemia) with or without oedema, provided that sodium restriction is not imperative.

Therapeutic Plasma Exchange as a replacement fluid for phoresed plasma.

Dosage and administration (a) *Administration:* Albuminar-5 is for intravenous infusion.

Albuminar-5 may be given intravenously without further dilution; 5% solution is approximately isotonic and isosmotic with citrated plasma.

When albumin solution is administered to patients with normal blood volume, particular attention should be given to the rate of infusion so that the plasma volume is not expanded too rapidly.

(b) *Standard dose: Urgent restoration of blood volume:* In the emergency treatment of shock, the amount of albumin and duration of therapy must be based on the responsiveness of the patient as indicated by blood pressure, central venous pressure, degree of pulmonary congestion and haematocrit. The initial dose may be followed by additional albumin within 15–30 minutes if the response is deemed inadequate. If there has been considerable loss of blood, transfusion with whole blood is indicated, or if there is continued loss of protein, blood or plasma it may also be desirable to give whole blood and/or other blood fractions.

Burns: Albuminar-5 may be used to prevent marked haemoconcentration and to maintain appropriate electrolyte balance. An optimal regimen involving the use of albumin, crystalloids and water has not been established. Suggested therapy in the treatment of burns includes administration of large volumes of crystalloid solution during the first 24 hours to maintain an adequate plasma volume, even when albumin is infused. Continuation of therapy beyond 24 hours usually requires more albumin and less crystalloid solution. Duration of treatment varies depending on the extent of protein loss through renal excretion, denuded areas of skin and decreased albumin synthesis. Attempts to raise the albumin level above 40 g/litre may only result in an increased rate of catabolism.

Conditions associated with hypoproteinaemia: In these conditions, 1,000 to 1,500 ml of Albuminar-5 may be required to reduce oedema and to bring serum protein values to normal. Since such patients usually have approximately normal blood volume, doses of more than 500 ml of Albuminar-5 should not be given faster than 500 ml in 30–45 minutes to avoid circulatory embarrassment. If slower administration is desired, e.g. in patients with hypertension or cardiac insufficiency, 1,000 ml of Albuminar-5 may be administered by continuous drip at a rate of 100 ml of this solution per hour. Unless the pathological condition responsible for the hypoproteinaemia can be corrected, albumin in any form can afford only symptomatic or supportive relief. The 5% solution should not be administered in situations where sodium restriction is imperative.

Therapeutic plasma exchange: In plasma exchange procedures the volume of plasma removed may be replaced with an equivalent volume of Albuminar-5.

(c) *Children:* The amount of albumin given and the duration of therapy must be determined by the child's condition, response and other parameters, as stated under 'Standard Dose'. However, when treating children, their body weight should also be taken into account.

Use in pregnancy: There is some experience of albumin

being used in the treatment of pre-eclampsia and eclampsia. However, there is very little experience of the use of albumin in the early stages of pregnancy. There is no evidence either in human pregnancy or in animal work that administration of albumin is free from hazard.

Pharmacology: Action: Albuminar-5 is active osmotically and is therefore important in regulating the volume of circulating blood. When the circulating blood volume has been depleted, the haemodilution following albumin administration persists for many hours. In individuals with normal blood volumes, it usually lasts only a few hours.

Contra-indications, warnings, etc *Contra-indications:* Albuminar-5 may be contra-indicated in patients with severe anaemia or cardiac failure.

Precautions: If dehydration is present additional fluids must accompany or follow the administration of Albuminar-5.

The rise in blood pressure which may follow rapid administration of albumin necessitates careful observation of the injured patient to detect bleeding points, which failed to bleed at the lower blood pressure; otherwise new haemorrhage and shock may occur.

Albuminar-5 should be administered with caution to patients with low cardiac reserve or with no albumin deficiency, because a rapid increase in plasma volume may cause circulatory embarrassment or pulmonary oedema. In cases of hypertension or cardiac insufficiency, a slower rate of administration is desirable, at a rate of 5 g of albumin (100 ml) per hour. A careful watch must be kept for the possible development of pulmonary oedema. Should pulmonary oedema occur, the infusion must be stopped immediately.

Warnings and adverse effects: Do not use if the solution is turbid or contains a deposit. Since the solution contains no preservative, it should be used within 3 hours after entering the vial.

The incidence of adverse reactions to Normal Serum Albumin (Human) 5% is low, although nausea, vomiting, increased salivation and febrile reactions may occasionally occur.

Toxicity and treatment of overdosage: Administration of large quantities of albumin should be supplemented with red cell concentrates or replaced by whole blood to combat the relative anaemia which would follow such use. If circulatory embarrassment or pulmonary oedema should develop, the infusion must be stopped immediately and specific treatment given.

Pharmaceutical precautions

(a) *Presentation and Composition:* Albuminar-5 is a sterile, clear, brownish, slightly viscous aqueous solution of human serum albumin. It is stabilised with 0.004 M sodium acetyltryptophanate and 0.004 M sodium caprylate and the pH of the solution is adjusted with sodium bicarbonate or acetic acid. The solution contains approximately 130–160 mmol/l of sodium and not more than 1 mmol/l of potassium. The solution contains no preservative.

(b) *Storage:* Albuminar-5 should be stored at a temperature between 2° and 25°C. Freezing will not harm the solution, but might damage the container and allow contamination of the contents.

Protect solution from light.

When stored as directed Albuminar-5 has a shelf-life of 3 years.

Legal category POM.

Package quantities

Albuminar-5 is supplied as a 5% solution in:

- 250 ml glass vials containing 12.5 grams of albumin
- 500 ml glass vials containing 25.0 grams of albumin
- 1,000 ml glass vials containing 50.0 grams of albumin.

Further information Albuminar-5 is prepared from blood that was non-reactive for hepatitis B surface antigen (HBsAg) when tested with licensed reagents. The likelihood of the presence of viable hepatitis viruses has been further minimised by pasteurising the product at 60°C for 10 hours. Such treatment has been shown to be effective in this respect even when prepared from plasma known to be infective and albumin so prepared, unlike whole blood or plasma, is considered free of the danger of homologous serum hepatitis. Albuminar-5 may be given in conjunction with other parenteral fluids, such as whole blood, plasma, saline, dextrose, or sodium lactate. It is convenient to use, since no cross-matching is required and the absence of cellular elements removes the danger of sensitisation with repeated infusions.

Albuminar-5 contains none of the recognised components of the clotting mechanism of normal blood or plasma. It does not interfere with the normal clotting of blood.

Product licence number 0231/0056.

ALBUMINAR-20

Presentation Albuminar-20 is a sterile aqueous solution of Normal Serum Albumin (Human) 20% obtained from large pools of adult human venous plasma. Each 100 ml of Albuminar-20 contains 20 g of human serum albumin which is osmotically equivalent to 400 ml of normal human plasma.

The product conforms to the monograph for Human Albumin BP.

Indications Albuminar-20 is indicated in: The emergency treatment of shock and in other conditions where the restoration of blood volume is urgent.

Serious burns to prevent haemoconcentration and to combat fluid and sodium losses.

Clinical situations associated with low plasma protein (hypoproteinaemia) with or without oedema.

As an adjunct to exchange transfusion for the treatment of hyperbilirubinaemia in haemolytic disease of the newborn.

In priming heart lung machines for cardiopulmonary by-pass surgery.

Dosage and administration

(a) **Administration:** Albuminar-20 is for intravenous infusion.

Albuminar-20 may be given intravenously without dilution or it may be diluted with normal saline or 5% dextrose before administration, 250 ml per litre gives a solution which is approximately isotonic and isosmotic with citrated plasma.

When undiluted albumin solution is administered to patients with normal blood volume, particular attention should be given to the rate of infusion so that the plasma volume is not expanded too rapidly.

(b) **Standard dose:** *Urgent restoration of blood volume:* In these conditions effectiveness of Albuminar-20 depends on its ability to draw tissue fluid into the blood stream, when such fluid is available. Therefore, if dehydration is present, other fluids must be administered

by any available route, either with albumin or following it. In the emergency treatment of shock, the amount of albumin and duration of therapy must be based on the responsiveness of the patient as indicated by blood pressure, central venous pressure, degree of pulmonary congestion and haematocrit. The initial dose may be followed by additional albumin within 15–30 minutes if the response is deemed inadequate. If there has been considerable loss of blood, transfusion with whole blood is indicated, or if there is continued loss of protein, blood or plasma it may also be desirable to give whole blood and/or other blood fractions.

Burns: Albuminar-20 may be used in conjunction with normal saline or dextrose to prevent marked haemoconcentration and to maintain appropriate electrolyte balance. An optimal regimen involving the use of albumin, crystalloids and water has not been established. Suggested therapy in the treatment of burns includes administration of large volumes of crystalloid solution during the first 24 hours to maintain an adequate plasma volume, even when albumin is infused. Continuation of therapy beyond 24 hours usually requires more albumin and less crystalloid solution. Duration of treatment varies depending on the extent of protein loss through renal excretion, denuded areas of skin and decreased albumin synthesis. Attempts to raise the albumin level above 40 g/litre may only result in an increased rate of catabolism.

Conditions associated with hypoproteinaemia: In these conditions, 200 to 300 ml of Albuminar-20 may be required to reduce oedema and to bring serum protein values to normal. Since such patients usually have approximately normal blood volume, doses of more than 100 ml of Albuminar-20 should not be given faster than 100 ml in 30–45 minutes to avoid circulatory embarrassment. If slower administration is desired, e.g. in patients with hypertension or cardiac insufficiency, 250 ml of Albuminar-20 may be mixed with 250 ml of 10% dextrose solution and administered by continuous drip at a rate of 100 ml of this dextrose solution per hour. Unless the pathological condition responsible for the hypoproteinaemia can be corrected, albumin in any form can afford only symptomatic or supportive relief.

Hyperbilirubinaemia in haemolytic disease of the newborn: In neonates, with serum bilirubin levels above 20 mg per 100 ml severe cerebral damage can develop due to kernicterus. In hypoalbuminaemia the reserve binding capacity for bilirubin is decreased and consequently bilirubin toxicity increases and with it the risk of cerebral damage. The risk of cerebral damage can be reduced by correction of the bilirubin binding capacity with Albuminar-20.

If immediate protection of the patient is required an intravenous injection of 1.0–1.5 g/kg albumin (5–7 ml Albuminar-20/kg bodyweight) can be given. Following this injection the exchange transfusion procedure should be instituted within 6 hours.

If albumin is intended for increasing the removal of bilirubin during exchange transfusion, it is suggested that 1.5–2.5 g albumin (7–12 ml Albuminar-20) is added to each 100 ml donor blood during exchange transfusion.

In Priming Heart Lung Machines for Cardiopulmonary By-Pass Surgery: Pre-operative dilution of the blood by use of a pump prime consisting of only albumin and crystalloid has been shown to be well tolerated during clinical studies. An albumin concentration of 5 g per cent has been widely used. A commonly employed pro-

gramme is an albumin and crystalloid pump prime adjusted so as to achieve a haematocrit reading of 20 per cent and a plasma albumin level of 2.5 g/100 ml in the patient.

(c) *Children:* The amount of albumin given and the duration of therapy must be determined by the child's condition, response and other parameters, as stated under 'Standard Dose'. However, when treating children, their body weight should also be taken into account.

Use in pregnancy: There is some experience of albumin being used in the treatment of pre-eclampsia and eclampsia. However, there is very little experience of the use of albumin in the early stages of pregnancy. There is no evidence either in human pregnancy or in animal work that administration of albumin is free from hazard.

Pharmacology: Action: Albuminar-20 is active oncologically and is therefore important in regulating the volume of circulating blood. When injected intravenously, 50 ml of Albuminar-20 draws approximately 3 volumes of additional fluid into the circulation within 15 minutes, except in the presence of marked dehydration. This extra fluid reduces haematocrit and blood viscosity. The degree of volume expansion is dependent on the initial blood volume. When circulating blood volume has been depleted, the haemodilution following albumin administration persists for many hours. In individuals with normal blood volume, it usually lasts only a few hours.

Contra-indications, warnings, etc

Contra-indications: Albuminar-20 may be contra-indicated in patients with severe anaemia or cardiac failure.

Precautions: If dehydration is present additional fluids must accompany or follow the administration of Albuminar-20.

The rise in blood pressure which may follow rapid administration of albumin necessitates careful observation of the injured patient to detect bleeding points, which failed to bleed at the lower blood pressure; otherwise new haemorrhage and shock may occur.

Albuminar-20 should be administered with caution to patients with low cardiac reserve or with no albumin deficiency, because a rapid increase in plasma volume may cause circulatory embarrassment or pulmonary oedema. In cases of hypertension or cardiac insufficiency, a slower rate of administration is desirable: 250 ml of Albuminar-20 may be mixed with 250 ml of 10% dextrose solution and administered at a rate of 10 g of albumin (100 ml) per hour. A careful watch must be kept for the possible development of pulmonary oedema. Should pulmonary oedema occur, the infusion must be stopped immediately.

Warnings and adverse effects: Do not use if the solution is turbid or contains a deposit. Since the solution contains no preservative, it should be used within 3 hours after entering the vial.

The incidence of adverse reactions to Normal Serum Albumin (Human) 20% is low, although nausea, vomiting, increased salivation and febrile reactions may occasionally occur.

Toxicity and treatment of overdosage: Administration of large quantities of albumin should be supplemented with red cell concentrates or replaced by whole blood to combat the relative anaemia which would follow such use.

If circulatory embarrassment or pulmonary oedema should develop, the infusion must be stopped immediately and specific treatment given.

Pharmaceutical precautions

(a) *Presentation and composition:* Albuminar-20 is a sterile, clear, brownish, slightly viscous aqueous solution of human serum albumin. It is stabilised with 0.016 M sodium acetyltryptophanate and 0.016 M sodium caprylate and the pH of the solution is adjusted with sodium bicarbonate or acetic acid. The solution contains not more than 130 mmol/l of sodium and not more than 1 mmol/l of potassium. The solution contains no preservative.

(b) *Storage:* Albuminar-20 should be stored at a temperature between 2° and 25°C. Freezing will not harm the solution, but might damage the container and allow contamination of the contents. Protect solution from light.

When stored as directed, Albuminar-20 has a shelf-life of 3 years.

Legal category POM.

Package quantities Albuminar-20 is supplied as a 20% solution in:

- 50 ml vials containing 10.0 grams of albumin;
- 100 ml vials containing 20.0 grams of albumin.

Further information Albuminar-20 is prepared from blood that was non-reactive for hepatitis B surface antigen (HBsAg) when tested with licensed reagents. The likelihood of the presence of viable hepatitis viruses has been further minimised by pasteurising the product at 60°C for 10 hours. Such treatment has been shown to be effective in this respect even when prepared from plasma known to be infective and albumin so prepared, unlike whole blood or plasma, is considered free of the danger of homologous serum hepatitis.

Albuminar-20 may be given in conjunction with other parenteral fluids, such as whole blood, plasma, saline, dextrose, or sodium lactate. It is convenient to use, since no cross-matching is required with the absence of cellular elements removes the danger of sensitisation with repeated infusions.

Albuminar-20 contains none of the recognised components of the clotting mechanism of normal blood or plasma. It does not interfere with the normal clotting of blood.

Product licence number 0231/0057

ALBUMINAR-25

Presentation Albuminar-25 is a sterile aqueous solution of Normal Serum Albumin (Human) 25% obtained from large pools of adult human venous plasma. Each 100 ml of Albuminar-25 contains 25 g of human serum albumin which is osmotically equivalent to 500 ml of normal human plasma.

The product conforms to the monograph for Normal Serum Albumin (Human) USP.

Indications Albuminar-25 is indicated in: The emergency treatment of shock and in other conditions where the restoration of blood volume is urgent.

Serious burns to prevent haemoconcentration and to combat fluid and sodium losses.

Clinical situations associated with low plasma protein (hypoproteinaemia) with or without oedema.

As an adjunct to exchange transfusion for the treatment of hyperbilirubinaemia in haemolytic disease of the newborn.

In priming heart-lung machines for cardiopulmonary by-pass surgery.

Dosage and administration

(a) *Administration:* Albuminar-25 is for intravenous infusion.

Albuminar-25 may be given intravenously without dilution or it may be diluted with normal saline or 5% dextrose before administration; 200 ml per litre gives a solution which is approximately isotonic and isosmotic with citrated plasma.

When undiluted albumin solution is administered to patients with normal blood volume, particular attention should be given to the rate of infusion so that it is slow enough to prevent too rapid expansion of plasma volume.

(b) *Standard dose: Urgent restoration of blood volume:* In these conditions effectiveness of Albuminar-25 depends on its ability to draw tissue fluid into the blood stream, when such fluid is available. Therefore, if dehydration is present, other fluids must be administered by any available route, either with albumin or following it. In the emergency treatment of shock, the amount of albumin and duration of therapy must be based on the responsiveness of the patient as indicated by blood pressure, central venous pressure, degree of pulmonary congestion and haematocrit. The initial dose may be followed by additional albumin within 15–30 minutes if the response is deemed inadequate. If there has been considerable loss of blood, transfusion with whole blood is indicated, or if there is continued loss of protein, blood or plasma it may also be desirable to give whole blood and/or other blood fractions.

Burns: Albuminar-25 may be used in conjunction with normal saline or dextrose to prevent marked haemoconcentration and to maintain appropriate electrolyte balance. An optimal regimen involving the use of albumin, crystalloids and water has not been established. Suggested therapy in the treatment of burns includes administration of large volumes of crystalloid solution during the first 24 hours to maintain an adequate plasma volume, even when albumin is infused. Continuation of therapy beyond 24 hours usually requires more albumin and less crystalloid solution. Duration of treatment varies depending on the extent of protein loss through renal excretion, denuded areas of skin and decreased albumin synthesis. Attempts to raise the albumin level above 40 g/litre may only result in an increased rate of catabolism.

Conditions associated with hypoproteinaemia: In these conditions, 200 to 300 ml of Albuminar-25 may be required to reduce oedema and to bring serum protein values to normal. Since such patients usually have approximately normal blood volume, doses of more than 100 ml of Albuminar-25 should not be given faster than 100 ml in 30–45 minutes to avoid circulatory embarrassment. If slower administration is desired, e.g. in patients with hypertension or cardiac insufficiency, 200 ml of Albuminar-25 may be mixed with 300 ml of 10% dextrose solution and administered by continuous drip at a rate of 100 ml of this dextrose solution per hour. Unless the pathological condition responsible for the hypoproteinaemia can be corrected, albumin in any form can afford only symptomatic or supportive relief.

Hyperbilirubinaemia in haemolytic disease of the newborn: In neonates with serum bilirubin levels above 20 mg per 100 ml severe cerebral damage can develop due to kernicterus. In hypoalbuminaemia the reserve binding capacity for bilirubin is decreased and conse-

quently bilirubin toxicity increases and with it the risk of cerebral damage. The risk of cerebral damage can be reduced by correction of the bilirubin binding capacity with Albuminar-25.

If immediate protection of the patient is required an intravenous injection of 1.0–1.5 g/kg albumin (4–6 ml Albuminar-25/kg bodyweight) can be given. Following this injection the exchange transfusion procedure should be instituted within 6 hours.

If albumin is intended for increasing the removal of bilirubin during exchange transfusion, it is suggested that 1.5–2.5 g albumin (6–10 ml Albuminar-25) is added to each 100 ml donor blood during exchange transfusion.

In Priming Heart Lung Machines for Cardiopulmonary By-Pass Surgery: Pre-operative dilution of the blood by use of a pump prime consisting of only albumin and crystalloid has been shown to be well tolerated during clinical studies. An albumin concentration of 5 g per cent has been widely used. A commonly employed programme is an albumin and crystalloid pump prime adjusted so as to achieve a haematocrit reading of 20 per cent and a plasma albumin level of 2.5 g/100 ml in the patient.

(c) *Children:* The amount of albumin given and the duration of therapy must be determined by the child's condition, response and other parameters, as stated under 'Standard Dose'. However, when treating children, their body weight should also be taken into account.

Use in pregnancy: There is some experience of albumin being used in the treatment of pre-eclampsia and eclampsia. However, there is very little experience of the use of albumin in the early stages of pregnancy. There is no evidence either in human pregnancy or in animal work that administration of albumin is free from hazard.

Pharmacology: Action: Albuminar-25 is active oncologically and is therefore important in regulating the volume of circulating blood. When injected intravenously, 50 ml of Albuminar-25 draws approximately 175 ml of additional fluid into the circulation within 15 minutes, except in the presence of marked dehydration. This extra fluid reduces haematocrit and blood viscosity. The degree of volume expansion is dependent on the initial blood volume. When circulating blood volume has been depleted, the haemodilution following albumin administration persists for many hours. In individuals with normal blood volume, it usually lasts only a few hours.

Contra-indications, warnings, etc

Contra-indications: Albuminar-25 may be contra-indicated in patients with severe anaemia or cardiac failure.

Precautions: If dehydration is present additional fluids must accompany or follow the administration of Albuminar-25.

The rise in blood pressure which may follow rapid administration of albumin necessitates careful observation of the injured patient to detect bleeding points, which failed to bleed at the lower blood pressure; otherwise new haemorrhage and shock may occur.

Albuminar-25 should be administered with caution to patients with low cardiac reserve or with no albumin deficiency, because a rapid increase in plasma volume may cause circulatory embarrassment or pulmonary oedema. In cases of hypertension or cardiac insufficiency, a slower rate of administration is desirable: 200 ml of Albuminar-25 may be mixed with 300 ml of 10% dextrose solution and administered at a rate of 10 g of albumin (100 ml) per hour. A careful watch must be kept for the possible development of pulmonary oedema.

Should pulmonary oedema occur, the infusion must be stopped immediately.

Warnings and adverse effects: Do not use if the solution is turbid or contains a deposit. Since the solution contains no preservative, it should be used within 3 hours after entering the vial.

The incidence of untoward reactions to Normal Serum Albumin (Human) 20% is low, although nausea, vomiting, increased salivation and febrile reactions may occasionally occur.

Toxicity and treatment of overdosage: Administration of large quantities of albumin should be supplemented with red cell concentrates or replaced by whole blood to combat the relative anemia which would follow such use.

If circulatory embarrassment or pulmonary oedema should develop, the infusion must be stopped immediately and specific treatment given.

Pharmaceutical precautions

(a) **Presentation and composition:** Albuminar-25 is a sterile, clear, brownish, slightly viscous aqueous solution of human serum albumin. It is stabilised with 0.02 M sodium acetyltryptophanate and 0.02 M sodium caprylate and the pH of the solution is adjusted with sodium bicarbonate or acetic acid. The solution contains approximately 130–160 mmol/l of sodium and not more than 1 mmol/l of potassium. The solution contains no preservative.

(b) **Storage:** Albuminar-25 should be stored at a temperature between 2° and 25°C. Freezing will not harm the solution, but might damage the container and allow contamination of the contents. Protect solution from light.

When stored as directed, Albuminar-25 has a shelf-life of 3 years.

Legal category POM.

Package quantities Albuminar-25 is supplied as a 25% solution in:

- 20 ml vials containing 5.0 grams of albumin.
- 50 ml vials containing 12.5 grams of albumin;
- 100 ml vials containing 25.0 grams of albumin.

Further information Albuminar-25 is prepared from blood that was non-reactive for hepatitis B surface antigen (HBsAg) when tested with licensed reagents. The likelihood of the presence of viable hepatitis viruses has been further minimised by pasteurising the product at 60°C for 10 hours. Such treatment has been shown to be effective in this respect even when prepared from plasma known to be infective and albumin so prepared, unlike whole blood or plasma, is considered free of the danger of homologous serum hepatitis.

Albuminar-25 may be given in conjunction with other parenteral fluids, such as whole blood, plasma, saline, dextrose, or sodium lactate. It is convenient to use, since no cross-matching is required and the absence of cellular elements removes the danger of sensitisation with repeated infusions.

Albuminar-25 contains none of the recognised components of the clotting mechanism of normal blood or plasma. It does not interfere with the normal clotting of blood.

Product licence number 0231/0045

CALCITARE*

Presentation For intramuscular or subcutaneous use only. Each vial contains 160 international units porcine calcitonin with a vial of gelatin diluent.

Uses Paget's disease of bone

Hypercalcaemia: The calcium lowering effect of calcitonin is usually rapid. Treatment should be regarded as an adjunct to more specific long-term measures. The fall in serum calcium is more pronounced in hypercalcaemic patients with a raised bone turnover, e.g. Paget's disease and thyrotoxicosis. Treatment may also be beneficial in patients with hypercalcaemia due to immobilisation in Paget's disease, malignancy, vitamin D intoxication and hyperparathyroidism. Calcitonin is of particular value when such patients have concurrent renal or cardiac failure.

Dosage and administration Calcitare can be given subcutaneously or intramuscularly.

1. **Paget's disease of bone:** Clinical and biochemical improvement has been observed with dosage regimens ranging from 80 international units three times a week to 160 international units daily in single or divided doses.

Daily injections of 80 international units or 160 international units are recommended for three to six months in patients with bone pain or nerve compression syndromes.

Clinical improvement is usually seen within three months but may occasionally be delayed for as long as a year. When clinical improvement occurs, an attempt to reduce the dose and/or frequency of injection may be made, consistent with maintaining a remission. Alternatively, treatment can be stopped and restarted at a later date when necessary.

Biochemical improvement is shown by a reduction in serum alkaline phosphatase and urinary hydroxyproline excretion, the fall in urinary hydroxyproline often occurring in a matter of days. The fall in serum alkaline phosphatase occurs in a matter of weeks. Serum alkaline phosphatase and urinary hydroxyproline levels return slowly towards pre-treatment values (at different rates) on withdrawal of calcitonin therapy. Long-term treatment with calcitonin may be needed in those asymptomatic patients with rapidly advancing and potentially disabling disease.

Radiological and histological improvement has also been observed with long-term treatment and this reconstructive action of calcitonin on bone has been shown to be dose-dependent.

When changing from synthetic salmon calcitonin (Calsynar) to porcine calcitonin (Calcitare), 80 international units of Calcitare may be conveniently substituted for 50 international units of Calsynar and 160 international units for 100 international units respectively.

2. **Hypercalcaemia:** The optimum dosage pattern must essentially be gauged by the magnitude of the hypocalcaemic response obtained in a particular patient. In general the greatest response will be observed in cases of rapid bone turnover. Four international units per kg per day of Calcitare may produce a fall in serum calcium. However, larger doses of calcitonin may be necessary, but are inconvenient to administer as Calcitare, in which case treatment with Calsynar is advised.

Contra-indications, warnings and side-effects

Calcitonin may cause nausea, vomiting, facial flushing and tingling of the hands. An unpleasant taste and

inflammatory reactions at the injection site have been reported. The nausea and flushing are usually transient and rarely necessitate withdrawal of treatment. If necessary, the injections can be administered at night with an antiemetic.

In any patient with a history of allergy; a scratch (or intradermal) test should be conducted prior to administration of Calcitare using a 1:100 dilution in Sodium Chloride Injection BP. To detect gelatin sensitivity a similar test should be carried out using gelatin diluent in the same dilution.

Some patients will develop porcine calcitonin binding antibodies after several months of treatment. The antibodies are generally of low titre and are more likely to occur in patients on the higher doses. The development of these antibodies is not usually related to loss of clinical efficacy. It is possible that this may be analogous to treated diabetic patients in whom insulin binding antibodies frequently develop, but who rarely manifest clinical resistance to insulin. The presence of these antibodies appears to bear no relationship to allergic reactions which are very rare. Secondary hyperparathyroidism is not thought to occur following calcitonin therapy.

Reproductive studies performed with salmon calcitonin showed a decrease in foetal birth weight in rabbits when given in doses of 14–56 times the dose recommended for human use. Since calcitonin does not cross the placental barrier this finding may be due to metabolic effects of calcitonin on the pregnant animal. There are no studies in pregnant women. Salmon calcitonin, and by inference porcine calcitonin, should be used only when clearly needed in women who are or who may become pregnant.

Calcitonin has been shown to inhibit lactation in animals and should not be administered to nursing mothers.

Following injections of calcitonin serum calcium levels may be transiently lowered to below normal values. This effect is noted most frequently on therapy where bone turnover is abnormally high, but diminishes as osteoclastic activity is reduced with Calcitare. Whilst this phenomenon does not usually give rise to complications, care should be exercised in patients who are receiving concurrent cardiac glycosides as dosage adjustments of these drugs may be necessary in view of the fact that their effect may be modified by changes in cellular electrolyte concentrations. Trace amounts of T_3/T_4 are present in Calcitare. Experience over a number of years has not revealed any significant metabolic effects due to T_3 and T_4 , when Calcitare has been given at the maximum recommended dose for Paget's disease of 160 international units daily. At higher doses (e.g. 8 i.u./kg) used in the treatment of hypercalcaemia, the amounts of T_3/T_4 normally detected in the product are most unlikely to have any adverse effect, except in highly susceptible patients such as those with significant ischaemic heart disease.

Pharmaceutical precautions Calcitare is presented as a sterile, lyophilised powder providing 160 international units porcine calcitonin per vial. Using aseptic technique the contents of a vial of the freeze-dried powder are reconstituted with an appropriate volume of sterile gelatin diluent so that the final injection volume will be 1–2 ml. Once reconstituted any unused solution should be administered within 24 hours, or if refrigerated (2–10°C) used within seven days.

The lyophilised powder when stored at less than 25°C will retain its potency for three years.

Legal category POM.

Package quantities For intramuscular or subcutaneous use: Boxes of 5 vials Calcitare 160 international units per vial sterile, lyophilised, with 5 vials gelatin diluent, sterile.

Boxes of 10 vials Calcitare 160 international units per vial sterile, lyophilised, with 10 vials gelatin diluent, sterile.

Further information The calcium lowering ability of the calcitonins is measured in international units. The international unit is based on a rat bioassay in which one fortieth of the weight of salmon calcitonin, as compared with weights of porcine and human calcitonin, produces the same fall in serum calcium. The weights of pure calcitonin equivalent to 100 international units in this assay are: human calcitonin, 1 mg, porcine calcitonin, 1 mg, and salmon calcitonin, 0.025 mg.

Product licence number 0231/0011.

CALSYNAR* (SALCATONIN)

Presentation *Multidose vials:* each multidose vial contains 400 international units of synthetic salmon calcitonin in 2 ml of saline acetate diluent (i.e. 200 international units of approximately 0.05 mg synthetic salmon calcitonin per ml). For subcutaneous or intramuscular use only.

Ampoules: each clear glass ampoule contains 100 international units of synthetic salmon calcitonin in 1 ml saline acetate diluent. For subcutaneous or intramuscular use only.

Uses *Paget's disease of bone.*

Hypercalcaemia: The calcium lowering effect of calcitonin is usually rapid. Treatment should be regarded as an adjunct to more specific long-term measures. The fall in serum calcium is more pronounced in hypercalcaemic patients with a raised bone turnover, e.g. Paget's disease and thyrotoxicosis. Treatment may also be beneficial in patients with hypercalcaemia due to immobilisation in Paget's disease, malignancy, vitamin D intoxication and hyperparathyroidism.

Calcitonin is of particular value when such patients have concurrent renal or cardiac failure.

Pain associated with advanced metastatic bone cancer: The use of Calsynar has been reported to be beneficial in the relief of pain in some patients with advanced metastatic bone cancer.

Dosage and administration (a) *Paget's disease of bone:* Clinical and biochemical improvement has been observed with dosage regimens ranging from 50 international units three times a week to 100 international units daily in single or divided doses.

Daily injections of 50 international units or 100 international units are recommended for three to six months in patients with bone pain or nerve compression syndromes.

Clinical improvement is usually seen within three months but may occasionally be delayed for as long as a year. When clinical improvement occurs an attempt to reduce the dose and/or frequency of the injections may be made consistent with maintaining a remission.

Alternatively, treatment can be stopped and restarted at a later date when necessary.

Biochemical improvement is shown by a reduction in serum alkaline phosphatase and urinary hydroxyproline excretion, the fall in urinary hydroxyproline often occurring in a matter of days, the fall in serum alkaline phosphatase occurring in a matter of weeks. Serum alkaline phosphatase and urinary hydroxyproline levels return slowly towards pre-treatment values (at different rates) on withdrawal of calcitonin therapy. Long-term treatment with calcitonin may be needed in those asymptomatic patients with rapidly advancing and potentially disabling disease.

Radiological and histological improvement has also been observed with long-term treatment and this reconstructive action of calcitonin on bone has been shown to be dose-dependent.

When changing from porcine calcitonin (Calcitare) to synthetic salmon calcitonin (Calsynar) 50 international units of Calsynar may be conveniently substituted for 80 international units of Calcitare and 100 international units for 160 international units of Calcitare.

(b) *Hypercalcaemia*: Calsynar should be given by subcutaneous or intramuscular injection. Treatment should be adjusted to the patient's clinical and biochemical response.

Severe hypercalcaemia may require high doses of Calsynar and initially 400 international units may be given six or eight-hourly. Lower doses may be satisfactory in some patients and dosage may be adjusted according to the patient's clinical and biochemical response. There is no additional benefit to be gained from doses in excess of 8 international units per kg six-hourly.

(c) *Pain associated with advanced metastatic bone cancer*: The use of Calsynar has been reported to be beneficial in the relief of pain in some patients with advanced metastatic bone cancer. Subcutaneous or intramuscular administration of 200 iu six-hourly for 48 hours has been shown to be effective in some patients and to permit reduction in the dose of concomitantly administered analgesics. Relief of pain may last for one week or longer. Treatment may be repeated at the discretion of the physician.

Contra-indications, warnings and side-effects

Calcitonin may cause nausea, vomiting, facial flushing, tingling of the hands, and an unpleasant taste. Inflammatory reactions at the injection site have been reported. The nausea and flushing are usually transient and rarely necessitate withdrawal of treatment. If necessary, the injections can be administered at night with an antiemetic.

In any patient with a history of allergy, a scratch (or intradermal) test should be conducted prior to administration of Calsynar using a 1:100 dilution in Sodium Chloride Injection BP.

Some patients will develop salmon calcitonin binding antibodies after several months of treatment. The antibodies are generally of low titre and are more likely to occur in patients on the higher doses. The development of these antibodies is not usually related to loss of clinical efficacy. It is possible that this may be analogous to treated diabetic patients in whom insulin binding antibodies frequently develop, but who rarely manifest clinical resistance to insulin. The presence of antibodies appears to bear no relationship to allergic reactions which are very rare.

Secondary hyperparathyroidism is not thought to occur following calcitonin therapy.

Salmon calcitonin has been shown to cause decrease in foetal birth weight in rabbits when given in doses of 14–56 times the dose recommended for human use. Since calcitonin does not cross the placental barrier this finding may be due to metabolic effects of calcitonin on the pregnant animal. Studies have not been carried out in pregnant women. Whenever possible, treatment should be avoided in women of child-bearing potential.

Calcitonin has been shown to inhibit lactation in animals and should not be administered to nursing mothers.

Following injections of calcitonin serum calcium levels may be transiently lowered to below normal values. This effect is noted most frequently on initiation of therapy where bone turnover is abnormally high, but diminishes as osteoclastic activity is reduced with Calsynar. Whilst this phenomenon does not usually give rise to complications, care should be exercised in patients who are receiving concurrent cardiac glycosides as dosage adjustments of these drugs may be necessary in view of the fact that their effect may be modified by changes in cellular electrolyte concentrations.

Pharmaceutical precautions Calsynar multidose vials contain a sterile solution of 400 international units of synthetic salmon calcitonin in 2 ml of saline acetate diluent per vial. Calsynar multidose vials, when stored between 2–10°C will retain their potency for 3 years. Do not freeze.

Calsynar ampoules contain a sterile solution of 100 international units of synthetic salmon calcitonin in 1 ml saline acetate diluent. Calsynar ampoules 100 international units when stored between 2–10°C will retain their potency for two years. Do not freeze.

Legal category POM.

Package quantities For subcutaneous or intramuscular use only:

Boxes of 1 multidose vial of Calsynar 400 international units per vial in 2 ml saline acetate diluent.

Cartons of six ampoules and 10 ampoules, each ampoule containing 100 international units in 1 ml saline acetate diluent.

Further information The calcium lowering ability of the calcitonins is measured in international units. The international unit is based on a rat bioassay in which one fortieth of the weight of salmon calcitonin, as compared with weights of porcine and human calcitonin, produces the same fall in serum calcium. The weights of pure calcitonin equivalent to 100 international units in this assay are approximately: human calcitonin, 1 mg, porcine calcitonin, 1 mg and salmon calcitonin, 0.025 mg.

Product licence numbers

Multidose vials – 0231/0027.

Ampoules – 0231/0055.

CHYMOCYCLAR*

Presentation Each pink, gelatin capsule contains:

50,000 Armour units of proteolytic activity supplied by a purified enzyme concentrate containing trypsin and chymotrypsin.

250 mg Tetracycline Hydrochloride BP.

Uses Infections due to tetracycline-sensitive organisms.

Dosage and administration

For administration to adults only: One or two capsules to be taken four times a day, half an hour before meals. The capsules should be swallowed whole since damage to the enteric coated core results in loss of proteolytic activity.

Absorption of tetracycline is impaired by the concomitant administration of food or drugs of high calcium content.

Contra-indications, warnings, etc

Precautions: In the presence of renal or hepatic impairment accumulation of tetracycline may occur and special attention to dosage is necessary. If possible, serum antibiotic levels should be controlled in such patients. Special care should be exercised with the use of tetracycline during pregnancy.

Side-effects: Tetracycline is known to produce gastrointestinal disturbances and may facilitate monilial infection in some cases. Although no specific reports relating to Chymocyclar have been received, tetracycline has been recorded as causing haemolytic anaemia, eosinophilia, thrombocytopenia, hepatotoxicity, allergic skin reactions and photosensitivity.

Tetracycline has also been reported to reduce the efficacy of oral steroid contraceptives.

Contra-indications: Patients with known sensitivities to enzymes and tetracycline. During the period of tooth development, last trimester of pregnancy and early childhood, it is possible that tetracycline may cause yellowish brown discolouration of the teeth and enamel hyperplasia in prolonged high dosage.

Pharmaceutical precautions Chymocyclar should be stored in a cool dry place, protected from light – Shelf-life 3 years.

Legal category POM.

Package quantities Bottles of 30, 100 and 500 capsules.

Further information In conditions where inflammatory oedema is associated with infections, the administration of the proteolytic enzymes may be directly advantageous, and the beneficial clinical results obtained with combination therapy of this nature have been reported in the literature.

Product licence number 0231/5001.

**CHYMORAL®
CHYMORAL® FORTE**

Presentation Enteric-coated tablets containing a purified proteolytic enzyme concentrate providing trypsin and chymotrypsin activity.

Chymoral – 50,000 Armour units.

Chymoral Forte – 100,000 Armour units.

Uses Resolution of acute, inflammatory oedema associated with: Accidental and surgical trauma. Episiotomies. Intervertebral disc herniation (sciatica). Thrombophlebitis. Vasectomies. Reduction in viscosity of mucus and sputum associated with bronchitis, rhinitis and sinusitis.

Dosage and administration *Chymoral:* 2 tablets four times a day. Children 1 tablet four times a day.

Chymoral Forte: 1 tablet four times a day. Not for administration to children.

The tablets must be taken half an hour before meals and swallowed whole without crushing, since damage to the enteric coating rapidly causes loss of potency.

Contra-indications, warnings, etc

Precautions: Patients with known sensitivity to enzymes.

After many years of widespread clinical use, there is no reason to believe that Chymoral is, or may be, teratogenic in humans. However, it is a sound medical principle to exercise precaution in prescribing any medication during the first three months of pregnancy.

Side-effects: Occasional slight gastric disturbance.

Pharmaceutical precautions The tablets should be stored in a cool dry place – shelf-life is three years for Chymoral and two years for Chymoral Forte.

Legal category P.

Package quantities *Chymoral:* Bottles of 50 and 500 tablets.

Chymoral Forte: Bottles of 30, 200 and 500 tablets.

Further information Nil.

Product licence numbers

Chymoral 0231/5021

Chymoral Forte 0231/5020

DIORALYTE®

Presentation Foil/laminate sachets each containing:

Sodium Chloride BP	0.20 g
Potassium Chloride BP	0.30 g
Sodium Bicarbonate BP	0.30 g
Dextrose Monohydrate BP	8.00 g

Uses Oral correction of fluid and electrolyte loss in infants, children and adults. In the treatment of watery diarrhoea of varying aetiologies, including gastroenteritis, in all age groups.

The product has been formulated to treat fluid and electrolyte loss associated with infantile diarrhoea, but is also appropriate for the treatment of older children and adults.

Dosage and administration *Reconstitution:* The contents of each sachet should be dissolved in sufficient freshly boiled and cooled water to make up to 200 ml (approximately 7 fluid ounces). An infant's feeding bottle is a convenient measure of this volume. The solution should be made up immediately prior to feeding and any solution remaining an hour after reconstitution should be discarded. However, the solution may be used for up to 24 hours if stored in a refrigerator immediately after reconstitution.

The reconstituted solution must not be boiled.

Dosage: For oral administration only.

The volume of reconstituted Dioralyte needed each day should be determined by the physician, taking into account the weight of the patient and severity of the condition.

For the treatment of infantile diarrhoea, a number of different regimens are used by different physicians, but the basic principle is to stop all foods including milk initially, whilst maintaining adequate fluid intake. Milk can then be reintroduced to provide calories, but to avoid worsening or prolonging the diarrhoea this should be gradual. A suggested regimen for the treatment of severe

infantile diarrhoea based on body weight in kilograms is given below.

Day	Volume of Dioralyte solution (ml)	Volume of milk (ml)	Total volume in 24 hours (ml)
1	150 × wt†	0	150 × wt
2	120 × wt	30 × wt	150 × wt
3	90 × wt	60 × wt	150 × wt
4	60 × wt	90 × wt	150 × wt
5	30 × wt	120 × wt	150 × wt
6	0	150 × wt	150 × wt

† Weight in kilograms.

Simplified dosage scheme: Alternatively, for milder cases, the following simplified regimen may be adopted.

During the first 24–28 hours, the infant is offered Dioralyte in the same quantities as are used for the usual feeds. When the vomiting and diarrhoea have subsided, the Dioralyte solution is substituted with half strength milk feeds. Normal feeding may be resumed as the appetite returns. For toddlers and older children, Dioralyte may be given freely until the thirst is satisfied.

These dosage schemes are only a general guide and the volume of Dioralyte per feed and the speed of re-introduction of milk or other feeds is at the discretion of the physician.

In those patients who are vomiting at the start of treatment, it may be advisable to offer very small volumes initially until vomiting is under control. If the vomiting and diarrhoea show no sign of moderating the patient should be reassessed.

Diarrhoea is uncommon in breast fed infants. However, if treatment with Dioralyte becomes necessary it is suggested that for each feed the chosen regimen is followed, such that the infant is given the appropriate volume of Dioralyte for that feed and then put to the breast until satisfied. Expression of residual milk from the breasts may be necessary during this period.

Contra-indications, warnings, etc

Warnings: For oral administration only.

The contents of each sachet should always be made up to 200 ml with freshly boiled and cooled water (the product must not be reconstituted in diluents other than water, e.g. must not be included in milk solutions). A weaker solution than recommended will fail to provide adequate sugar and electrolytes and a stronger solution than recommended may give rise to hypernatraemia.

The reconstituted solution must not be boiled.

Contra-indications: There are no known contra-indications to Dioralyte. However, there may be a number of conditions where treatment with Dioralyte will be inappropriate, e.g. intestinal obstruction requiring surgical intervention.

Pharmaceutical precautions The sachet should be stored in a cool, dry place.

Legal category P.

Package quantities Cartons containing 20 sachets, together with a professional package insert and two tear-off Patient Instruction leaflets.

Cartons of 4 sachets with patient instruction leaflet.

Further information Dioralyte (Glucose Electrolyte Supplement) is Compound Sodium Chloride and Dextrose Oral Powder BP.

A litre of made up solution (5 sachets, 5 × 200 ml

quantities) contains: 35 mmol Sodium (Na⁺); 20 mmol Potassium (K⁺); 37 mmol Chloride (Cl⁻); 18 mmol Bicarbonate (HCO₃⁻); 200 mmol Dextrose. The total osmolality is 310 mmol per litre.

Product licence number 0231/0043.

FACTORATE*

Presentation Dried Human Antihaemophilic Fraction Factorate is a stable lyophilised concentrate of Factor VIII (AHF, AHG) prepared from pooled human plasma.

Each vial contains the labelled amount of antihaemophilic activity in International Units (one International Unit is the activity equivalent to the average Factor VIII content of 1 ml aliquots of 167 samples of fresh normal plasma, as determined in an international collaborative study). Each vial also contains sufficient sodium chloride to make the reconstituted solution approximately isotonic when sterile Water for Injections BP is added as directed.

Uses For use in therapy of classic haemophilia (Haemophilia A).

Dosage and administration Factorate is for intravenous administration only. As a general rule one unit of Factor VIII activity per kg will increase by 2% the circulating Factor VIII level, and although dosage must be adjusted according to the needs of the patient (weight, severity of haemorrhage, presence of inhibitors) the following general dosages are suggested.

1. **Overt bleeding:** Initially 20 units per kg of body weight followed by 10 units per kg every eight hours for the first 24 hours and the same dose every 12 hours for the next 3 or 4 days. For massive wounds, give until bleeding stops and maintain with 20 units per kg 8-hourly to achieve a minimum Factor VIII level of 40%.

2. **Muscle haemorrhages:** (a) Minor haemorrhages in extremities or non-vital areas: 10 units per kg once a day for 2 or 3 days.

(b) Massive haemorrhages in non-vital areas: 10 units per kg by infusion at 12 hour intervals for 2 days and then once a day for 2 more days.

(c) Haemorrhages near vital organs (neck, throat, subperitoneal): 20 units per kg, initially; then 10 units per kg every 8 hours. After 2 days the dose may be reduced by one-half.

3. **Joint haemorrhages:** 10 units per kg every 8 hours for a day; then twice daily for 1 or 2 days. If aspiration is carried out, 10 units per kg just prior to aspiration with additional infusions of 10 units per kg 8 hours later and again on the following day.

4. **Surgery:** Dosages of 30 to 40 units per kg body weight prior to surgery are recommended. After surgery 20 units per kg every 8 hours should be administered. Close laboratory control to maintain the blood level of Factor VIII above 40% of normal for at least 10 days post-operatively is suggested.

5. **Dental extractions:** For simple extractions a pre-operative dose of 20–25 units per kg sufficient to raise the Factor VIII level to 50% should be given, followed by intravenous administration of epsilon aminocaproic acid. For multiple extractions further doses of Factor VIII may be advisable 24 or 36 hours after the operation.

Recommended reconstitution: Reconstitute Factorate using 20 ml sterile Water for Injections BP using standard aseptic precautions.

Warm both diluent and Factorate vials to between 20°C and 25°C. Direct diluent down the side of the vial and gently rotate the vial until contents are dissolved. **DO NOT SHAKE VIAL.** Vigorous shaking will cause frothing and prolong the reconstitution time. Complete solution usually takes less than 5 minutes. The solution is now ready for administration. If a gel forms on reconstitution, the preparation should not be used.

Administration: Standard aseptic techniques should be used at all times.

Intravenous injection: Plastic disposable syringes are recommended with Factor VIII solution. The ground glass surfaces of all-glass syringes tend to stick with solutions of this type.

1. Attach a filter needle to a sterile disposable syringe. Insert filter needle into stopper of Factor VIII vial; inject air and withdraw the reconstituted solution from the vial.

2. Discard the filter needle and attach a suitable intravenous needle.

3. Administer solution by slow intravenous injection (20 ml in about five minutes).

Intravenous infusion: The infusion equipment used should comply with that described in sections 3 or 4 of British Standard 2463:1962, Transfusion Equipment for Medical Use.

1. Prepare solution of Factorate as recommended under 'Reconstitution'.

2. Attach suitable infusion set.

3. If more than one vial is to be administered to the same patient the infusion set may be transferred to the second vial.

4. When infusion of Factorate is complete, the infusion set may be flushed with sterile isotonic saline to avoid loss of any of the reconstituted solution.

5. After use, discard infusion set, needles and vials together with any unused solution.

Contra-indications, warnings, etc

Warning: Factor VIII is prepared from human plasma, each donation of which has been found negative for hepatitis B surface antigen (HBsAg) by the radioimmunoassay (RIA) method. In addition, each batch, after reconstitution as recommended, has been tested and found negative by the RIA method. However, since no completely reliable laboratory test is yet available to detect all potentially infectious plasma donations, the risk of transmitting viral hepatitis is still present.

Side-effects: Products of this type are known to cause mild chills, nausea or stinging at the infusion site.

Contra-indications: There are no known contra-indications to antihæmophilic fraction.

Precautions: Factor VIII contains low levels of group A and B isohaemagglutinins. When large volumes are given to patients of blood groups A, B or AB, the possibility of intravascular haemolysis should be considered. Such patients should be monitored by means of a haematocrit and direct Coombs test for signs of progressive anaemia.

Pharmaceutical precautions Factorate is to be stored at refrigerator temperature (2°C–6°C). When stored as directed, it will maintain its labelled potency for the dating period indicated on the label but within this period may be stored at room temperature (not exceeding 30°C or 86°F) for up to six months.

Legal category POM.

Package quantities Factorate is supplied in single dose vials (potency is stated on each vial label).

Further information Haemophilia A, a hereditary disorder of blood coagulation occurring almost exclusively in males results in profuse bleeding in joints, muscles or internal organs as a result of minor trauma. The disease appears to be due to a deficiency of a specific plasma protein, antihæmophilic factor, Factor VIII: Factorate provides temporary replacement of the missing clotting factor.

Affected individuals frequently require therapy following minor trauma. Surgery, when required in such individuals must be preceded by temporary correction of the clotting abnormality with fresh plasma transfusions, cryoprecipitate or by injections of Factor VIII concentrates. Obvious advantages of the use of concentrates of Factor VIII are the avoidance of hyper-proteinaemia, overloading the circulatory system and possible kidney dysfunction resulting from large volume transfusions.

Several different concentrations of Factor VIII have been used successfully. These range from Fraction 1 of Cohn to highly purified potent preparations. Dried Human Antihæmophilic Fraction – Factorate is in an intermediate category, being purified cryoglobulin complying with the standards of the BP.

Product licence number 0231/0038.

HIGH POTENCY FACTORATE*

Presentation Dried Human Antihæmophilic Fraction High Potency Factorate is a stable lyophilised concentrate of Factor VIII (AHF, AHG) prepared from pooled human plasma. It conforms to the monograph for Dried Human Antihæmophilic Factor BP.

Each vial contains the labelled amount of antihæmophilic activity in International Units (one International Unit is the activity equivalent to the average Factor VIII content of 1 ml aliquots of 167 samples of fresh normal plasma, as determined in an international collaborative study). Each vial also contains sufficient sodium chloride to make the reconstituted solution approximately isotonic when Water for Injections BP is added as directed.

Uses For use in therapy of classic haemophilia (Haemophilia A).

Dosage and administration High Potency Factorate is for intravenous administration only. As a general rule one unit of Factor VIII activity per kg will increase by 2% the circulating Factor VIII level, and although dosage must be adjusted according to the needs of the patient (weight, severity of haemorrhage, presence of inhibitors) the following general dosages are suggested.

1. **Overt bleeding:** Initially 20 units per kg of body weight followed by 10 units per kg every eight hours for the first 24 hours and the same dose every 12 hours for the next 3 or 4 days. For massive wounds, give until bleeding stops and maintain with 20 units per kg 8-hourly to achieve a minimum Factor VIII level of 40%.

2. **Muscle haemorrhages:** (a) Minor haemorrhages in extremities or non-vital areas: 10 units per kg once a day for 2 or 3 days.

- (b) Massive haemorrhages in non-vital areas: 10 units per kg by infusion at 12 hour intervals for 2 days and then once a day for 2 more days.

- (c) Haemorrhages near vital organs (neck, throat, subperitoneal), 20 units per kg, initially; then 10 units per kg every 8 hours. After 2 days the dose may be reduced by one-half.

3. **Joint haemorrhages:** 10 units per kg every 8 hours for a day; then twice daily for 1 or 2 days. If aspiration is

carried out, 10 units per kg just prior to aspiration with additional infusions of 10 units per kg 8 hours later and again on the following day.

4. Surgery: Dosages of 30 to 40 units per kg body weight prior to surgery are recommended. After surgery 20 units per kg every 8 hours should be administered. Close laboratory control to maintain the blood level of Factor VIII above 40% of normal for at least 10 days post-operatively is suggested.

5. Dental extractions: For simple extractions a pre-operative dose of 20–25 units per kg sufficient to raise the Factor VIII level to 50% should be given, followed by intravenous administration of tranexamic acid. For multiple extractions further doses of Factor VIII may be advisable 24 or 36 hours after the operation.

Recommended reconstitution: Reconstitute High Potency Factorate using 30 ml sterile Water for Injections BP using standard aseptic precautions.

Warm both diluent and High Potency Factorate vials to between 20°C and 30°C. Direct diluent down the side of the vial and gently rotate the vial until contents are dissolved. **DO NOT SHAKE VIAL.** Vigorous shaking will cause frothing and prolong the reconstitution time. Complete solution usually takes approximately 10 minutes. The solution is now ready for administration. If a gel forms on reconstitution, the preparation should not be used. The solution should be used within 3 hours of reconstitution.

Administration: Standard aseptic techniques should be used at all times.

Intravenous injection: Plastic disposable syringes are recommended with Factor VIII solution. The ground glass surfaces of all-glass syringes tend to stick with solutions of this type.

1. Attach a filter needle to a sterile disposable syringe. Insert filter needle into stopper of Factor VIII vial; inject air and withdraw the reconstituted solution from the vial.

2. Discard the filter needle and attach a suitable intravenous needle.

3. Administer solution by slow intravenous injection, at a rate comfortable to the patient, and not exceeding 2 ml per minute.

Intravenous infusion: The infusion equipment used should comply with that described in sections 3 or 4 of British Standard 2463:1962, Transfusion Equipment for Medical Use.

1. Prepare solution of High Potency Factorate as recommended under 'Reconstitution'.

2. Attach suitable infusion set.

3. If more than one vial is to be administered to the same patient the infusion set may be transferred to a second vial.

4. When infusion of High Potency Factorate is complete, the infusion set may be flushed with sterile isotonic saline to avoid loss of any of the reconstituted solution.

5. After use, discard infusion set, needles and vials together with any unused solution.

Contra-indications, warnings, etc

Warning: Factor VIII is prepared from human plasma, each donation of which has been found negative for hepatitis B surface antigen (HBsAg) by the radio-immunoassay (RIA) method. In addition, each batch, after reconstitution as recommended, has been tested and found negative by the RIA method. However, since no completely reliable laboratory test is yet available to

detect all potentially infectious plasma donations, the risk of transmitting viral hepatitis is still present.

Side-effects: Products of this type are known to cause mild chills, nausea or stinging at the infusion site.

Contra-indications: There are no known contra-indications to antihaemophilic fraction.

Precautions: Factor VIII contains low levels of group A and B isohaemagglutinins. When large volumes are given to patients of blood groups A, B or AB, the possibility of intravascular haemolysis should be considered. Such patients should be monitored by means of a haematocrit and direct Coombs test for signs of progressive anaemia.

Pharmaceutical precautions High Potency Factorate is to be stored at refrigerator temperature (2°C–6°C). When stored as directed, it will maintain its labelled potency for the period indicated on the label but within this period it may be stored at room temperature (not exceeding 30°C or 86°F) for up to six months.

Legal category POM.

Package quantities High Potency Factorate is supplied in single dose vials (potency is stated on each vial label).

Further information Haemophilia A, a hereditary disorder of blood coagulation occurring almost exclusively in males results in profuse bleeding in joints, muscles or internal organs as a result of minor trauma. The disease appears to be due to a deficiency of a specific plasma protein, antihaemophilic factor, Factor VIII; High Potency Factorate provides temporary replacement of the missing clotting factor.

Affected individuals frequently require therapy following minor trauma. Surgery, when required in such individuals must be preceded by temporary correction of the clotting abnormality with fresh plasma transfusions, cryoprecipitate or by injections of Factor VIII concentrates. Advantages of the use of concentrates of Factor VIII are the avoidance of hyperproteinaemia, overloading the circulatory system and possible kidney dysfunction resulting from large volume transfusions. Several different concentrations of Factor VIII have been used successfully. These range from Fraction 1 of Cohn to highly purified potent preparations. Dried Human Antihaemophilic Fraction – High Potency Factorate is a purified preparation with lower levels of fibrinogen and other non-AHF protein per international unit than 'Intermediate Purity' AHF preparations.

Product licence number 0231/0044.

SYRTUSSAR*

Presentation A red syrupy liquid. Each 5 ml contains:

Dextromethorphan Hydrobromide BP	10 mg
Pheniramine Maleate USNF XII	7.5 mg

Uses Coughs.

Dosage and administration **Adults:** One to two 5 ml spoonfuls three to four times a day.

Children over 6: Half the adult dose three to four times a day.

Children 2–6 years: Half a 5 ml spoonful three times a day.

Note: If required, Syrtussar may be diluted with Syrup BP.

Contra-indications, warnings, etc The preparation may cause drowsiness. If affected, do not drive or operate machinery. Avoid alcoholic drink.

Pharmaceutical precautions Store in a cool place – Shelf life 5 years.

Legal category P.

Package quantities Bottles of 100 ml and 1 litre dispensing pack.

Further information Dextromethorphan hydrobromide is an effective antitussive agent which, combined with antihistamine, provides a therapy for coughs.

Product licence number 0231/5019.

**Trade Mark*

Astra Pharmaceuticals Limited
St Peter's House
2 Bricket Road
St Albans Herts AL1 3JW

ASTRA

BETALOC*

Presentation White tablets containing either 50 mg metoprolol tartrate coded A/BB or 100 mg metoprolol tartrate coded A/ME.

Uses In the management of hypertension and angina pectoris. Cardiac arrhythmias, especially supraventricular tachyarrhythmias. Adjunct to the treatment of thyrotoxicosis.

Dosage and administration The dose must always be adjusted to the individual requirements of the patient. The following are guide lines:

Hypertension: Total daily dose 100–400 mg to be given as a single or twice daily dose.

The starting dose is 100 mg per day. This may be increased by 100 mg per day at weekly intervals.

If full control is not achieved using a single daily dose, a.b.d. regimen should be initiated. Combination therapy with a diuretic or other hypotensive agent may also be considered.

Angina: Usually 50–100 mg twice or three times daily.

Cardiac arrhythmias: 50 mg b.i.d. or t.i.d. should usually control the condition. If necessary the dose can be increased up to 300 mg per day in divided doses.

Following the treatment of an acute arrhythmia with Betaloc injection, continuation therapy with Betaloc tablets should be initiated 4–6 hours later. The initial oral dose should not exceed 50 mg t.i.d.

Thyrotoxicosis: 50 mg four times a day.

Contra-indications, warnings, etc

Contra-indications: A V block. Digitalis refractory heart failure.

Warnings: In labile and insulin-dependent diabetes it may be necessary to adjust the hypoglycaemic therapy.

Betaloc therapy must be reported to the anaesthetist prior to general anaesthesia.

Digitalisation should be considered for patients with a previous history of heart failure, or patients known to have a poor cardiac reserve.

Betaloc has proved safe in a large number of asthmatic patients; although it is a selective beta-blocker it is prudent to exercise care in the treatment of patients with chronic obstructive pulmonary disease.

Until further clinical experience is available, it is recommended that treatment with Betaloc be avoided during pregnancy.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenoceptor blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuation of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-blocker should be gradual.

Side-effects: These are mild and have been infrequently reported. The commonest appear to be lassitude, GI disturbances, and disturbance of sleep pattern. In many

cases these effects have been transient, or have disappeared after a reduction in dosage.

Pharmaceutical precautions Protect from light, heat and moisture.

Legal category POM.

Package quantities Securitainers of 100 and 500.

Further information *Treatment of overdose:* Marked bradycardia may be treated by intravenous atropine sulphate (0.25–2.0 mg) and in severe cases by slow intravenous infusion of about 5 mcg per minute of isoprenaline.

Metoprolol undergoes biotransformation in the liver and thereafter is mainly excreted as inactive metabolites by the kidney.

Product licence numbers

Tablets 50 mg 0017/0073

Tablets 100 mg 0017/0074

BETALOC* I.V. INJECTION ▼

Presentation *Ampoules:* Each ampoule of 5 ml contains 5 mg metoprolol tartrate.

Uses Control of tachyarrhythmias, especially supraventricular tachyarrhythmias.

Dosage and administration Initially up to 5 mg injected i.v. at a rate of 1–2 mg per minute. The injection can be repeated at 5 minute intervals until a satisfactory response has been obtained.

A total dose of 10–15 mg generally proves sufficient. Because of the risk of a pronounced drop of blood pressure, the i.v. administration of Betaloc to patients with a systolic blood pressure below 100 mm Hg should only be given with special care.

During anaesthesia: 2–4 mg injected slowly i.v. at induction is usually sufficient to prevent the development of arrhythmias during anaesthesia. The same dosage can also be used to control arrhythmias developing during anaesthesia. Further injections of 2 mg may be given as required to a maximum overall dose of 10 mg.

Contra-indications, warnings, etc

Contra-indications: AV Block. Digitalis refractory heart failure. Severe bradycardia. Cardiogenic shock.

Warnings: In labile and insulin dependent diabetes, it may be necessary to adjust the hypoglycaemic therapy.

Betaloc therapy must be reported to the anaesthetist prior to general anaesthetic.

Digitalisation should be considered for patients with a previous history of heart failure, or patients known to have a poor cardiac reserve.

Betaloc has proved safe in a large number of asthmatic patients; although it is a selective beta-blocker it is prudent to exercise care in the treatment of patients with chronic obstructive pulmonary disease. In patients

suffering from asthma, additional therapy with a β_2 -stimulant (e.g. terbutaline) may be advisable.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenoceptor blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuation of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-blocker should be gradual.

Betaloc therapy should be avoided during pregnancy. If there are overwhelming clinical reasons for its use during the second or third trimesters, particular attention should be paid to its β -blocking effects (especially bradycardia) in the mother, foetus and neonate.

In a patient under beta-blockade, the anaesthetic selected should be one exhibiting as little negative inotropic activity as possible (e.g. halothane/nitrous oxide).

Side-effects: As in the case of other beta-blockers, a marked fall in blood pressure may sometimes occur following intravenous injection of Betaloc.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities 4 x 5 ml ampoules.

Further information *Treatment of overdose:* Marked bradycardia may be treated by intravenous atropine sulphate (0.25 to 2.0 mg) and in severe cases by slow intravenous infusion of about 5 mcg/minute of isoprenaline.

Betaloc is a cardioselective β_1 -receptor blocker exhibiting no intrinsic sympathomimetic activity. Betaloc injection is suitable for the treatment of cardiac arrhythmias, especially supraventricular tachyarrhythmias. Its use often re-establishes normal sinus rhythm in patients with paroxysmal atrial tachycardia or reduces the ventricular rate. Also where atrial fibrillation or flutter exists it can not only reduce ventricular rate but may also restore sinus rhythm. It also reduces the number of ventricular extrasystoles.

Product licence number 0017/0072.

BETALOC-SA

Presentation White tablets (coded A MD) containing 200 mg metoprolol tartrate Durules (sustained action).

Uses In the management of angina pectoris and hypertension.

Dosage and administration Oral, once daily in the morning. In rare cases two tablets may be indicated.

Administration of Betaloc-SA results in a controlled release of active substance which means that the peak plasma levels are reduced. Compared to Betaloc tablets the absorption phase is prolonged and the duration of effect is extended. The substance is completely absorbed and the maximal beta-blocking effect is reached after about four hours.

These factors may lead to a more convenient dosage and an improved degree of beta₁-selectivity.

The effect on the pulse and blood pressure remain pronounced 24 hours after administration.

Betaloc-SA tablets should be swallowed whole and not broken or chewed.

Metoprolol undergoes bio-transformation in the liver

and thereafter is mainly excreted as inactive metabolites by the kidney.

Contra-indications, warnings, etc

Contra-indications: AV block. Digitalis refractory heart failure.

Warnings: In labile and insulin-dependent diabetes, it may be necessary to adjust the hypoglycaemic therapy.

Betaloc therapy must be reported to the anaesthetist prior to general anaesthetic.

Digitalisation should be considered for patients with a previous history of heart failure or patients known to have a poor cardiac reserve.

Betaloc has proved safe in a large number of asthmatic patients; although it is a selective beta-blocker it is prudent to exercise care in the treatment of patients with chronic obstructive pulmonary disease. Use of a beta₂-bronchodilator may be advisable in some asthmatics.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenoceptor blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuation of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-blocker should be gradual.

Until further clinical experience is available, it is recommended that treatment with Betaloc-SA be avoided during pregnancy.

Side-effects: These are mild and have been infrequently reported. The commonest appear to be lassitude, GI disturbances and disturbances of sleep pattern. In many cases these effects have been transient, or have disappeared after a reduction in dosage.

Pharmaceutical precautions Store in a cool dry place.

Legal category POM.

Package quantities Calendar pack of 28 tablets. Securainers of 300 tablets.

Further information *Treatment of overdose:* Marked bradycardia may be treated by intravenous atropine sulphate (0.25–2.0 mg) and in severe cases by slow intravenous infusion of about 5 mcg per minute of isoprenaline.

Product licence number 0017/0093.

BRICANYL* SPACER INHALER BRICANYL* INHALER

Presentation *Bricanyl Spacer inhaler:* Metered aerosol with extended mouthpiece, delivering 0.25 mg terbutaline sulphate per actuation.

Bricanyl inhaler: Metered aerosol delivering 0.25 mg terbutaline sulphate per actuation.

Uses A selective beta₂-adrenergic stimulant recommended for the relief of allergic and intrinsic asthma, chronic bronchitis, emphysema and other bronchopulmonary disorders in which bronchospasm is a complicating factor.

Dosage and administration Bricanyl Spacer inhaler is particularly recommended to enable patients with difficulty coordinating conventional aerosols to derive greater therapeutic benefit.

Adults and children: One or two inhalations as required, with a short interval between each inhalation. Not more

than eight inhalations should be necessary in any 24 hours.

See package insert for simple operating instructions.

Contra-indications, warnings, etc No contra-indications are known. Bricanyl should not be used with non-selective beta-blocking agents, but may be used with agents which selectively block cardiac β_1 -receptors. Care should be taken with patients suffering from myocardial insufficiency or thyrotoxicosis. Although no teratogenic effects have been observed in animal experiments, caution is recommended during the first trimester of pregnancy.

Side-effects: The frequency of side-effects is low, and those which have been recorded, e.g. tremor and palpitations, are all characteristic of sympathomimetic amines. Whenever these have occurred, the majority have resolved spontaneously within the first week of treatment.

Precautions: Care should be taken when aminophylline or related compounds are given to patients receiving Bricanyl by injection.

Pharmaceutical precautions None.

Legal category POM.

Package quantities *Bricanyl Spacer Inhaler:* aerosol containing 400 metered doses complete with extended mouth piece.

Bricanyl Inhaler: Aerosol containing 400 metered doses.

Further information Bricanyl is also available as Respirator Solution, Tablets, Syrup, Injection, Expecto-rant and Compound Tablets.

Product licence numbers

Bricanyl Spacer Inhaler 0017/0061
Bricanyl Inhaler 0017/0061

BRICANYL* TABLETS BRICANYL* SYRUP

Presentation *Bricanyl Tablets:* Off-white scored tablet containing terbutaline sulphate 5 mg.

Bricanyl Syrup: Clear aqueous solution containing 0.3 mg terbutaline sulphate per ml.

Uses A bronchodilator recommended for relief of allergic and intrinsic asthma, chronic bronchitis, emphysema and other broncho-pulmonary disorders in which bronchospasm is a complicating factor. Bricanyl Expecto-rant is recommended in these conditions where secretion is a complicating factor.

Dosage and administration

Bricanyl Tablets: Adults: 1 tablet twice a day; or three times a day at eight-hourly intervals.

Children: 7-15 years: $\frac{1}{2}$ tablet twice a day; or three times a day at eight-hourly intervals.

Bricanyl Syrup: Adults: 2-3 $\times$ 5 ml spoonfuls three times a day at eight-hourly intervals.

Children: 7-15 years: 1-2 $\times$ 5 ml spoonfuls three times a day at eight-hourly intervals.

3-7 years: $\frac{1}{2}$ -1 $\times$ 5 ml spoonful three times a day at eight-hourly intervals.

Contra-indications, warnings, etc No contra-indications are known. Bricanyl should not be used with non-selective beta-blocking agents, but may be used

with agents which selectively block cardiac β_1 receptors. Care should be taken with patients suffering from myocardial insufficiency or thyrotoxicosis. Although no teratogenic effects have been observed in animal experiments, caution is recommended during the first trimester of pregnancy.

Side-effects: The frequency of side-effects is low, and those which have been recorded, e.g. tremor and palpitations, are all characteristic of sympathomimetic amines. Whenever these have occurred, the majority have been spontaneously reversible within the first week of treatment.

Pharmaceutical precautions No special storage conditions are necessary for any of the Bricanyl preparations. The recommended diluent for Bricanyl Syrup is water.

Legal category POM.

Package quantities *Bricanyl Tablets:* Bottles of 100 and 500 tablets.

Bricanyl Syrup: Bottles of 300 ml and 1 litre.

Further information When Bricanyl is prescribed orally a suitable regime for providing eight-hourly administration is: on rising, in the mid-afternoon, on retiring.

Product licence numbers

Bricanyl Tablets 0017/0047
Bricanyl Syrup 0017/0058

BRICANYL* INJECTION

Presentation Clear aqueous solution for injection containing 0.5 mg terbutaline sulphate per ml.

Uses

1. *For bronchodilatation.* A selective β_2 adrenergic stimulant recommended for the relief of allergic and intrinsic asthma, chronic bronchitis, emphysema and other broncho-pulmonary disorders in which bronchospasm is a complicating factor.

2. *For the management of uncomplicated premature labour.*

Dosage and administration

1. *For bronchodilatation.* When a rapid therapeutic response is required, Bricanyl can be administered by any of the three standard parenteral routes: subcutaneous, intramuscular, or i.v. bolus. The preferred routes will usually be subcutaneous or intramuscular. When given as an i.v. bolus the injection must be made slowly noting patient response.

Adults: $\frac{1}{2}$ -1 ampoule (0.25-0.5 mg) up to four times a day.

Children: 2-15 years. 0.01 mg/kg body weight to a maximum of 0.3 mg total.

Age	Average weight		mg terbutaline	ml volume
	kg	(lb)		
<3	10	(22)	0.1	0.2
3	15	(33)	0.15	0.3
6	20	(44)	0.2	0.4
8	25	(55)	0.25	0.5
10+	30+	(66+)	0.3	0.6

By infusion: 3 to 5 ampoules (1.5–2.5 mg) in 500 ml dextrose, saline or dextrose/saline solution given by continuous intravenous infusion at a rate of 10–20 drops (0.5–1 ml) per minute for 8 to 10 hours. Corresponding reduction in dosage should be made for children.

2. For management of premature labour. The dose must be individually titrated with reference to suppression of contractions, increase in pulse rate and changes in blood pressure, which are limiting factors.

These parameters should be carefully monitored during treatment. A maternal heart rate of more than 135 beats/min should be avoided. 10 mcg/min i.v. should be infused during the first hour. This can be increased by 5 mcg/min at 10 min intervals until the contractions stop. The highest dose should be 25 mcg/min. During the next seven hours, the dose should be decreased in 30 minute periods by 5 mcg/min to the lowest maintenance dose that produces continued suppression of the contractions. After this initial treatment, subcutaneous injections (0.25 mg) should be given four times a day for three days. During this period, oral treatment should be started (5 mg three times a day). The oral treatment should be continued until the end of the 36th week of pregnancy. Suggestion for dilution: 5 mg (10 ampoules) in 1,000 ml of dextrose solution (40 drops contain approximately 10 mcg).

Contra-indications, warnings, etc

1. For bronchodilatation. No contra-indications are known. Bricanyl should not be used with non-selective beta-blocking agents, but may be used with agents which selectively block cardiac receptors. Care should be taken with patients suffering from myocardial insufficiency or thyrotoxicosis. Although no teratogenic effects have been observed in animal experiments, caution is recommended during the first trimester of pregnancy.

Side-effects: When used as a bronchodilator the frequency of side-effects is low, and those which have been recorded, e.g. tremor and palpitations, are all characteristic of sympathomimetic amines. Whenever these have occurred, the majority have resolved spontaneously within the first week of treatment.

Precautions: When used for bronchodilatation care should be taken when aminophylline or related compounds are given to patients receiving Bricanyl by injection.

2. For management of premature labour. The following are contra-indications: ante-partum haemorrhage due to any cause, toxæmia of pregnancy, cord compression. Any condition of the mother or foetus in which prolongation of pregnancy is hazardous.

In premature labour in a patient with known or suspected cardiac disease a physician experienced in cardiology should assess the suitability of treatment before i.v. infusion with Bricanyl.

Warnings: In treatment of premature labour, hyperglycaemia and ketoacidosis have been found in pregnant women with diabetes after treatment with β_2 -stimulants. It may therefore be necessary to adjust the insulin dose when β_2 -stimulants are used in the treatment.

During infusion treatment in pregnant women with β_2 -stimulants in combination with corticosteroids a rare complication with a pathological picture resembling pulmonary oedema, has been reported.

Increased tendency to uterine bleeding has been reported in connection with Caesarian section. However,

this can be effectively stopped by propranolol 1–2 mg injected intravenously.

Pharmaceutical precautions No special storage conditions are necessary. The recommended diluent is water for injection, or sterile saline or dextrose.

Legal category POM.

Package quantities Packs of 5 × 1 ml ampoules.

Further information Nil.

Product licence number 0017/0048.

BRICANYL* COMPOUND TABLETS BRICANYL* EXPECTORANT

Presentation *Compound Tablets:* Plain white tablets each containing:

Terbutaline sulphate	2.5 mg
Guaiphenesin	100 mg

Expectorant: Clear aqueous solution containing:

Terbutaline sulphate	0.3 mg/ml
Guaiphenesin	13.3 mg/ml

Uses Bronchodilator and expectorant recommended for relief of bronchial asthma, bronchitis, emphysema and other broncho-pulmonary disorders where bronchospasm and secretion are complicating factors.

Dosage and administration *Compound Tablets:* Two tablets three times daily at eight-hourly intervals. Not recommended for children.

Expectorant: *Adults:* 2–3 × 5 ml spoonfuls three times daily at eight-hourly intervals. Not recommended for children.

Contra-indications, warnings, etc No contra-indications are known. Bricanyl should not be used with non-selective beta-blocking agents, but may be used with agents which selectively block cardiac β_1 receptors. Care should be taken with patients suffering from myocardial insufficiency or thyrotoxicosis. Although no teratogenic effects have been observed in animal experiments, caution is recommended during the first trimester of pregnancy.

Side-effects: The frequency of side-effects is low. Those which have been recorded, e.g. tremor and palpitations, are all characteristic of sympathomimetic amines. Whenever these have occurred, the majority have been spontaneously reversible within the first week of treatment.

Pharmaceutical precautions No special storage conditions required. Recommended diluent for expectorant is water.

Legal category POM.

Package quantities *Compound Tablets:* Bottles of 100.

Expectorant: Bottles of 300 ml and 1 litre.

Further information Bricanyl is also available as ampoules, plain tablets, syrup, pressurised aerosol and respirator solution.

Product licence numbers

Compound Tablets	0017/0067
Expectorant	0017/0068

BRICANYL[®] RESPIRATOR SOLUTION

Presentation A solution containing 10 mg/ml terbutaline sulphate.

Uses For the relief of severe bronchospasm.

Dosage and administration *Adults:* The usual dose of terbutaline by wet aerosol is 2–5 mg or in severe cases up to 10 mg. Administration of terbutaline solution can be via a nebuliser or an IPPV machine.

The terbutaline solution must be diluted with sterile physiological saline to ensure delivery of the correct dose. Such dilution will depend on two factors: the period of time over which the dose of terbutaline is to be delivered; the design of the equipment used to deliver the solution – its capacity, dead-space, etc.

For example, administration over a short period of time in a machine capable of completely utilising small volumes of liquid (e.g. Bird Respirator) may indicate little if any dilution (e.g. 3–5 ml). At the other extreme, use of a nebuliser such as Ventimask, Wright's or De Vilbiss would require a dilution suited to the equipment and administration time. For such chronic administration terbutaline should be given at a rate of 1–2 mg per hour in a solution of 100 mcg/ml (1 : 100 dilution).

Children: The doses in the table below are based on the adult dosage for severe bronchospasm of 10 mg terbutaline.

Acute usage: table below based on adult dosage for severe bronchospasm of 10 mg terbutaline.

Age	Average weight		mg terbutaline	ml undiluted solution
	kg	lb		
<3	10	22	2.0	0.2
3	15	33	3.0	0.3
6	20	44	4.0	0.4
8	25	55	5.0	0.5
10+	30+	66+	6.0	0.6

Chronic usage: Pro rata to adult chronic administration.

Contra-indications, warnings, etc No contra-indications are known. Bricanyl should not be used with non-selective beta-blocking agents, but may be used with agents which selectively block cardiac β_1 receptors. Care should be taken with patients suffering from myocardial insufficiency or thyrotoxicosis. Although no teratogenic effects have been observed in animal experiments, caution is recommended during the first trimester of pregnancy.

Side-effects: The frequency of side-effects is low and those which have been recorded, e.g. tremor and palpitations, are all characteristic of sympathomimetic amines. Whenever these have occurred, the majority have been spontaneously reversible within the first week of treatment.

Pharmaceutical precautions Bricanyl Respirator solution should be stored in a cool place away from light.

Whilst the usual diluent will be sterile physiological saline, water for injection can also be used.

Solution in nebulisers should be replaced daily.

Legal category POM.

Package quantities 10 ml.

Further information Nil.

Product licence number 0017/0078

BRICANYL[®] SA

Presentation White tablet with engraving ^A_{BD} containing 7.5 mg terbutaline sulphate in a sustained-release formulation.

Uses For relief of bronchospasm in bronchial asthma and in chronic bronchitis, emphysema and other pulmonary disorders in which bronchospasm is a complicating factor.

Dosage and administration *Adults:* 1 tablet morning and evening. The tablet may not be divided or chewed, but must be swallowed whole together with liquid.

Contra-indications, warnings, etc Bricanyl should not be used with non-selective β -blocking agents. (Non-selective β -blockers can completely or to some extent nullify the effect of β -receptor stimulants) but may be used with agents which selectively block cardiac β_1 -receptors. Care should be taken with patients suffering from myocardial insufficiency, thyrotoxicosis and diabetes. Bricanyl is contra-indicated when there is known hypersensitivity to sympathomimetic amines.

Although no teratogenic effects have been observed in animal experiments, caution is recommended during the first trimester of pregnancy. It is not known if terbutaline sulphate passes over to maternal milk.

Side-effects: The frequency of side effects is low and those which have been recorded, e.g. tremor and palpitations are all characteristic of sympathomimetic amines. Whenever these have occurred the majority have been spontaneously reversible within the first week of treatment.

As with other β -stimulants cramps may occur in hands and feet at high dosage.

Pharmaceutical precautions No special storage conditions are necessary.

Legal category POM.

Package quantities Glass bottles containing 60 tablets.

Further information The inactive components in Bricanyl SA form a matrix which is insoluble in the digestive juices. The empty matrix may sometimes pass through the digestive system unchanged and be excreted.

Product licence number 0017/0110

CITANEST[®]

Presentation Sterile clear aqueous solution for local anaesthesia. Each ml contains:

0.5% solution: Prilocaine hydrochloride 5 mg.

1% solution: Prilocaine hydrochloride 10 mg.

Uses Infiltration anaesthesia, nerve blocks, intravenous regional blocks, analgesia.

Dosage and administration Basically it should be remembered that the smallest dose to produce the required effect should be given. The maximum adult dose (body weight 70 kg) should not exceed 400 mg; for children and debilitated patients smaller amounts and weaker concentrations directly proportionate to weight are indicated.

Contra-indications, warnings, etc Known hypersensitivity to anaesthetics of the amide type.

Adverse reactions: Systemic effects are practically unknown due to the small dosages employed. However, at the recommended maximum dosage there is a transient increase of the methaemoglobin value, sometimes with a concomitant cyanosis. If considered desirable intravenous methylene blue treatment (1 mg/kg body weight) may be instituted.

If toxic reactions occur as a result of overdosage, faulty injection technique or possible hypersensitivity, treatment is the same as for other local anaesthetics. The type of toxic reaction is unpredictable, and depends on dosage, route of administration and state of the patient. Reactions are primarily of two types typified by stimulation and depression of the cerebral cortex and medulla respectively.

Precautions: Care should be observed in patients suffering from epilepsy.

Pharmaceutical precautions Store at room temperature.

Legal category POM.

Package quantities 0.5% and 1% solution: Vials of 20 ml and 50 ml.

Further information Citanest multidose vials contain methylhydroxybenzoate 1 mg/ml.

Product licence numbers

0.5% 0017/5047

1% 0017/5048

CITANEST* 3% WITH ADRENALINE 1 : 300,000

Presentation Sterile clear aqueous solution for dental anaesthesia: prilocaine hydrochloride 30 mg/ml, Adrenaline BP 1 : 300,000.

Uses For dental infiltration anaesthesia where there is no necessity for profound ischaemia in the area injected. For all dental nerve-block techniques.

Dosage and administration Infiltration – 1 ml. Nerve block – 1.5–2 ml.

The recommended maximum dosage is higher than that recommended for a plain solution, but total dosage should not exceed 600 mg in a healthy adult of body weight 70 kg. The total dose should not exceed 20 ml. In children, aged and debilitated patients the dose may be reduced and calculated in relation to body weight.

Contra-indications, warnings, etc Known hypersensitivity to anaesthetics of the amide type.

Precautions: All established precautions on the use of adrenaline should be observed, e.g. cardiac patients, hypertension, thyrotoxicosis, in patients taking tricyclic antidepressants. If toxic reactions occur as a result of overdosage, faulty injection technique or possible hypersensitivity, treatment is the same as for other local anaesthetics. Care should be observed in patients suffering from epilepsy.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Glass cartridges of 2 ml in boxes of 100.

Further information Citanest 3% with adrenaline

1 : 300,000 solutions contain methylhydroxybenzoate 1 mg/ml.

Product licence number 0017/5002.

CITANEST* 3% WITH OCTAPRESSIN*

Presentation Sterile clear aqueous solution for dental anaesthesia: prilocaine hydrochloride 30 mg/ml, felypressin 0.03 i.u. per ml.

Uses Local anaesthetic solution with vasoconstrictor for dental infiltration anaesthesia where there is no necessity for profound ischaemia in the area injected. For all dental nerve-block techniques.

Dosage and administration 1–2 ml should be sufficient for the majority of procedures. The addition of Octapressin decreases the rate of absorption of the injected solution. For this reason the recommended maximum dosage for Citanest with Octapressin is higher than that recommended for a plain solution, but total dosage of Citanest should not exceed 600 mg in a healthy adult of body weight 70 kg. The total dose should not exceed 20 ml. In aged and debilitated patients the dose must be reduced. In children the maximum dose is considerably less and should be calculated in relation to body weight.

Contra-indications, warnings, etc In known cases of ischaemic heart disease not more than four cartridges should be used at one sitting.

Known sensitivity to local anaesthetics of the amide type.

Adverse reactions: The type of toxic reaction is unpredictable and depends on dosage, route of administration and state of the patient. The reactions are primarily of two types, and typified by stimulation and depression of the cerebral cortex and medulla respectively. Slow onset – stimulation leading to nervousness, dizziness, blurred vision, nausea, tremors, convulsions and respiratory arrest. Rapid onset – depression leading to respiratory arrest, cardiovascular collapse and cardiac arrest. Symptoms occur rapidly and with little warning.

Precautions: Adequate resuscitation equipment must be available whenever local or general anaesthesia is administered. Though clinical tolerance is remarkably good, overdosage or accidental intravenous injection may give rise to toxic reactions. Care should be observed in patients suffering from epilepsy.

Pharmaceutical precautions Store at room temperature.

Legal category POM.

Package quantities Glass cartridges of 2 ml standard, and 2 ml self-aspirating, in boxes of 100.

Further information Citanest 3% with Octapressin solutions contain methylhydroxybenzoate 1 mg/ml.

Product licence number 0017/5003.

CITANEST* 4%

Presentation Sterile clear aqueous solution. Each millilitre contains prilocaine hydrochloride 40 mg.

Uses Local anaesthetic solution without vasoconstrictor for dental infiltration anaesthesia where there is no necessity for profound ischaemia in the area injected.

For all dental nerve-block techniques. For all dental injections where a vasoconstrictor is contra-indicated.

Dosage and administration 1–2 ml. In a healthy adult of a normal body weight (70 kg) the maximum dose should not exceed 400 mg. In aged and debilitated patients the dose must be reduced, and in children the maximum dose should be calculated in relation to body weight, i.e. 3 mg per lb or 6 mg per kg.

Contra-indications, warnings, etc Known hypersensitivity to anaesthetics of the amide type.

Side-effects: Systemic effects due to the use of Citanest in dental practice are practically unknown due to the small dosages employed.

Adverse reactions: The type of toxic reaction is unpredictable, and depends on dosage, route of administration and state of patient. Reactions are primarily of two types typified by stimulation and depression of the cerebral cortex and medulla respectively.

Precautions: Though clinical tolerance is remarkably good, overdosage or accidental intravenous injection may give rise to toxic reactions. These are best avoided by aspiration before making an injection, in order to avoid accidental intravascular injection. Care should be observed in patients suffering from epilepsy.

Pharmaceutical precautions Store at room temperature.

Legal category POM.

Package quantities Glass cartridges of 2 ml standard and 2 ml self-aspirating in boxes of 100.

Further information Citanest 4% solutions contain methylhydroxybenzoate 1 mg/ml.

Product licence number 0017/5050.

CO-BETALOC*

Presentation White scored tablets (coded A/MH) containing 100 mg metoprolol tartrate and 12.5 mg hydrochlorothiazide.

Uses In the management of mild or moderate hypertension. The combination product may be suitable for use when satisfactory control of arterial blood pressure cannot be obtained with either a diuretic or a beta-adrenoceptor blocking drug used alone.

Dosage and administration The dose will depend on patient response. Usually 1–3 tablets per day as a single or in divided dose.

Contra-indications, warnings, etc

Contra-indications: AV block.

Digitalis refractory heart failure.

Severe kidney and liver failure.

Manifest gout.

Anti-diuretic effect has been reported following concomitant treatment with diuretics and lithium. As with all products which contain diuretics, Co-Betaloc is contra-indicated during lithium therapy.

Warnings: In labile and insulin dependent diabetes, it may be necessary to adjust the hypoglycaemic therapy.

Co-Betaloc therapy must be reported to the anaesthetist prior to general anaesthesia.

Digitalisation should be considered for patients with a previous history of heart failure, or patients known to have a poor cardiac reserve.

Metoprolol has proved safe in a large number of asthmatic patients; although it is a selective beta-blocker it is prudent to exercise care in the treatment of patients with chronic obstructive pulmonary disease.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenoceptor blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuation of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-blocker should be gradual.

Until further evidence is available Co-Betaloc therapy should be avoided in pregnancy.

Side-effects: Are mild and infrequent. The most common are gastro-intestinal disturbance, lassitude and disturbances of sleep pattern. In many cases these effects are transient or have disappeared with a reduction in dosage. The familiar side-effects of thiazide diuretics may be expected.

Pharmaceutical precautions Store in a cool dry place.

Legal category POM.

Package quantities Calendar packs of 28 tablets. Securitainers of 300 tablets.

Further information The use of a selective beta-blocker in this combination may counteract the tendency to hyperglycaemia which the diuretic may provoke.

Treatment of overdosage: Marked bradycardia may be treated by intravenous atropine sulphate (0.25–2.0 mg) and in severe cases by slow intravenous infusion of about 5 mcg per minute of isoprenaline.

Product licence number 0017/0092.

DIRYTHMIN SA* ▼

Presentation White, film-coated sustained release tablets (Durules), engraved $\text{D}_\text{A}_\text{R}$ on one side containing 150 mg disopyramide base as the phosphate.

Uses Dyrhythm-SA is a Class I antiarrhythmic drug, indicated for treatment of a wide range of supraventricular and ventricular arrhythmias including:

Atrial or ventricular ectopic beats.

Paroxysmal atrial or ventricular tachycardia.

Arrhythmias associated with myocardial infarction.

Wolff-Parkinson-White syndrome.

Maintenance of sinus rhythm following electro-conversion.

Dyrhythm-SA can be used in both digitalised and non-digitalised patients.

Dosage and administration The dosage should be adjusted dependant on the patient response and tolerance. The normal adult dosage is 2 tablets 12 hourly (600 mg daily). Dosage should not normally exceed 900 mg daily.

In patients with moderate renal insufficiency (creatinine clearance > 40 ml/min) or hepatic insufficiency, dosage should be limited to 1 Dyrhythm-SA tablet b.d. In patients with creatinine clearance < 40 ml/min standard capsules are advised.

Dyrhythm-SA tablets should be swallowed whole.

Patients treated with conventional disopyramide capsules q.i.d. can be transferred to the equivalent dosage

of Dirythmin-SA e.g. 150 mg disopyramide q.i.d. is equivalent to 2 × 150 mg Dirythmin-SA tablets b.d.

Contra-indications, warnings, etc

Contra-indications: AV block II and III in absence of pacemaker. Known hypersensitivity. Cardiogenic shock.

Warnings: Disopyramide should not be administered to patients with cardiomyopathy, or uncompensated cardiac failure.

Treatment with disopyramide should be discontinued if any of the following develop: Hypotension, 2nd or 3rd degree heart block, significant QRS prolongation (> 25%) or QT prolongation.

Disopyramide has been associated with hypoglycaemia usually in patients with impaired liver function. Caution should be observed in patients with prostatic hypertrophy, glaucoma, myasthenia gravis or digitalis intoxication.

Disopyramide dosage should be reduced if 1st degree heart block develops and may require discontinuation if the block persists.

Patients should be digitalised prior to administration of disopyramide for the treatment of atrial flutter or fibrillation or blocked SVT.

Use of disopyramide with other Class I antiarrhythmics and/or beta-blockers is not recommended.

Disopyramide may be ineffective in the presence of marked hypokalaemia.

The safety and efficacy of disopyramide in children has not been established. The safety of disopyramide in pregnancy has not been established.

Side-effects: Side-effects reported are usually associated with the anticholinergic properties of disopyramide and include dry mouth, blurred vision and urinary retention.

Treatment of overdosage: Disopyramide should be discontinued and supportive or symptomatic treatment instigated.

Pharmaceutical precautions Store in a cool, dry place.

Legal category POM.

Package quantities Amber glass bottles of 100 tablets.

Further information Nil.

Product licence number 0017/0100.

HEMINEVRIN* 0.8% INFUSION

Presentation Colourless aqueous solution; chlormethiazole edisylate 8 mg/ml.

Uses Hypnotic and anticonvulsant for the treatment of pre-eclamptic toxemia, status epilepticus, acute alcohol withdrawal symptoms and delirium tremens.

Dosage and administration *Pre-eclamptic toxemia:* An intravenous infusion is set up with 30–50 ml Heminevrin 0.8%. The solution is run in quickly at 60 drops per minute (4 ml/min) until the patient feels drowsy. The exact amount given depends on the patient's response. The drip rate is then maintained at 15 drops/minute (= 1 ml/minute) or decreased to 10 drops per minute if the patient is very drowsy. As the patient responds very quickly to the change of dosage, the drip rate can be increased if the patient is restless, and reduced again once the patient is well sedated.

Status epilepticus: 40–100 ml of Heminevrin 0.8% infusion administered over a period of 5–10 minutes will usually stop convulsions. Thereafter an intravenous infusion of Heminevrin 0.8% may be required depending on the patient's response.

Acute alcohol withdrawal symptoms and delirium tremens: Either of the above regimes can be utilised depending on the patient's condition but if the rapid infusion method is used it will be necessary to continue with either an infusion of Heminevrin 0.8% or oral therapy with Heminevrin capsules due to the short half life (three to four hours) of chlormethiazole.

Contra-indications, warnings, etc *Side-effects:*

Heminevrin has a very low toxicity. The most common side-effect appears to be a tingling sensation in the nose and sneezing, occurring immediately after the start of the intravenous infusion. Conjunctival irritation has also been noted in some cases, and occasionally these symptoms may be severe and may be associated with severe headache. Intravenous administration of Heminevrin solution may be followed by a slight but temporary decrease in blood pressure, which is less pronounced the slower the infusion is given. Local reactions such as thrombophlebitis at the site of injection are exceedingly rare, except when using the continuous intravenous infusion. In these cases superficial phlebitis has been frequently reported, but only of a mild degree. Neither heparin nor cortisone has been shown to be helpful in preventing such reactions.

Precautions: Heminevrin may potentiate or be potentiated by centrally acting depressant drugs, including alcohol, thus when used concomitantly dosages should be appropriately reduced. The patient should be kept under close and constant observation by a nurse during the period of continuous drip infusion. With too high a rate of infusion the sleep induced with Heminevrin can pass unnoticed into deep unconsciousness with the consequent risk of mechanical airway obstruction. With gross overdosage there is always the possibility of causing centrally induced respiratory depression and circulatory collapse. In view of the possible risk of slight respiratory depression during routine Heminevrin intravenous therapy, caution should be observed when administering the solution to patients with a history of obstructive pulmonary disease. Because of the possible danger of mechanical airway obstruction occurring in deep sleep during Heminevrin therapy, the patient should be maintained where necessary by the use of an oral airway tube. In addition, an aspirator should always be close at hand.

Pharmaceutical precautions To be stored within the temperature range 5°C–8°C.

Legal category POM.

Package quantities Bottles of 500 ml.

Further information Nil.

Product licence number 0017/5007.

**HEMINEVRIN* CAPSULES
HEMINEVRIN* SYRUP**

Presentation *Capsules:* Off-white oval capsule containing chlormethiazole (base) 192 mg in arachis oil.

Syrup: Clear, colourless, aqueous solution containing chlormethiazole edisylate 50 mg/ml.

Uses Neuropharmacological studies in animals show that Heminevrin possesses sedative/hypnotic and anti-convulsant properties. Whilst the mode of action is uncertain, the anticonvulsant effect may involve direct or indirect actions on GABA-systems in the CNS. The sedative/hypnotic properties involve actions on both catecholaminergic and gabaergic systems.

Indications: In adults, Heminevrin is indicated in the management of restlessness and agitation in the elderly, in the short term treatment of insomnia in the elderly and in the control of symptoms arising from acute withdrawal from alcohol where close hospital supervision is also provided.

Heminevrin is not recommended for use in children.

Dosage and administration *Sleep disturbances in the elderly:* The usual dose will be two capsules or two 5 ml spoonful of syrup before going to bed. In rare cases, one capsule of 5 ml syrup will suffice.

Management of restlessness and anxiety: One capsule or 5 ml syrup three times daily.

Alcohol withdrawal states: Heminevrin is not a treatment for 'alcoholism'. Alcohol withdrawal should be treated in hospital or, in exceptional circumstances, on an out-patient basis by specialist units when the daily dosage of Heminevrin must be monitored closely by community health staff. The dosage should be adjusted to patient response. A suggested regimen is:

Initial dose: 2 to 4 capsules, if necessary repeated after some hours.

Day 1, first 24 hours: 9 to 12 capsules, divided into 3 or 4 doses.

Day 2: 6 to 8 capsules, divided into 3 or 4 doses.

Day 3: 4 to 6 capsules, divided into 3 or 4 doses.

Days 4 to 6: A gradual reduction in dosage until final dose.

Administration for more than nine (9) days is not recommended. 5 ml of Heminevrin syrup can be substituted for each capsule administered, if desired.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to chlormethiazole. Acute pulmonary insufficiency.

Precautions: Chronic pulmonary insufficiency. Chronic renal or hepatic disease. Heminevrin may potentiate or be potentiated by centrally acting depressant drugs including alcohol. Whilst the concurrent use of other central nervous system drugs should be avoided, if they are used, dosages should be appropriately reduced. Particular caution should be exercised when either chlormethiazole or another CNS depressant is given parenterally. Hypoxia, resulting from, for example, cardiac and/or respiratory insufficiency, may result in manifestations of symptoms of agitation and restlessness leading to a confusional state. Recognition and specific treatment of the cause is essential in such patients.

Warnings and adverse effects: The most common side-effect is nasal congestion and irritation, which may occur 15 to 20 minutes after drug ingestion. Conjunctival irritation has also been noted in some cases and, occasionally, these symptoms may be severe and may be associated with severe headache. Gastrointestinal disturbances have been reported.

Hangover effects in the elderly are uncommon but may occur.

Excessive sedation may occur, especially with higher

doses or when given to the elderly for daytime sedation. Paradoxical excitement or confusion may occur rarely. Large doses of chlormethiazole depress respiration. Performance at skilled tasks and alertness may be impaired.

Where relevant, patients should be warned of this hazard and advised not to drive or operate machinery during treatment.

When Heminevrin has been given at higher than recommended doses for other than recommended indications over prolonged periods of time, physical dependence, tolerance and withdrawal reactions have been reported.

Great caution is required in prescribing Heminevrin for patients with a history of chronic alcoholism, drug abuse or marked personality disorder.

Heminevrin should not be prescribed for alcoholics who continue to drink alcohol.

Overdose: The main symptoms to be expected with overdose of Heminevrin are: coma, respiratory depression, hypotension and hypothermia.

Hypothermia is thought to be due to a direct central effect as well as a result of lying unconscious for several hours. In addition, patients have increased secretion in the upper airways, which in one series was associated with a high incidence of pneumonia. The effects of overdosage are not usually severe in patients with no evidence of alcoholic liver disease, but they may be exacerbated when chlormethiazole is taken in combination with alcohol and/or CNS depressant drugs, particularly those that are metabolised by the liver. There is no specific antidote to chlormethiazole. Treatment of overdosage should therefore be carried out on a symptomatic basis, applying similar principles to those used in the treatment of barbiturate overdosage.

Further information Heminevrin has a short half life and therefore a low incidence of daytime sedation when prescribed as an hypnotic.

In the elderly, the safety and efficacy of Heminevrin has been established in controlled studies of up to three months duration. However, as with all psychotropic drugs, treatment should be kept to a minimum, reviewed regularly and discontinued as soon as possible.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities

Capsules: Bottles of 100.

Syrup: Bottles of 300 ml and 500 ml.

Product licence numbers

Capsules 0017/5009R

Syrup 0017/0063

HEWLETT'S* ANTISEPTIC CREAM

Presentation White scented cream: zinc oxide 8%, boric acid 2.5%, lanolin 4%.

Uses Topical ointment for nursing hygiene and care of skin.

Dosage and administration Applied as required.

Contra-indications, warnings, etc Not to be administered to large areas of broken skin.

Pharmaceutical precautions Store at room temperature.

Legal category P.

Package quantities 35 g tubes.

Further information Nil.

Product licence number 0017/5010.

HYPRENAN* ▼

Presentation A clear, colourless solution containing 1 mg per ml prenalterol hydrochloride in 5 ml ampoules.

Uses Hyprenan is indicated only in adults who require inotropic support in the treatment of heart failure associated with myocardial infarction, open heart surgery or shock, and for the reduction or abolition of the cardiac effects of beta-adrenoceptor blockade.

Dosage and administration 1. When inotropic support is required in the treatment of heart failure associated with myocardial infarction, open heart surgery or shock, Hyprenan should be given by slow intravenous infusion, at a rate of 0.5 mg per minute. However, the rate of the administration and duration of therapy should be adjusted according to patient response as determined by heart rate, blood pressure and, if possible, cardiac output. The maximum total dose used in clinical trials has been 20 mg.

2. To abolish or reduce the cardiac effects of beta-adrenoceptor blockade, Hyprenan should be given in doses of 2–5 mg i.v. Hyprenan should be administered cautiously, generally over a 5 minute period depending on the acuteness of the situation. The optimal effect of each dose is generally achieved within 2–5 minutes, after which further doses may be given to a maximum of 20 mg total. Larger doses of Hyprenan may be necessary in patients who have taken beta-adrenoceptor blocking agents in excess of the recommended dose.

Contra-indications, warnings, etc Hyprenan should not be given to patients with serious ventricular arrhythmias.

Pregnacy: Toxicology studies in animals have indicated an increased occurrence of undesirable effects on foetal development, manifest as abnormalities of the thoracic cage and cardiovascular system. The significance of this in man is, however, uncertain. Nevertheless, benefit: risk should be considered before administering prenalterol to pregnant women or women of child-bearing age.

Caution: Hypovolaemia should be corrected before giving Hyprenan. Hyprenan should be used with caution in patients with angina pectoris and recent myocardial infarction (during the first 6 weeks post infarction). Hyprenan should be used with caution in patients with hypokalaemia. Patients with uncontrolled or insulin-dependent diabetes should be kept under careful observation. Hyprenan should be used with great caution in patients with obstructive subvalvular cardiomyopathy as inotropic agents may exacerbate the obstruction to flow in these patients. If excessive increase in blood pressure or heart rate occurs and it is desired to counteract the effects of Hyprenan, a beta-adrenoceptor blocking agent should be given intravenously.

Side-effects: Palpitations and nervousness may occur. Isolated ventricular ectopic beats have been observed. In some patients with a history of angina pectoris, Hyprenan has caused an increase in anginal attacks.

Pharmaceutical precautions Recommended di-

luents are: sterile saline, Ringer's or 5% anhydrous glucose solution.

Legal category POM.

Package quantities 4 × 5 ml ampoules.

Further information Hyprenan has a more pronounced effect on cardiac contractility than on heart rate. Cardiac output increases mainly as a result of increased stroke volume. Hyprenan increases the systolic blood pressure with little or no effect on diastolic blood pressure. The plasma half life is about 2 hours. Excretion is mainly via the kidneys with 60% of the dose recoverable from the urine as unchanged drug.

Product licence number 0017/0109

JECTOFR*

Presentation Dark brown liquid for intramuscular injection; Iron Sorbitol Citric Acid Complex BP (50 mg elemental iron per ml).

Uses For the treatment of iron-deficiency anaemia and the rapid replenishment of iron stores.

Dosage and administration The recommended single dose of Jectofer is 1.5 mg per kg body weight by intramuscular injection to a maximum of 100 mg per injection. A series of daily injections of this single dose should be given to restore haemoglobin levels to normal and replenish iron stores based on the following table.

Hb gm/100 ml	5.0	6.0	7.0	8.0	9.0	10.0	11.0
Hb%	33	40	46	53	60	66	73
No. of injections	24	22	20	17	14	12	10

In patients who have a low tolerance threshold to intramuscular iron the injections should be given on alternate days. Not recommended in children under 3 kg (7 lb) body weight.

Contra-indications, warnings, etc Serious liver or kidney damage. Ineffective in aplastic or hypoplastic anaemias and acute leukaemia.

Side-effects: A few cases have been reported of serious reactions of a cardiovascular type with cardiac arrhythmia.

Precautions: The importance of using the correct recommended dose in relation to body weight is emphasised, especially in patients who are already markedly underweight. Oral Iron should be discontinued 24 hours before Jectofer is administered.

Pharmaceutical precautions Store at room temperature, do not refrigerate.

Legal category POM.

Package quantities 10 × 2 ml and 100 × 2 ml ampoules for intramuscular use.

Further information Nil.

Product licence number 0017/5011.

KINIDIN DURULES*

Presentation Film-coated white oval tablets. Each Durule contains 250 mg quinidine bisulphate (equivalent to 200 mg Quinidine Sulphate BP) in a sustained action form.

Uses Maintenance of sinus rhythm following electrical conversion of atrial fibrillation, extrasystoles (atrial, nodal, ventricular), paroxysmal atrial tachycardia, nodal tachycardia, atrial fibrillation, atrial flutter, ventricular paroxysmal tachycardia. Conversion of atrial fibrillation.

Dosage and administration Two to five Durules twice a day (morning and evening). In certain cases, e.g. conversion of atrial fibrillation, it may be necessary to increase this dosage. Should be swallowed whole.

Contra-indications, warnings, etc The presence of acute infections or toxic conditions, known hypersensitivity to quinidine, bundle branch block, untreated cardiac insufficiency, thrombocytopenia.

Side-effects: originating from CNS, termed as cinchonism (impaired hearing, blurred vision, headache, dizziness and vomiting). These symptoms are associated with overdosage and usually disappear on reduction of dosage. Gastro-intestinal irritation resulting in nausea, vomiting.

Adverse reactions: Hypersensitivity reactions are very rare and are manifested as urticaria, increased temperature, which may result in thrombocytopenia. Granulomatous hepatitis with raised liver enzymes, reversible on stopping therapy, has also been reported. Heart block, premature beats, ventricular tachycardia, ventricular fibrillation can occur and are usually a result of overdosage.

Precautions: A test dose of one Kinidin Durule should always be given in order to ascertain whether there is hypersensitivity. In digitalised patients quinidine may increase the concentration of digitalis in plasma by up to 100%. It may therefore be necessary to reduce the dose of digitalis in these patients.

Pharmaceutical precautions Not to be dispensed in a metal container.

Legal category POM.

Package quantities Bottles of 100 and 250.

Further information Nil.

Product licence number 0017/5015.

PROCAINAMIDE DURULES*

Presentation Slightly yellow, circular, convex tablets containing 500 mg procainamide hydrochloride.

Uses Supraventricular tachyarrhythmias (atrial premature beats, paroxysmal atrial tachycardia, atrial flutter, atrial fibrillation, AV junctional tachycardia and premature beats).

Ventricular arrhythmias (ectopic beats, premature beats, and tachycardia).

Digitalis induced arrhythmias.

Dystrophia myotonica; myotonica congenita (Thomsen).

Dosage and administration Ideally the dosage should be adjusted to maintain a serum concentration between 4–8 mcg per ml, usually 2–3 tablets three times a day (3–4.5 g daily).

Guidelines: Anti-arrhythmic prophylaxis after acute myocardial infarction, initially 3–4 Durules followed by 2–3 Durules thrice daily as maintenance. During transition from lignocaine therapy, treatment with Procainamide Durules should be initiated two hours prior to

discontinuation of infusion of lignocaine. It may occasionally be necessary to divide the daily dose into 4 doses per day.

The Durules should be swallowed whole, not broken or chewed.

Contra-indications, warnings, etc

Contra-indications: Procainamide hypersensitivity. Second or third degree AV-block and bifascicular block with AV-block type I if the patient does not have a pacemaker. Bronchial asthma, myasthenia gravis and SLE are relative contra-indications.

Precautions: In patients with renal insufficiency or heart failure, accumulation of procainamide may occur; caution should therefore be observed and the dose adjusted if necessary. Accumulation leads to an impairment of hepatic and/or renal function.

Side-effects: Procainamide is generally well tolerated, but anorexia, nausea and vomiting and diarrhoea may occur. Occasional cases of flushing, skin rash, pruritis, depression, vertigo, psychosis with hallucinations, shivering, fever, joint and muscle pain, 'bitter taste' and muscle weakness have been reported. A possible lupus erythematosus-like syndrome may occur during treatment. Serological tests for ANF should therefore be made before commencement of treatment and regularly thereafter. The blood should also be examined for LE-type cells at the same time. If the ANF titre rises or LE cells appear, then cessation of treatment should be considered. Usually these increases are noted before overt clinical symptoms are detectable. The syndrome is usually completely reversible. Serious side-effects in the form of leucopenia and agranulocytosis may occur during long-term treatment.

Pharmaceutical precautions Procainamide Durules may be stored at room temperature.

Legal category POM.

Package quantities 500 mg tablets in bottles of 100.

Further information Procainamide Durules are a sustained release formulation which enable therapeutic blood levels of procainamide to be conveniently attained and maintained.

Product licence number 0017/0071.

TONOCARD* ▼

Presentation Yellow, biconvex, film coated tablets containing tocainide hydrochloride, either 400 mg (coded A/TT) or 600 mg (coded A/TC).

Injection vials of 15 ml, each 1 ml of clear aqueous sterile solution for injections contains 50 mg tocainide hydrochloride.

Uses Tonocard can be used for both treatment and prophylaxis of acute and chronic ventricular arrhythmias, including those complicating myocardial infarction.

Dosage and administration *Acute Treatment:* 500–750 mg by slow intravenous injection (or by infusion, diluted in 50–100 ml saline or glucose) given over 15–30 minutes, followed immediately by 600–800 mg orally.

Maintenance treatment: 8 hours after acute treatment, commence maintenance therapy with 1200 mg daily, divided into two or three oral doses.

Chronic ventricular arrhythmias: 1200 mg daily, divided into two or three oral doses.

The oral daily dosage of Tonocard may be increased to 1800–2400 mg in divided doses, if necessary.

Not to be administered to children.

Contra-indications, warnings, etc *Contra-indications:* Known hypersensitivity to amide drugs. Second or third degree A.V. block, in the absence of a pacemaker.

Precautions: Like other drugs, Tonocard should be used with caution in patients with severe hepatic or renal disease and in the elderly because of the potential risk of accumulation. Caution is also advised in patients with uncompensated heart failure and in patients receiving other antiarrhythmic agents.

Reproduction studies in animals have shown maternal and foetal toxicity. The safety of Tonocard in human pregnancy has not been tested and the potential benefit should be weighed against possible hazard.

Side-effects: Side effects during Tonocard treatment are generally mild and transient. Reported side effects are mainly neurological or gastro-intestinal. CNS symptoms are usually dose-related and may include tremor, dizziness, lightheadedness, convulsions and paraesthesia. Gastro-intestinal symptoms include nausea and vomiting. Rash and fever have been reported. Bradycardia and hypotension may occur after i.v. injection. Positive ANF titres, clinical manifestation of LE syndrome and fibrosing alveolitis have been reported during Tonocard therapy. Agranulocytosis or transient neutropenia has occurred in a few patients taking Tonocard, although a causal relationship has not been established.

Pharmaceutical precautions Recommended diluents for i.v. injection are sterile glucose solution or sterile saline.

Legal category POM.

Package quantities *Tablets:* 400 mg, bottle of 100 tablets; 600 mg, bottle of 100 tablets.

Injection: Packs of 5 × 15 ml injection vials.

Further information Tonocard is a primary amine analogue of lignocaine, with a high oral bio-availability. Its electro-physiological properties are similar to lignocaine and, as such, Tonocard has been shown to be effective in the treatment of ventricular arrhythmias. In therapeutic plasma concentration, no clinically significant adverse haemodynamic changes have been reported, even in patients with acute myocardial infarction or those pre-treated with beta-blockers.

Product licence numbers

400 mg tablets	0017/0106
600 mg tablets	0017/0107
50 mg/ml i.v. Solution	0017/0108

XYLOCAINE*

Presentation Clear aqueous sterile solution for injection. Each millilitre contains:

0.5% solution:	lignocaine hydrochloride anhydrous	5 mg
1% solution:	lignocaine hydrochloride anhydrous	10 mg
1.5% solution:	lignocaine hydrochloride anhydrous	15 mg
2% solution:	lignocaine hydrochloride anhydrous	20 mg

Uses Local anaesthetic solution without vasoconstrictor for infiltration anaesthesia, nerve blocks, intravenous regional blocks and analgesia.

Dosage and administration The dosage for local anaesthetics must be judged for each individual patient. Basically it should be remembered that the smallest dose producing the desired result should be given. Maximum dosage for adults of average body weight (70 kg) is 200 mg. Dosages for debilitated and aged patients should be appropriately reduced. For children, smaller amounts in lower concentrations should be administered, dependent on body weight.

The 1% solution in doses up to 20 ml and 2% solution in doses up to 10 ml should be reserved for nerve blocks.

Contra-indications, warnings, etc Known hypersensitivity to anaesthetics of the amide type.

Adverse reactions: The type of toxic reaction is unpredictable and depends on dosage, route of administration and state of the patient. The reactions are primarily of two types typified by stimulation and depression of the cerebral cortex and medulla respectively. Adequate resuscitation equipment must be available whenever local or general anaesthesia is administered. Though clinical tolerance is remarkably good, overdosage or accidental intravenous injection may give rise to toxic reactions.

Special precautions: Care should be observed in patients suffering from epilepsy.

Pharmaceutical precautions Store at room temperature.

Legal category POM.

Package quantities

Vials:

0.5% solution	– 20 ml, 50 ml.
1.0% solution	– 20 ml, 50 ml.
2.0% solution	– 20 ml, 50 ml.

Ampoules:

0.5% solution	– 10 ml.
1% solution	– 2 ml, 10 ml.
1.5% solution	– 25 ml.
2% solution	– 5 ml.

Further information Multidose vial preparations of Xylocaine contain methylhydroxybenzoate 1 mg/ml.

Product licence numbers

0.5%	0017/5031
1%	0017/5032
1.5%	0017/5033
2%	0017/5034

XYLOCAINE* WITH ADRENALINE 1 : 200,000

Presentation Clear sterile aqueous solution for injection. Each millilitre contains:

0.5% solution:	lignocaine hydrochloride anhydrous	5 mg, Adrenaline BP 0.005 mg.
1% solution:	lignocaine hydrochloride anhydrous	10 mg, Adrenaline BP 0.005 mg.
2% solution:	lignocaine hydrochloride anhydrous	20 mg, Adrenaline BP 0.005 mg.

Uses Local anaesthetic solution with vasoconstrictor for infiltration anaesthesia, nerve blocks and analgesia.

Dosage and administration The dosage for local

anaesthetics must be judged for each individual patient. Basically it should be remembered that the smallest dose producing the desired result should be given. Maximum dosage for adults of average body weight (70 kg) is 500 mg. Dosage for debilitated and aged patients should be appropriately reduced. For children, smaller amounts in lower concentrations should be administered, dependent on body weight.

In operative fields the 0.5% solution may be used for infiltration anaesthesia. The 1% solution in doses up to 50 ml and the 2% solution in doses up to 25 ml should be reserved for nerve blocks.

Contra-indications, warnings, etc Hypersensitivity to local anaesthetics of the amide type. The use of vasoconstrictor is contra-indicated for analgesia of fingers, toes, tip of nose, ears and penis.

Adverse reactions: The type of toxic reaction is unpredictable and depends on dosage, route of administration and state of the patient. The reactions are primarily of two types, typified by stimulation and depression of the cerebral cortex and medulla respectively. Adequate resuscitation equipment must be available whenever local or general anaesthesia is administered. Though clinical tolerance is remarkably good, overdosage or accidental intravenous injection may give rise to toxic reactions.

Precautions: Care should be observed in patients taking tricyclic antidepressants; patients suffering from epilepsy. Xylocaine solutions containing vasoconstrictors are suitable for routine use. Whenever possible solutions containing vasoconstrictors should be used to prolong anaesthesia and to reduce systemic absorption. This is especially important in highly vascularised areas.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities

Vials:

0.5% solution – 20 ml, 50 ml.

1.0% solution – 20 ml, 50 ml.

2.0% solution – 20 ml, 50 ml.

Ampoules:

1.0% solution – 10 ml.

Further information Multidose vial preparations of Xylocaine with adrenaline 1 : 200,000 contain methylhydroxybenzoate 1 mg/ml.

Product licence numbers

0.5% 0017/5028

1% 0017/5029

2% 0017/5030

XYLOCAINE* 2%

Presentation Sterile aqueous solution for injection: lignocaine hydrochloride 20 mg/ml.

Uses Local anaesthetic solution without vasoconstrictor for dental anaesthesia where there is no need for profound ischaemia in the area injected. For all dental nerve-block techniques.

Dosage and administration Infiltration – 1 ml. Nerve block – 1.5–2 ml.

In adults the maximum total dose of Xylocaine is 200 mg.

In children the maximum dose is considerably less and should be calculated in relation to body weight.

Contra-indications, warnings, etc Known hypersensitivity to local anaesthetics of the amide type.

Adverse reactions: The type of toxic reaction is unpredictable and depends on dosage, route of administration and state of the patient. The reactions are primarily of two types, typified by stimulation and depression of the cerebral cortex and medulla respectively. Slow onset – stimulation leading to nervousness, dizziness, blurred vision, nausea, tremor convulsions and respiratory arrest. Rapid onset – depression leading primarily to respiratory arrest, cardiovascular collapse and cardiac arrest.

Precautions: Adequate resuscitation equipment must be available whenever local or general anaesthesia is administered. Though clinical tolerance is extremely good, overdosage or accidental intravenous injection may give rise to toxic reactions.

Pharmaceutical precautions Store at room temperature.

Legal category POM.

Package quantities 2 ml glass cartridges in boxes of 100.

Further information Dental cartridges of Xylocaine 2% contain methylhydroxybenzoate 1 mg/ml.

Product licence number 0017/5026.

XYLOCAINE* 2% WITH ADRENALINE 1 : 80,000

Presentation Sterile clear aqueous solution: lignocaine hydrochloride 20 mg/ml, Adrenaline BP 1 : 80,000.

Uses Local anaesthetic solution with vasoconstrictor for dental infiltration anaesthesia where a vasoconstrictor is indicated. For all dental nerve-block techniques.

Dosage and administration Infiltration – 1 ml. Nerve block – 1.5–2 ml. Extensive surgery – 3–5 ml. Adult maximum dose 500 mg.

In children the maximum dose is considerably less and should be calculated in relation to the body weight.

Contra-indications, warnings, etc Patients with thyrotoxicosis and cardiac disease, particularly with arrhythmia or hypertension. Known hypersensitivity to local anaesthetics of the amide type.

Adverse reactions: The type of toxic reaction is unpredictable and depends on dosage, route of administration and state of patient, the reactions are primarily of two types, typified by stimulation and depression of the cerebral cortex and medulla respectively. Slow onset – stimulation leading to nervousness, dizziness, blurred vision, nausea, tremor convulsions and respiratory arrest. Rapid onset – depression leading primarily to respiratory arrest, cardiovascular collapse and cardiac arrest. Symptoms occur rapidly and with little warning.

Precautions: Adequate resuscitation equipment must be available whenever local or general anaesthesia is administered. Though clinical tolerance is remarkably good, overdosage or accidental intravenous injection may give rise to toxic reactions. These are best avoided by aspiration before making an injection in order to avoid accidental intravascular injection.

Care should be observed in patients taking tricyclic anti-depressants.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Glass cartridges of 2 ml standard, and 2 ml self-aspirating, in boxes of 100.

Further information Dental cartridges of Xylocaine 2% with adrenaline 1 : 80,000 contain methylhydroxybenzoate 1 mg/ml.

Product licence number 0017/5027.

XYLOCAINE* ANTISEPTIC GEL

Presentation Clear sterile viscous gel. Each millilitre contains Lignocaine Hydrochloride BP 21.4 mg (equivalent to 20 mg lignocaine hydrochloride anhydrous), Chlorhexidine Gluconate Solution BPC 0.0025 ml in a water-miscible base.

Uses Anaesthetic gel for anaesthesia of the urethra and topical application on mucous membrane wherever an anaesthetic/antiseptic effect is required.

Dosage and administration *Men:* 10 ml injected initially, followed by 3–5 ml.

Women: 3–5 ml injected into the urethra.

Contra-indications, warnings, etc Known hypersensitivity to anaesthetics of the amide type.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities 15 ml tubes.

Further information Nil.

Product licence number 0017/5035.

XYLOCAINE* 4% EYE DROPS

Presentation Sterile clear aqueous solution (isotonic). Each millilitre contains lignocaine hydrochloride anhydrous 40 mg.

Uses To anaesthetise the cornea and conjunctiva for removal of foreign bodies. Surgical procedures. Inflammation due to excessive glare (as in welders), and in conjunction with tonometric procedures.

Dosage and administration One or two drops as necessary.

Contra-indications, warnings, etc Known hypersensitivity to anaesthetics of the amide type.

Pharmaceutical precautions To be stored at room temperature.

Legal category POM.

Package quantities 4 ml dropper bottles.

Further information Nil.

Product licence number 0017/5036.

XYLOCAINE* GEL

Presentation Sterile clear gel. Each millilitre contains

Lignocaine Hydrochloride BP 21.4 mg (equivalent to 20 mg lignocaine hydrochloride anhydrous).

Uses Gel for anaesthesia of the urethra.

Dosage and administration *Men:* 10 ml injected initially, followed by 3–5 ml.

Women: 3–5 ml injected into the urethra.

Contra-indications, warnings, etc Known hypersensitivity to anaesthetics of the amide type.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities 20 g tubes.

Further information Nil.

Product licence number 0017/5037.

XYLOCAINE* OINTMENT 5%

Presentation White cream. Each gramme contains lignocaine base 50 mg in a water-miscible vehicle.

Uses Local anaesthetic for topical use in dentistry for surface anaesthesia of the gums, and for the relief of soreness of the nipples in nursing mothers, pain relief in pruritus ani and vulvae, haemorrhoids, herpes zoster and labialis. As a lubricant for proctoscope and cystoscope.

Dosage and administration In dentistry, apply to dry gum and rub gently. For soreness of nipples, apply on a small piece of lint or gauze (to be washed off immediately before next feeding). For other indications, apply when required.

Contra-indications, warnings, etc Known hypersensitivity to anaesthetics of the amide type.

Pharmaceutical precautions Xylocaine ointment is not intended for use with aseptic techniques, nor is it bactericidal.

Legal category P.

Package quantities 15 g tubes.

Further information Nil.

Product licence number 0017/5038.

XYLOCAINE* SPRAY

Presentation Clear spray solution. Each gram contains 100 mg lignocaine base, 0.1 mg cetyl pyridinium chloride.

Uses Anaesthetic solution for surface analgesia of mucous membrane in ENT surgery, obstetrics and dental surgery.

Dosage and administration The spray is supplied in metered spray bottles. Each metered dose contains 10 mg of lignocaine base. The number of sprays needed depends upon the extent of the area to be anaesthetised. Maximum adult dosage based on body weight of 70 kg is 200 mg, equal to 20 spray doses. Maximum dosage in children is proportionately lower according to body weight.

Contra-indications, warnings, etc Known hypersensitivity to anaesthetics of the amide type.

Side-effects: Does not produce side-effects when used at the recommended dosage.

Adverse reactions: The type of toxic reaction is unpredictable and depends on dosage and state of the patient. The reactions are primarily of two types, typified by stimulation and depression of the cerebral cortex and medulla respectively.

Precautions: The spray should not come in contact with the eyes. Accidental application should be counteracted by immediate instillation of pure liquid paraffin followed by a boric acid (2–3%) wash.

Pharmaceutical precautions Store in a cool place. Keep away from excessive heat and direct sunlight. Empty container must not be thrown on to a fire or other source of heat.

Legal category P.

Package quantities Supplied in spray bottles of 80 g (approx. 800 spray doses) with a metering valve complete with adjustable spray nozzle which can be steam sterilised at 115°C or 121°C.

Further information Nil.

Product licence number 0017/5039.

XYLOCAINE* 4% TOPICAL

Presentation Clear aqueous solution. Each millilitre contains 40 mg lignocaine hydrochloride anhydrous.

Uses Anaesthesia of mucous membrane in bronchoscopy and bronchography; biopsy in the mouth and throat; puncture of the maxillary sinus or polypectomy; tonsillectomy; resection of nasal turbinates; in dentistry.

Dosage and administration *Bronchoscopy and bronchography:* With a suitable spray 2–3 ml Xylocaine 4% may be applied to the mouth, pharynx, larynx and trachea.

Biopsy: 3–4 ml may be sprayed on the area or the solution may be applied for a few minutes with a swab. Adrenaline may be added to this solution in order to produce vasoconstriction (add 1–2 drops, 0.05 ml, 1 : 1,000, solution to 5 ml Xylocaine 4% solution).

Puncture of maxillary sinus or polypectomy: A swab soaked in the solution may be applied for two to three minutes. The addition of adrenaline is advised in these procedures, made up on the lines indicated above.

The maximum adult dose (70 kg body weight) should not exceed 5 ml (200 mg). For the debilitated, the aged and children the dosage should be reduced. In children the maximum dose is calculated as 1.4 mg per lb, or 3 mg/kg.

Contra-indications, warnings, etc Known hypersensitivity to anaesthetics of the amide type.

Precautions: Adrenaline added to the solution as described above decomposes fairly rapidly. A freshly prepared solution should be made up and used within a few hours or discarded.

Pharmaceutical precautions Store at room temperature.

Legal category P.

Package quantities Bottles of 25 ml.

Further information Nil.

Product licence number 0017/5040.

XYLOCAINE* VISCOUS

Presentation Viscous clear liquid. Each millilitre contains Lignocaine Hydrochloride BP 21.4 mg (equivalent to 20 mg lignocaine hydrochloride anhydrous).

Uses Topical anaesthetic solution for:

1. Mucous membrane lesions of mouth and throat following tonsillectomy, and post-tonsillectomy sore throat.
2. Introduction of instruments and catheters into the stomach.
3. Oesophagoscopy, oesophagitis, pharyngitis and stomatitis.
4. Severe hiccough.

Dosage and administration

1. One teaspoonful (5 ml) swished around the mouth and swallowed slowly. (Not more than six times in 24 hours.)
2. One tablespoonful (15 ml).
3. One dessertspoonful (10 ml) swished around the mouth and swallowed slowly. (Not more than three times in 24 hours.)
4. One dessertspoonful (10 ml) swallowed quickly in one gulp. (Not more than three times in 24 hours.)

The maximum dose for adults of normal body weight is 15 ml. This should be reduced for debilitated and aged patients.

Contra-indications, warnings, etc Known hypersensitivity to anaesthetics of the amide type. There are no known side-effects or adverse reactions.

Precautions: No food or drink should be taken for three hours after administration. Not more than 30 ml to be administered in 24 hours. Minimal interval between doses – four hours.

Pharmaceutical precautions None.

Legal category P.

Package quantities Bottles of 150 ml.

Further information Nil.

Product licence number 0017/5041.

XYLOCARD*

Presentation *Xylocard 100 mg Intravenous bolus injection:* Clear aqueous sterile solution in pre-loaded syringe 5 ml: lignocaine hydrochloride anhydrous 20 mg/ml.

Xylocard 1 g and 2 g: Sterile aqueous solution in pre-loaded 5 ml or 10 ml syringe: lignocaine hydrochloride anhydrous 200 mg/ml.

Uses Prevention of ventricular tachyarrhythmias in patients with suspected or proven acute myocardial infarction. Treatment of ventricular tachyarrhythmias associated with acute myocardial infarction. Ventricular extrasystoles and ventricular tachycardia. As anti-arrhythmic cover in cases of ventricular fibrillation being DC converted.

Dosage and administration *Adults:* *Xylocard 100 mg Intravenous:* 1 mg/kg body weight Normal dose

(adults) 50–100 mg (2.5–5 ml) as initial treatment to be injected slowly over a period of two minutes. When necessary injection can be repeated once or twice at 5–10 minute intervals. Effect can be observed within two minutes.

Xylocard 1 g and 2 g for addition to I.V. Infusion: A concentration of 0.2% lignocaine infusion may be recommended for most cases. This is achieved by adding 1 × Xylocard 1 g syringe (or $\frac{1}{2}$ × Xylocaine 2 g syringe) to 500 ml infusion solution. Normal dose (adults) 2–4 mg/min. Based on a concentration of 0.2% this is equivalent to an infusion rate of 1–2 ml/min.

Not to be administered to children.

Contra-indications, warnings, etc Lignocaine is contra-indicated in patients with a known history of hypersensitivity.

Arterioventricular block is an absolute or relative contra-indication, according to severity.

Other serious conduction disturbances, and cardiac decompensation not dependent on treatable tachyarrhythmias, are also contra-indications.

Side-effects: *CNS (cortex):* Agitation, drowsiness, disorientation, blurred vision, euphoria, tremor and convulsions.

CNS (medullary): Nausea, pallor, cold sweat, respiratory depression.

Cardiovascular: Fall in blood pressure, bradycardia, cardiac arrest.

Patients with severe liver damage should be given lower doses and the effect carefully monitored. Manifest renal insufficiency calls for special care in infusion therapy.

Pharmaceutical precautions Store in a cool place.

The content of the Xylocard 1 g and 2 g syringe is for dilution in infusion fluid only. Under no circumstances are they to be administered undiluted.

Legal category POM.

Package quantities *Xylocard 100 mg 5 ml (20 mg/ml):* Pre-loaded syringe for immediate use. Box of 5.

Xylocard 1 g (5 ml) and Xylocard 2 g (10 ml) both 200 mg/ml: Pre-loaded syringe for addition to infusion bottles and bags. Box of 10.

Further information All Xylocard syringes are free of bacteriostat and preservatives.

Product licence numbers

Xylocard 100 mg I.V. bolus	0017/5018
Xylocard 1 g I.V. infusion	0017/0064
Xylocard 2 g I.V. infusion	0017/0064

XYLODASE*

Presentation White cream. Each gram contains lignocaine (base) 50 mg, Hyaluronidase BP 50 units (0.015%) in water-miscible base.

Uses Surface anaesthesia in dental procedures: surface analgesia before any injection, opening of abscesses, preparation of sensitive cervical cavities, deep scaling, extraction of deciduous teeth not embedded deeply in the bone, wiring of teeth.

Dosage and administration $\frac{1}{2}$ –1 g or as required.

Contra-indications, warnings, etc Known hypersensitivity to anaesthetics of the amide type.

Pharmaceutical precautions To be stored at room temperature.

Legal category P.

Package quantities Boxes of 12 × 15 g tubes.

Further information Nil.

Product licence number 0017/5042.

XYLOPROCT* OINTMENT

Presentation White water-miscible cream. Each gram contains: Xylocaine (lignocaine) 50 mg, Hydrocortisone Acetate BP 2.75 mg, Zinc Oxide BP 180 mg, aluminium acetate 35 mg.

Uses External and prolapsed haemorrhoids and other painful perianal conditions.

Pruritus ani – pruritus vulva.

Dosage and administration To be applied several times a day according to the severity of the condition.

Contra-indications, warnings, etc There are no known contra-indications or side-effects.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities *Tubes:* 30 g ointment complete with special applicator.

Further information Nil.

Product licence number 0017/5023.

XYLOPROCT* SUPPOSITORIES

Presentation White cone-shaped suppositories. Each suppository contains: Xylocaine (lignocaine) 60 mg, hydrocortisone Acetate BP 5 mg, Zinc Oxide BP 400 mg, Aluminium acetate 50 mg.

Uses For the treatment of internal haemorrhoids and other disorders of the anal canal such as proctitis, fissure in ano, anal fissure and anal fistula.

Dosage and administration Removing protective foil, use 1 suppository at night before retiring and repeat the treatment after each bowel action.

Contra-indications, warnings, etc There are no known contra-indications or side-effects.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Packs containing 10 separate foil-protected suppositories.

Further information Nil.

Product licence number 0017/5024.

ZELMID* ▼

Presentation Zelmid (zimelidine dihydrochloride, INN) is available as white film coated tablets: Zelmid 100 mg, round, marked $\frac{Z}{100}$, Zelmid 200 mg, oval marked $\frac{Z}{200}$.

Uses The molecular structure of Zelmid is different to that of tricyclic antidepressants. As a result of this, it has different pharmacological properties.

Zelmid inhibits the re-uptake of 5-hydroxytryptamine (5-HT) into CNS pre-synaptic nerve terminals. It has only a minor effect on the re-uptake of noradrenaline and is without a direct effect on dopamine. Zelmid, therefore, preferentially enhances transmission in 5-HT neuronal systems. The anticholinergic action of Zelmid is extremely weak and it has no antihistaminic activity.

Indications: In the management of major depressive illness.

Dosage and administration *Route of Administration:* Oral.

Dosage: *Adults: Non-Elderly:* 200 mg as a single dose during the day. This can be taken in two divided doses if needed. In non-responders at 200 mg the dosage may be increased to 300 mg in divided daily doses.

Elderly: As a reduction in eliminatory capacity may be present in this age group, a single daily dose of 100 mg is recommended. Non-responders at this dose level may receive 200 mg daily in 2 divided doses.

Children: Not recommended, as currently no clinical data is available.

Contra-indications, warnings, etc *Contra-indications:* Mania, severe liver disease, patients who are hypersensitive to Zelmid. Do not use in pregnancy nor in nursing mothers.

Precautions: Until further clinical experience is obtained, care must be exercised in patients suffering from uncontrolled epilepsy and lowered seizure threshold.

Although Zelmid has only weak anticholinergic properties it should be used cautiously in patients with conditions which would worsen under anticholinergic influence (e.g. narrow angled glaucoma, urinary retention, increased intra-ocular pressure, etc.) until further clinical experience is gained.

As with all drugs, patients suffering from hepatic, renal or cardiac insufficiency, recent myocardial infarction, heart block or arrhythmias should be carefully monitored during Zelmid therapy. Animal work has shown adverse effects on sexual performance and this effect might occur in patients.

As a general principle, elderly and debilitated patients should be carefully monitored during therapy with antidepressants, including Zelmid.

Patients with severe depression who pose a high suicide risk should be kept under close surveillance, particularly during the early stages of treatment.

Interactions: The use of monoamine oxidase inhibitors should be discontinued 2 weeks before the start of Zelmid therapy.

Although interaction between Zelmid and antihypertensive drugs has not been recorded a review of

antihypertensive therapy during Zelmid treatment is advisable.

Although interaction with sympathomimetic agents has not been reported with Zelmid, care should be taken when given concomitantly with adrenaline, ephedrine, isoprenaline, noradrenaline, phenylephrine, and phenylpropanolamine.

The possibility that Zelmid might potentiate the CNS depressant effect of alcohol has not been excluded.

Warnings and adverse reactions: Anticholinergic side-effects have been reported less frequently with Zelmid than with standard antidepressants.

As with all drugs, if surgery is necessary Zelmid therapy must be reported to the anaesthetist.

Although Zelmid does not induce sedation which can lead to impairment of psychomotor skills, depressed patients should be warned to exercise extra care when driving or operating hazardous machinery.

Zelmid is generally well tolerated. Side effects reported to date have been mild and transient in nature. The most common side effects observed are headache, nausea, indigestion and perspiration. Single cases of postural hypotension and clinically non-significant ECG changes have been reported. Isolated cases of allergic reaction, reversible anaemia, leucopaenia, thrombocytopenia and transient increases in transaminases have been reported.

Overdosage: There is no specific antidote to Zelmid. Patients should be monitored carefully and given supportive treatment when necessary.

Pharmaceutical precautions Store in cool place.

Legal category POM.

Package quantities 100 mg: bottles of 100.
200 mg: blister packs of 28.

Further information Zelmid does not increase appetite, and unlike tricyclic antidepressants, inappropriate weight gain does not occur. Zelmid does not enhance the CNS depressant effect of benzodiazepines. This could be of advantage if concomitant use is necessary.

At levels of Zelmid which effectively prevent 5-HT re-uptake, the effect on other pharmacological systems is negligible or not measurable. The risk of a direct pharmacological interaction between Zelmid and other groups of drugs (e.g., antihypertensives, anticholinergics, alcohol, etc.) is, therefore, less than for those antidepressants which have a wide spectrum of pharmacological activity.

Product licence numbers

100 mg 0017/0104

200 mg 0017/0105

***Trade Mark**

Ayerst Laboratories Limited

South Way
Andover
Hampshire SP10 5LT



ANTEPSIN[®] TABLETS ▼

Presentation Antepsin Tablets 1 gram are white, oblong, biconvex, uncoated tablets scored on one side branded 1239 and Ayerst and containing 1 gram sucralfate.

Uses For the treatment of duodenal ulcer, gastric ulcer and chronic gastritis.

Dosage and administration For oral administration: *Adults*: Usual dose 1 gram 4 times a day. Maximum daily dose 8 grams. Tablets to be taken 1 hour before meals and at bedtime.

Four to six weeks' treatment is usually needed for ulcer healing but up to twelve weeks may be needed in resistant cases.

Antacids may be used as required for relief of pain.

Contra-indications, warnings, etc

Contra-indications: There are no known contra-indications.

Precautions: 1. Concomitant administration with some oral anti-infectives such as tetracyclines may interfere with absorption of the latter.

2. The product should only be used with caution in patients with renal dysfunction.

3. As with all medicines Antepsin should not be used in early pregnancy unless considered essential.

Side-effects: A low incidence of mild side-effects, e.g. constipation has been reported.

Pharmaceutical precautions No special requirements for storage are necessary.

Legal category POM.

Package quantities Antepsin 1 gram: Securitainers of 100.

Further information Antepsin is not significantly absorbed. It forms a chemical complex which selectively binds to the ulcer site, establishing a protective barrier against the actions of pepsin bile and gastric acid.

Product licence number 0607/0045.

BC 500[®]

Presentation BC 500 is a high-potency B complex and C vitamin tablet. Each tablet contains:

Thiamine mononitrate (vit. B ₁)	25 mg
Riboflavin (vit. B ₂)	12.5 mg
Nicotinamide	100 mg
Pyridoxine hydrochloride (vit. B ₆)	10 mg
Calcium pantothenate	20 mg
Cyanocobalamin (vit. B ₁₂)	5 mcg
Ascorbic acid (vit. C) as sodium ascorbate	500 mg

BC 500 is an orange, oblong, film-coated tablet printed 'Ayerst 824'.

Uses BC 500 is indicated whenever the administration of high-potency B complex and C vitamins is needed. Such conditions include: Convalescence. Chronic alcoholism. Old age and associated poor diet. Prolonged antibiotic therapy. Debilitating disease, including ulcerative colitis, colostomy, gastric and duodenal ulcer.

Dosage and administration Recommended only for adults. One tablet daily.

Contra-indications, warnings, etc As is usual with water-soluble vitamins there are no known contra-indications.

Precautions: Pyridoxine may antagonise laevodopa when given for Parkinson's Disease.

Overdosage: BC 500 contains only water soluble vitamins and overdosage is unlikely to be a problem.

Pharmaceutical precautions No special requirements for storage are necessary.

Legal category P.

Package quantities Securitainers of 100 and 500 tablets.

Further information BC 500 contains high doses of the B complex and 500 mg vitamin C. This means that a once a day dosage provides adequate vitamins even when requirements are high.

Product licence number 0607/0011.

BC 500[®] WITH IRON

Presentation BC 500 with Iron tablets contain high potency B complex and C vitamins with ferrous fumarate. Each tablet contains:

Ferrous Fumarate	200 mg
Thiamine Mononitrate	25 mg
Riboflavin	12.5 mg
Nicotinamide	100 mg
Pyridoxine Hydrochloride	10 mg
Calcium Pantothenate	20 mg
Ascorbic Acid as Sodium Ascorbate	500 mg

BC 500 with Iron is a red film-coated round biconvex tablet printed Ayerst 1143.

Uses BC 500 with Iron tablets are recommended for the treatment of iron deficiency when therapeutic doses of water soluble vitamins are also required.

Dosage and administration One tablet daily or as recommended by the physician. Recommended only for adults. Keep out of reach of children.

Contra-indications, warnings, etc **Precautions:** Iron chelates with tetracyclines and may impair absorption of both agents. Pyridoxine may antagonise laevodopa when given for Parkinson's Disease.

Side-effects: As with all iron preparations, nausea,

gastro-intestinal irritation and constipation may rarely occur.

Overdose: In the event of overdose emesis and/or gastric lavage is indicated. Immediate injection of 2 g desferrioxamine mesylate in water for injection is required. After gastric lavage 5 g of desferrioxamine mesylate in 50–100 ml of water may be left in the stomach.

Pharmaceutical precautions No special requirements for storage are necessary.

Legal category P.

Package quantities Securitainers of 100 and 500 tablets.

Further information The dose of Vitamin C is sufficient both to treat deficiency of this vitamin and to enhance the absorption of iron.

Product licence number 0607/0028.

CALTHOR* TABLETS ▼ CALTHOR* SUSPENSION ▼

Presentation Calthor Tablets are white, round, flat and scored one side, containing 250 mg or 500 mg ciclacillin. The 250 mg tablets are 10 mm in diameter and 4.4 mm thick. The 500 mg tablets are 13 mm in diameter and 5 mm thick.

Calthor Suspension 125 mg is presented as a granular off-white powder. When reconstituted it is a pale orange, homogenous suspension with a characteristic fruity smell, containing 125 mg ciclacillin per 5 ml. Calthor Suspension 250 mg is presented as a granular off-white powder. When reconstituted it is an off-white, homogenous suspension with a characteristic fruity smell containing 250 mg ciclacillin per 5 ml.

Uses Calthor is an orally active broad spectrum penicillin. Calthor is indicated for the oral treatment of a wide range of bacterial infections caused by commonly occurring pathogens.

Calthor is active against the following organisms *in vitro*: Group A beta-haemolytic streptococci, *Strep. faecalis* (enterococci), alpha-haemolytic streptococci, *Strep. pneumoniae*, non-penicillinase-producing staphylococci, *Haemophilus influenzae*, *Escherichia coli*, *Proteus mirabilis*, *Neisseria gonorrhoeae*. All strains of pseudomonas and most strains of klebsiella and enterobacter are resistant: some strains of *E. coli* and *H. influenzae* may be resistant. Calthor should not be used in any infections caused by *E. coli* and *P. mirabilis* other than urinary tract infections. Efficacy against salmonella infections has not been established.

Calthor is indicated for the treatment of the following infections, due to susceptible organisms:

Respiratory Tract infections, *e.g.*: Tonsillitis, pharyngitis, bronchitis, pneumonia,
Otitis Media,
Skin and Skin Structure (Integumentary) infections,
Urinary Tract infections.

Dosage and administration *Preparation of the suspension:* 125 mg/5 ml – add 57 ml of water to the powder for reconstitution and shake well.

250 mg/5 ml – add 74 ml of water to the powder for reconstitution and shake well.

Adults: Respiratory Tract Infections: Tonsillitis and Pharyngitis 250 mg qid in equally spaced doses.

Bronchitis and Pneumonia:

Mild or moderate infections – 250 mg qid in equally spaced doses.

Chronic infections – 500 mg qid in equally spaced doses.

Otitis Media: 250 mg to 500 mg qid in equally spaced doses depending on severity.

Skin and Skin Structure Infections: 250 mg to 500 mg qid in equally spaced doses depending on severity.

Urinary Tract Infections: 500 mg qid in equally spaced doses.

Children: 2 months to 10 years – half adult dose. Over 10 years – adult dose.

All recommended dosages are a guide only. In severe infections dosages may be increased.

In infections caused by Group A beta-haemolytic streptococci a minimum of 10 days of treatment is recommended to guard against the risk of rheumatic fever or glomerulonephritis.

In the treatment of chronic urinary tract infection frequent bacteriological and clinical appraisal is necessary during therapy and may be required for several months afterwards. Persistent infection may require treatment for several weeks.

Calthor should not be used in children under 2 months of age.

Patients with renal failure: Each patient should be individually considered. Based on a dosage of 500 mg qid the following adjustment in dosage interval is recommended:

Patients with a creatinine clearance of 50 ml/min need no dosage interval adjustment.

Patients with a creatinine clearance of 30–50 ml/min should receive a full dose every 12 hours.

Patients with a creatinine clearance of between 15–30 ml/min should receive full doses every 18 hours.

Patients with a creatinine clearance of between 10–15 ml/min should receive full doses every 24 hours.

In patients with a creatinine clearance of ≤ 10 ml/min or serum creatinine values of ≥ 10 mg per 100 ml, serum ciclacillin levels are recommended to determine the subsequent dosage and frequency.

Contra-indications, warnings, etc

Contra-indications: Calthor should not be given to patients with a history of hypersensitivity to penicillin.

Precautions: Animal experiments show no teratogenic effect but, as with all medicines, Calthor should not be administered during pregnancy unless considered essential. Because many drugs are excreted in human milk, caution should be exercised when Calthor is administered to a nursing mother.

Prolonged use of an anti-infective may result in overgrowth of non-sensitive organisms.

Side-effects: Calthor is generally very well tolerated and side-effects are rare. Diarrhoea, nausea, vomiting and skin reactions have occasionally been observed.

Penicillins may cause an acute anaphylactic reaction which can be fatal. This reaction appears to occur more frequently in patients with bronchial asthma or other allergic disorders.

Overdosage: Since Calthor is a penicillin problems of overdosage are unlikely to be encountered.

Pharmaceutical precautions Store in a cool place.

After reconstitution the suspension should be stored in a refrigerator and the unused portion discarded after 14 days. When stored at room temperature discard

unused portion after 8 days. The suspension may be diluted with syrup BP.

Legal category POM.

Package quantities

Tablets: Cartons of 120 tablets in blister packs of twelve.

Suspension: Bottles containing powder to give 120 ml reconstituted suspension.

Further information Ciclacillin is very rapidly and well absorbed from the gastro-intestinal tract after oral administration to give exceptionally high peak levels within 30–40 minutes. A high proportion is excreted unchanged in the urine within 6 hours.

Product licence numbers

Calthor tablets 250 mg	0607/0036
Calthor tablets 500 mg	0607/0037
Calthor suspension 125 mg/5 ml	0607/0040
Calthor suspension 250 mg/5 ml	0607/0038

EVADYNE* TABLETS

Presentation Evadyne Tablets 25 mg are orange, film-coated, round, bi-convex tablets containing butriptyline 25 mg as the hydrochloride.

Evadyne Tablets 50 mg are pink, film-coated, round, bi-convex tablets containing butriptyline 50 mg as the hydrochloride.

Uses Evadyne is indicated for the relief of depression with or without associated anxiety.

Evadyne is particularly useful in ambulatory patients because it is generally well tolerated and shows, after an early relief of anxiety, a gradual mood elevation with a disappearance of symptoms of self-deprecation, disinterest, fatigue, apathy and anorexia when present.

Evadyne has proved useful in cases resistant to other presently available antidepressant therapy. The drug may relieve depressive reactions and associated anxiety accompanying chronic illness.

Dosage and administration *Adults: Initial dosage:* Usually 25 mg three times daily (75 mg total daily dose).

Adjustment: The initial dose may be increased in steps of 25 mg every day or every other day to attain a level of 100–150 mg maximum total daily dose.

Maintenance dosage: When a satisfactory response is achieved the dose may be gradually reduced to 25 mg three times a day.

Formulations for children are not yet available.

Contra-indications, warnings, etc

Contra-indications: Combined use with other psychotropic drugs should be undertaken only with due recognition of the possibility of potentiation. Patients having received monoamine oxidase inhibitors (MAOI) should not be given Evadyne until at least two weeks after cessation of MAOI therapy. Evadyne is not recommended for use in pregnant patients as clinical experience and follow-up have as yet been limited. However, animal reproductive studies have shown no foetal malformations.

Precautions: As in the case of all psychotropic compounds, Evadyne may impair alertness in some patients; thus, activities made hazardous by diminished alertness should be avoided (e.g. driving). It should be used with caution in patients with a history of epileptiform seizures.

Patients should be cautioned against the ingestion of alcohol during therapy due to the danger of potentiation.

Evadyne may interact with adrenergic drugs and care must be taken if such a combination is to be used.

As with other dibenzocycloheptene derivatives, Evadyne should not be used in patients with glaucoma or those who would be expected to experience urinary retention.

Patients with known cardiovascular disorders should be watched closely; frequent ECG monitoring is recommended.

Side-effects: Side-effects experienced with Butriptyline are usually mild and transitory in nature. Evidence of anticholinergic activity such as dry mouth and blurred vision, accommodation disturbances, constipation, paralytic ileus and urinary retention may be seen; however, these are usually dose related. In the majority of patients, these adverse reactions do not interfere with therapy and tend to diminish with continued treatment.

Because of pharmacological similarities between tricyclic antidepressant drugs, cardiovascular, CNS and neuromuscular adverse reactions, which have not particularly been reported with Evadyne, should also be considered.

Overdosage: There is no specific antidote for overdosage with tricyclic compounds. Induced emesis and gastric lavage are recommended.

If the patient is stuporous but responds to stimuli, only close watching may be required for a few days; if comatose, supportive measures will be required. Maintain an open airway and adequate fluid intake; regulate body temperature. Anticonvulsants may be given to control convulsions. Central nervous system depression may be treated with nonconvulsant doses of CNS stimulants.

Digitalis should be considered if cardiovascular abnormalities occur. Standard measures such as oxygen and i.v. fluids may be used to manage circulatory shock.

Pharmaceutical precautions No special pharmaceutical precautions are necessary.

Legal category POM.

Package quantities Evadyne Tablets 25 mg are packed in Securitainers of 100.

Evadyne Tablets 50 mg are packed in Securitainers of 100.

Further information Nil.

Product licence numbers

Evadyne Tablets 25 mg	0607/0019
Evadyne Tablets 50 mg	0607/0020

HRF AYERST*

Presentation HRF Ayerst contains leutinising hormone/follicle stimulating hormone releasing hormone (LH/FSH-RH; gonadorelin) in a freeze-dried form. HRF Ayerst is available in 2 strengths, 100 mcg and 500 mcg, and is supplied with an ampoule of sterile diluent for injection.

Uses HRF Ayerst stimulates the release of gonadotrophins from a functional pituitary and is of diagnostic value in cases where determinations of pituitary reserve are required, e.g.

Female: Primary or secondary amenorrhoea, hypogonadotropic hypogonadism, Sheehan's Syndrome.

Male: Hypogonadotrophic hypogonadism, cryptorchism, Klinefelter's Syndrome, Frohlich's Syndrome.

Male and Female: Pituitary ablation, acromegaly, Cushing's Syndrome, Simmond's Syndrome, Kallman's Syndrome, etc.

In the differential diagnosis of delayed puberty and hypogonadotrophic hypogonadism, etc.

Dosage and administration *Routine determination of pituitary function:* For a rapid and simple determination of pituitary response capability, a single intravenous dose of 100 mcg is suggested.

Refined determination of pituitary function: To determine the threshold of pituitary response an initial dose of 25 mcg is recommended. This may be increased in steps until the pituitary threshold is determined. Doses as high as 500 mcg have been used for this purpose.

Blood samples: Venous blood samples should be taken before and at intervals after administration of HRF Ayerst. Arrangements should be made with a radio-immunoassay centre for measurement of LH and FSH in the samples.

Interpretation of results. The normal adult: In the normal adult an injection of 25–100 mcg of HRF Ayerst causes an increase in LH/FSH in a dose related manner. Peak circulating levels of LH are obtained within 10–30 minutes. An increase in serum FSH follows the same course but not to the same degree. Levels gradually fall during the next few hours, LH being elevated above base-line for four to six hours, and FSH for three to five hours. Frequent sampling shows that the secretion of gonadotrophins is pulsatile and synchronous. In the female the influence of gonadal steroids on pituitary responsiveness is less clear, as there is a cyclical variation in responsiveness depending upon the phase of the menstrual cycle, the maximum response being during the luteal phase. In the male feedback effects may be seen when gonadal steroids are administered in physiological and higher doses.

Absent response is defined as one in which the 100 mcg HRF Ayerst administration fails to produce a rise greater than three times the basal level of the gonadotrophins. An impaired response is said to occur if the elevation in circulating gonadotrophins is found but not within the normal range at 20–60 minutes. If the 60 minute value is the same or exceeds that at 20 minutes, the response is defined as delayed. Values outside the normal range at 20 or 60 minutes are considered to be exaggerated. Absent, impaired or exaggerated responses imply endocrine dysfunction. Delayed responses are not in themselves suggestive of pathology.

Reference to current literature will assist interpretation of results in pathological states.

Prepubertal children: In boys tested with HRF Ayerst there is an increasing LH response as puberty progresses from stage one to stage three. FSH secretion is less than for LH in all three stages of puberty and there are no significant differences between the results obtained at different stages.

In girls, FSH levels increase more markedly at stage one and then change little during puberty. LH response is slight at stage one and after stage two the levels achieved exceed that of FSH response resembling the normal adult pattern.

Contra-indications, warnings, etc Existing clinical experience has not shown any contra-indications to HRF Ayerst, but it should not be administered in

pregnancy. Administration during the follicular phase of a normal menstrual cycle may result in premature ovulation, and appropriate measures are advised to prevent an unwanted pregnancy in these circumstances.

Overdosage: with HRF Ayerst has never been reported and is unlikely to be a problem.

Pharmaceutical precautions HRF Ayerst has a shelf-life of four years. Store at room temperature. Use within 24 hours of reconstitution.

Legal category POM.

Package quantities Packs comprise a vial containing 100 mcg or 500 mcg freeze-dried material and a 2 ml ampoule of sterile diluent.

Further information HRF Ayerst is a synthetic decapeptide identical to the LH/FSH-RH identified by Schally and co-workers.

Combined test of pituitary function: Gonadorelin may be used in conjunction with TRH for a more complete evaluation of the hypothalamic-anterior pituitary-gonadal axis. TRH injection (2 ml) may be used in place of the diluent supplied with HRF Ayerst to prepare a combined injection. The HRF Ayerst/TRH mixture has been shown to be stable for 24 hours.

Product licence numbers

HRF Ayerst 100 mcg 0607/0016

HRF Ayerst 500 mcg 0607/0017

ISORDIL*

Presentation Isordil Sublingual Tablets, containing isosorbide dinitrate 5 mg, are small, pink tablets specially formulated for sublingual administration.

Isordil Tablets, containing isosorbide dinitrate 10 mg, are white, convex, scored tablets for normal oral administration.

Isordil Tablets containing isosorbide dinitrate 30 mg are pale yellow biconvex tablets, scored one side.

Uses *Angina pectoris:* Sublingually for the acute attack. Orally for protection against anginal attacks.

Acute congestive heart failure including after myocardial infarction and *chronic congestive heart failure* as adjunctive therapy.

Dosage and administration *Acute attack of angina:* 1 tablet Isordil 5 mg sublingually as required with a maximum of 1 or 2 tablets every two hours.

Protection against anginal attacks: 40–120 mg daily in divided doses. In selected cases daily doses of up to 240 mg Isordil have been administered.

Chronic congestive heart failure: As adjunctive therapy.

Initial dosage: Sublingual Isordil 5 mg in doses of 5–10 mg every two hours or as needed.

Maintenance: The oral form of Isordil in doses of 10 mg to 60 mg four times daily.

Acute congestive heart failure including after myocardial infarction: Sublingual Isordil 5–15 mg every two to three hours or as needed. The oral form of Isordil may be administered in doses of 10–60 mg four times daily or as needed.

The therapeutic use of Isordil in selected cases of acute and chronic congestive heart failure should be considered as an adjunct to the more conventional modes of therapy such as the cardiac glycosides and

diuretics etc. Continuous haemodynamic monitoring of the patient under treatment is desirable and optimal dose regimens should be determined for individual cases depending on these results.

Contra-indications, warnings, etc

Contra-indications: Idiosyncrasy to this drug.

Precautions:

1. Tolerance to this drug and cross tolerance to other nitrates and nitrites, may occur.
2. In congestive heart failure, as a rule, pulmonary capillary pressure should not be allowed to fall below 15 mmHg or systolic blood pressure below physiological range in normal or hypertensive patients. In patients with hypotension in the range of 90–100 mmHg of systolic pressure there should be no fall at all. As with other vasodilators in sensitive patients Isordil may cause paradoxical side-effects which may increase ischaemia and may even lead to extension of myocardial damage and advanced congestive heart failure.

Adverse reactions: The adverse reactions due to Isordil are common to all nitrates used for the treatment of angina pectoris.

1. Cutaneous vasodilation with flushing.
2. Headache is common and in some patients may be severe and persistent. Analgesics have been useful in some cases.
3. Transient episodes of dizziness and weakness and other signs of cerebral ischaemia associated with postural hypotension may occur.
4. This drug can act as a physiological antagonist to noradrenaline, acetylcholine, histamine and many other agents.

Treatment of overdosage: Isordil is very safe (the LD₅₀ of isosorbide dinitrate in rodents is of the order of 1,000 mg per kg), so dangerous overdosage is extremely rare. In such cases, however, gastric lavage is indicated. Passive exercise of the extremities of the recumbent patient will promote venous return.

Pharmaceutical precautions *Storage:* Unlike glyceryl trinitrate, Isordil Tablets are stable and no special storage conditions are necessary.

Legal category P.

Package quantities Isordil Sublingual Tablets 5 mg in Securitainers of 100.

Isordil Tablets 10 mg in Securitainers of 100.
Isordil Tablets 30 mg in Securitainers of 100.

Further information Isordil has a very high solubility compared with other nitrates and therefore acts sublingually to abort the acute attack of angina pectoris quickly. In addition Isordil can be administered orally to give a prolonged effect. Because Isordil is physically and chemically stable it is reliable in use.

Product licence numbers

Isordil Tablets 5 mg 0607/0006
Isordil Tablets 10 mg 0607/0007
Isordil Tablets 30 mg 0607/0027

ISORDIL* TEMBIDS* CAPSULES

Presentation Isordil tembids capsules containing isosorbide dinitrate 40 mg in a sustained release formulation are gelatin capsules with a colourless, transparent body and opaque blue cap for oral administration.

Uses Prophylaxis of angina pectoris.

Dosage and administration For oral administration – One capsule 2 or 3 times a day.

Contra-indications, warnings, etc

Contra-indications: Idiosyncrasy to this drug.

Precautions: Tolerance to this drug, and cross-tolerance to other nitrates and nitrites may occur.

Adverse Reactions: The adverse reactions due to Isordil are common to all nitrates used for the treatment of angina pectoris.

1. Cutaneous vasodilation with flushing.
2. Headache is common and in some patients may be severe and persistent. Analgesics have been useful in some cases.
3. Transient episodes of dizziness and weakness and other signs of cerebral ischaemia associated with postural hypotension may occur.
4. This drug can act as a physiological antagonist to noradrenaline, acetylcholine, histamine and many other agents.

Treatment of overdosage: Isordil is very safe (the LD₅₀ of isosorbide dinitrate in rodents is of the order of 1,000 mg/kg), so dangerous overdosage is extremely rare. In such cases, however, gastric lavage is indicated. Passive exercise of the extremities of the recumbent patient will promote venous return.

Pharmaceutical precautions *Storage:* Unlike glyceryl trinitrate, Isordil Tembids are stable and no special storage conditions are necessary.

Legal category P.

Package quantities Securitainers of 100.

Further information Isosorbide dinitrate is released from the slow release formulation over a 6 hour period to provide up to 12 hours of sustained effect.

Product licence number 0607/0041.

MICROLET* MICRO-ENEMA

Presentation A disposable polyethylene tube with a 2" pliable nozzle which contains 5 ml of a clear, virtually colourless, viscous liquid, comprising 45 mg sodium lauryl sulphoacetate, 450 mg sodium citrate and 625 mg glycerol, together with potassium sorbate, citric acid, sorbitol and water.

Uses Microlet combines the action of sodium citrate, a 'peptizing' agent which liberates water present in the faeces; sorbitol which enhances this action; sodium lauryl sulphoacetate, a wetting agent, and glycerol which promotes peristalsis and evacuation of the lower bowel.

Microlet is indicated whenever an enema is necessary for chronic and acute constipation in the rectum and sigmoid colon. Constipation during pregnancy, encopresis, coprostasis, pre- and post-operative constipation, and as a preliminary to rectoscopic and sigmoidoscopic examinations.

Dosage and administration

Adults and Children Aged 3 years and Over: Lubricate the nozzle with one drop of the contents, insert full length of nozzle into the rectum and squeeze tube until total contents have been administered. Two tubes may be necessary in severe cases.

Children Under 3 years: Insert half the length of the nozzle into the rectum following the instructions as above.

Contra-indications, warnings, etc Very occasionally, a slight cramp may occur. Prolonged use may interfere with the absorption of some vitamins. Excessive use of Microlet Micro-enema may cause diarrhoea and fluid loss. In such cases Microlet should be discontinued and appropriate therapy instituted.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities Packs of 12.

Further information Nil.

Product licence number 0607/0042.

PHOSPHOLINE IODIDE*

Presentation Each pack contains:

1. Ecothiopate iodide BP in a sterile, freeze-dried form mixed with 40 mg potassium acetate in a vial sufficient for: 5 ml of 0.03%, or 5 ml of 0.06%, or 5 ml of 0.125%, or 5 ml of 0.25%.

2. 5 ml sterile aqueous diluent containing chlorbutanol 0.5%, mannitol 1.2%, boric acid 0.06%, exsiccated sodium phosphate 0.026%.

3. A sterile dropper.

The 0.06%, 0.125% and 0.25% preparations are all Ecothiopate Eye Drops BNF.

Uses Chronic open-angle glaucoma. Chronic angle-closure glaucoma after iridectomy. Certain non-uveitic secondary types of glaucoma. Accommodative esotropia.

Dosage and administration *Early simple glaucoma:* Phospholine iodide 0.03% instilled twice daily; before retiring, and in the morning.

Advanced simple glaucoma and glaucoma secondary to cataract surgery: These cases may respond satisfactorily to Phospholine iodide 0.03% twice a day as above, but one of the higher strengths, 0.06%, 0.125% or 0.25%, may be needed. In this case, a brief trial with the 0.03% eyedrops will be advantageous in that the higher strengths will then be more easily tolerated. A single dose before retiring has been used, but twice daily is normal. More frequent dosage is undesirable. When a patient has been transferred from other therapy a brief trial with 0.03% may be useful.

Concomitant therapy: Phospholine iodide may be used concomitantly with adrenaline, a carbonic anhydrase inhibitor, or both.

Accommodative esotropia: In diagnosis: One drop 0.125% once daily in both eyes on retiring for two to three weeks. A favourable response may be noted within a few hours if the esotropia is accommodative.

In treatment: After initial period of treatment for diagnostic purposes, 0.125% every other day or 0.06% daily. Dosage can be lowered as treatment progresses. Maximum recommended dose 0.125% once daily.

Digital compression of the nasolachrymal ducts for a minute or two following instillation minimises drainage into the nasal chamber and hence reduces the incidence of any systemic side-effects.

Contra-indications, warnings, etc

Contra-indications: Most cases of angle-closure glaucoma. Active uveal inflammation. Hypersensitivity. Bronchial asthma.

Precautions: Pilocarpine eye drops should be administered for at least two months before initiating high-strength Phospholine iodide therapy in adults. The drops should be temporarily discontinued if (otherwise inexplicable) persistent diarrhoea, urinary incontinence, profuse sweating, muscle weakness or cardiac irregularities should occur. Anticholinesterase drugs should be used with extreme caution, if at all, in patients with bronchial asthma, marked vagotonia, peptic ulcer, pronounced bradycardia and hypotension, recent infarction, epilepsy, parkinsonism, etc. which may respond adversely to vagotonic effects. Anticholinesterase therapy should be avoided where there is a history of uveitis and used prior to ophthalmic surgery only as a considered risk because of the possible occurrence of hyphaema. While systemic effects are infrequent, digital compression of the naso-lachrymal ducts for a minute or so following instillation is necessary. The muscle relaxant succinylcholine should not be used prior to general anaesthesia in patients who are under treatment with 'Phospholine iodide', since cholinesterase inhibitors in general potentiate the effects of this drug. Caution should be observed in treating patients with myaesthesia gravis who are at the same time undergoing treatment with a systemic anticholinesterase. Phospholine iodide should be used with great caution, if at all, where there is a history of retinal detachment. The safety of anticholinesterase drugs in pregnancy has not been established.

1. Brow-ache, stinging, conjunctival reddening, and blurring due to accommodative spasm may occur when therapy is started but will disappear after 5–10 days of continuing treatment. Very few patients will be unable to tolerate the drug if reassurance is provided by the physician.

2. Lens opacities during Phospholine iodide therapy have been reported in adults, but the cause has not been established. Lens opacities have not been reported in adults following pilocarpine therapy or when using low-strength Phospholine iodide. Lens opacities have not been reported in children.

3. Iris cysts occur only occasionally in adults but fairly frequently in children. They usually do not interfere with continuation of treatment and will regress on reduction of dosage, or frequency of instillation.

4. Paradoxical increase in intra-ocular pressure may follow anticholinesterase instillation. This may be alleviated by prescribing a sympathomimetic, e.g. phenylephrine.

Accidental overdosage: Antidotes are atropine 2 mg parenterally; pralidoxime salts 25 mg/kg intravenously; artificial respiration should be given if necessary.

Pharmaceutical precautions Phospholine iodide has a shelf-life of 18 months in the dry form. After reconstitution the drops are stable for one month at room temperature or until the expiry date if kept in a refrigerator.

Legal category POM.

Package quantities Package for 5 ml of 0.03%. Package for 5 ml of 0.06%. Package for 5 ml of 0.125%. Package for 5 ml of 0.25%.

Further information Phospholine iodide is a potent, long-acting miotic which is both reliable and safe. It

offers a great advantage over short-acting miotics in that it continues to provide a protection against rising intra-ocular pressure during the night-time hours, which may otherwise lead to permanent retinal damage and narrowing of vision. The effects of 'Phospholine Iodide' are constant and stable, and the incidence of side-effects remarkably low once the dosage has been established.

Product licence numbers

0.03% Eye Drops	0607/5003
0.06% Eye Drops	0607/5004
0.125% Eye Drops	0607/5005
0.25% Eye Drops	0607/5006

PREMARIN* TABLETS

Presentation Premarin Tablets contain natural conjugated oestrogens.

Premarin Tablets 0.625 mg are maroon, oval, sugar-coated tablets printed 'Ayerst'.

Premarin Tablets 1.25 mg are yellow, oval, sugar-coated tablets printed 'Ayerst'.

Premarin Tablets 2.5 mg are purple, oval, sugar-coated tablets printed 'Ayerst'.

Uses Menopausal and post-menopausal oestrogen replacement therapy and allied disorders such as post-menopausal osteoporosis, atrophic vaginitis and post-menopausal atrophic urethritis. Functional amenorrhoea. Palliation of selected cases of breast cancer in women more than five years post menopausal. Inoperable prostatic carcinoma.

Dosage and administration *Menopausal and post-menopausal oestrogen deficiency:* Premarin 0.625–1.25 mg daily is the usual starting dose. Cyclic administration is recommended (three weeks' dosage followed by one week's rest). For maintenance the lowest effective dose should be used. If the patient has not menstruated within the last two months or more, cyclic administration is started arbitrarily. If the patient is menstruating, cyclic administration is started on day five of bleeding. In some cases the addition of a progestogen is advisable. When hormone replacement is contemplated, it is recommended that a complete physical examination including endometrial assessment, whenever possible, be performed at the time of the initial examination. The patient should be seen at 6 to 12 month intervals and the endometrium should be assessed regularly where possible. Any breakthrough bleeding is an indication for endometrial evaluation. Treatment should be discontinued prior to surgery if this entails a risk of thrombosis.

Atrophic vaginitis, kraurosis vulvae: 0.625–1.25 mg or more daily and cyclically depending on the response of the individual patient.

Post-menopausal osteoporosis: Cyclically 0.625–1.25 mg daily.

Functional Amenorrhoea: 1.25–3.75 mg daily in divided doses for 21 days. For the last seven days progestogen therapy should be added.

Breast cancer: In selected cases of mammary cancer oestrogens may be used for palliation in women who are at least five years post-menopausal. The suggested dose of Premarin is up to 10 mg three times a day for a period of at least three months.

Prostatic carcinoma: 3.75–7.5 mg daily in divided doses as palliative therapy.

Contra-indications, warnings, etc

Contra-indications: Uterine leiomyomata. Endometriosis. Cancer of the breast, uterus and other oestrogen dependent neoplasia. Hepatic, renal and severe cardiac disease. Undiagnosed genital bleeding. Pregnancy.

Although Premarin is a natural oestrogen in contrast to the synthetic preparations which may cause thrombosis, it should not be given to patients with a personal history of thrombosis or thromboembolic disease (including coronary thrombosis, cerebrovascular accident, etc).

Precautions: In the male – continuous therapy over prolonged periods of time may produce gynaecomastia, loss of libido and testicular atrophy. In the female – prolonged use of unopposed oestrogen may increase the risk of endometrial carcinoma.

Mastopathy.

Some women may develop cholelithiasis during oestrogen therapy.

When oestrogens are administered to patients with hypertension supervision is necessary and blood pressure should be monitored at regular intervals. In a diabetic patient for whom HRT is required Prempak should be considered in preference to unopposed oestrogen.

Because larger doses of oestrogen may increase thyroid binding globulin leading to increased circulating total thyroid hormone care should be taken in prescribing oestrogens for patients with thyrotoxicosis.

Side-effects: Although side-effects associated with Premarin tablets are extremely rare, the following may occur: Gastro-intestinal symptoms, headaches, breast tenderness, salt and water retention.

Overdosage: Reports of ingestion of large doses of oestrogen-containing products indicate that acute serious ill effects do not occur and overdosage is unlikely to be a problem.

Pharmaceutical precautions No special requirements for storage are required.

Legal category POM.

Package quantities

Premarin 0.625 mg: Bubble packs of 21 and Securitainers of 100.

Premarin 1.25 mg: Bubble packs of 21 and Securitainers of 100.

Premarin 2.5 mg: Securitainers of 100 tablets.

Further information Premarin is a mixture of natural oestrogens in the proportions physiologically maintained by nature. Unlike synthetic hormones Premarin is comparatively free from side-effects; in particular its effect on blood platelet behaviour is different from synthetic oestrogens. Amelioration of the individual's mental outlook, especially in the menopause, is generally associated with clinical improvement and is described by the patient as a gratifying sense of 'well being'.

Product licence numbers

Premarin Tablets 2.5 mg	0607/0002
Premarin Tablets 1.25 mg	0607/5001
Premarin Tablets 0.625 mg	0607/5000

PREMARIN* VAGINAL CREAM

Presentation Premarin Vaginal Cream contains 0.625 mg per gram of conjugated oestrogens in a non-liquefying base.

Uses Atrophic vaginitis and postmenopausal atrophic urethritis. Before and after urogenital surgery in the postmenopausal woman. Pruritis vulvae. Kraurosis vulvae.

Dosage and administration 1–2 g daily intravaginally or topically depending on the severity of the condition. A total daily dosage of 4 g should not be exceeded. The lowest dose that will control symptoms should be chosen. Administration should be cyclic (e.g. 3 weeks on and one week off). In postmenopausal surgery therapy is suggested 10 days before and 10 days following intervention.

If the patient has not menstruated within the last two months or more, cyclic administration is started arbitrarily. If the patient is menstruating, cyclic administration is started on day five of bleeding. When hormone replacement is contemplated, it is recommended that a complete physical examination including endometrial assessment, whenever possible, be performed at the time of the initial examination. Regular follow-up examinations, including endometrial assessments are recommended every 6–12 months. Breakthrough bleeding is an indication for medical evaluation.

Contra-indications, warnings, etc

Due to the possibility of systemic oestrogen absorption following the application of Premarin Vaginal Cream, prolonged administration might result in effects similar to those associated with prolonged use of Premarin Tablets. Therefore, the following contra-indications, precautions and possible side effects should be considered, although none of these have been reported directly with Premarin Vaginal Cream therapy.

Contra-indications: Uterine leiomyomata, endometriosis, cancer of the breast, uterus and other oestrogen dependent neoplasia, hepatic, renal and severe cardiac disease, undiagnosed genital bleeding, pregnancy.

Although Premarin is a natural oestrogen in contrast to the synthetic preparations which may cause thrombosis it should not be given to patients with a personal history of thrombosis or thromboembolic disease (including coronary thrombosis, cerebrovascular accident, etc.).

Precautions: Prolonged use of unopposed oestrogen may increase the risk of endometrial carcinoma.

Mastopathy.

Use in atrophic lesions of the vulva does not preclude the necessity for diagnostic measures to eliminate the possibility of neoplasia nor does it preclude the requirement for antimicrobial therapy in the presence of trichomonal, monilial or bacterial infection.

Some women may develop cholelithiasis during oestrogen therapy.

When oestrogens are administered to patients with hypertension supervision is necessary and blood pressure should be monitored at regular intervals.

In a diabetic patient insulin requirement may be altered.

Because larger doses of oestrogen may increase thyroid binding globulin leading to increased circulating total thyroid hormone, care should be taken in prescribing oestrogens for patients with thyrotoxicosis.

Side-effects: Although side-effects associated with Premarin Vaginal Cream are extremely rare, the following may occur: breast tenderness, headaches, salt and water retention, abnormal or excessive bleeding.

Overdosage: Reports of ingestion of large doses of oestrogen-containing products indicate that acute seri-

ous ill effects do not occur and overdosage is unlikely to be a problem.

Pharmaceutical precautions No special requirements for storage are necessary.

Legal category POM.

Package quantities Each pack contains 42.5 g of the non-liquefying cream with one calibrated applicator.

Further information Due to the low bulk of each application there is little likelihood of leakage.

Product licence number 0607/0005.

PREMPAK*

Presentation Prempak 0.625 contains 21 tablets natural conjugated oestrogens (Premarin) 0.625 mg plus 7 tablets norgestrel 0.5 mg.

Prempak 1.25 contains 21 tablets natural conjugated oestrogens (Premarin) 1.25 mg plus 7 tablets norgestrel 0.5 mg.

Uses For menopausal and postmenopausal oestrogen replacement therapy and allied disorders such as postmenopausal osteoporosis and senile vaginitis.

Dosage and administration *Menopausal and postmenopausal oestrogen deficiency:* Premarin 0.625 mg or 1.25 mg daily cyclically. One norgestrel tablet should be taken daily from day 15 to 21 of Premarin therapy. This should be followed by 7 tablet-free days. The pack carries patient instructions.

For maintenance, the lowest effective dose is recommended. If the patient has not menstruated within the last two months or more, cyclic administration is started arbitrarily. If the patient is menstruating, cyclic administration is started on day 5 of bleeding. If withdrawal bleeding is heavy, then the dose of Premarin may be reduced and periodical gynaecological examinations are advised for patients on long term therapy. In women with obesity, diabetes, low parity or a familial history of endometrial carcinoma, for whom hormone replacement therapy is required, Prempak should be considered in preference to unopposed oestrogen therapy. Prempak provides both oestrogens and a progestogen to restore endocrine balance, whilst avoiding endometrial hyperstimulation – this is achieved by endometrial shedding which occurs as a result of Prempak therapy. This also provides a form of cycle regulation in women who are still menstruating but irregularly. Before therapy commences it is recommended that the patient should have a complete physical examination.

Atrophic vaginitis: Premarin 0.625 mg – 1.25 mg daily for 21 days with 1 tablet norgestrel from day 15 to 21 of the cycle.

Postmenopausal osteoporosis: Premarin cyclically 0.625 mg to 1.25 mg daily on a 21-day cycle. 1 tablet norgestrel daily should be taken from day 15 to 21 of the Premarin cycle.

Contra-indications, warnings, etc

Contra-indications: Uterine leiomyomata. Endometriosis. Cancer of the breast, uterus and other oestrogen dependent neoplasia. Hepatic, renal and severe cardiac disease. Undiagnosed genital bleeding. Pregnancy. Although Premarin is a natural oestrogen in contrast to the synthetic preparations which may cause thrombosis, it should not be given to patients with a personal history

of thrombosis or thromboembolic disease (including coronary thrombosis, cerebrovascular accident, etc.).

Precautions: In a diabetic patient insulin requirement may be altered.

Mastopathy.

Some women may develop cholelithiasis during oestrogen therapy.

When oestrogens are administered to patients with hypertension supervision is necessary and blood pressure should be monitored at regular intervals.

Because larger doses of oestrogen may increase thyroid binding globulin leading to increased circulating total thyroid hormone, care should be taken in prescribing oestrogens for patients with thyrotoxicosis.

Prempak is not an oral contraceptive, neither will it restore fertility.

Side-effects: Although side-effects associated with Prempak are extremely rare, the following may occur: Gastrointestinal symptoms, headaches, breast tenderness, salt and water retention.

Overdosage: Reports of ingestion of large doses of oestrogen-containing products indicate that acute serious ill effects do not occur and overdosage is unlikely to be a problem.

Pharmaceutical precautions No special requirements for storage are required.

Legal category POM.

Package quantities Bubble pack of 21 Premarin tablets 0.625 mg or 1.25 mg plus 7 norgestrel tablets 0.5 mg.

Further information Prempak provides cycled oestrogen/progestogen therapy for the menopausal syndrome and associated disorders. The bubble pack contains 21 tablets of Premarin. From day 15 to day 21 inclusive each bubble contains in addition one norgestrel 0.5 mg tablet. The two tablets should be taken together for these seven days. The specially designed pack avoids the use of tablets containing more than one active compound.

Product licence numbers

Prempak 0.625 mg 0607/0029

Prempak 1.25 mg 0607/0030

*Trade Mark

Bayer UK Limited
Pharmaceutical Division
Burrell Road, Haywards Heath
West Sussex RH16 1TP



ADALAT*

Presentation *Adalat/Adalat 5*: Orange, soft gelatin capsules containing a yellow viscous liquid. Adalat capsules contain 10 mg nifedipine. Adalat 5 capsules contain 5 mg nifedipine.

Adalat Retard: Pink-grey lacquered tablets one side marked 1U, the reverse side with the Bayer Cross each containing 20 mg nifedipine.

Uses *Mode of action*: Adalat is a potent calcium antagonist. Its most important effect is to protect the heart against excessive oxygen utilisation during physical activity. There is a reduction in cardiac work and in myocardial oxygen demand. Adalat also causes peripheral vasodilatation and thus reduces peripheral resistance and heart work load. Adalat has no therapeutic anti-arrhythmic effect. Since Adalat does not cause a rise in intraocular pressure, it can be used in patients with glaucoma.

Indications: For the treatment and prophylaxis of angina pectoris and for the treatment of hypertension.

Dosage and administration For oral administration, the capsules should be taken with a little fluid during or after meals. The recommended dose is one 10 mg capsule three times daily. If necessary, up to two capsules three times daily may be taken.

If an immediate effect is required, the capsule should be bitten open and the liquid contents allowed to remain in the mouth.

Adalat 5 capsules permit titration of initial dosage in the elderly and those patients on concomitant medication. The recommended dose is one Adalat 5 capsules three times daily.

In the treatment of hypertension the recommended dose of Adalat Retard is one 20 mg tablet twice daily swallowed after food with a little fluid. If necessary the dose may be increased to 40 mg twice daily.

Treatment may be continued indefinitely.

Contra-indications, warnings, etc

Contra-indications: Must not be given to women capable of child-bearing.

Warnings and precautions: Adalat is not a beta-blocker and therefore gives no protection against the dangers of abrupt beta-blocker withdrawal; any such withdrawal should be by gradual reduction of the dose of beta-blocker, preferably over 8-10 days.

Adalat may be used in combination with beta-blocking drugs and other antihypertensive agents, but the possibility of an additive effect resulting in postural hypotension should be borne in mind. Adalat will not prevent possible rebound effects after cessation of anti-hypertensive therapy.

Adalat should be used with caution in patients whose cardiac reserve is poor.

Ischaemic pain has been reported in some patients, commonly within 30 minutes of the introduction of

Adalat therapy. Patients experiencing this effect should discontinue Adalat.

The use of Adalat in diabetic patients may require adjustment of their control. There is no known drug incompatibility.

Side-effects: Adalat is well tolerated. Minor side-effects, usually associated with vasodilatation are mainly headache, flushing and lethargy. These are transient and invariably disappear with continued treatment.

Overdosage: Standard measures such as atropine and noradrenaline may be used for resultant bradycardia and hypotension. Intravenous calcium gluconate may be of benefit.

Pharmaceutical precautions The capsules should be protected from strong light and stored in the manufacturer's original container.

Legal category POM.

Package quantities Adalat and Adalat 5 capsules are available in foil strips of 10 in packs of 100.

Adalat Retard tablets are also available in foil strips of 10 in packs of 100.

Further information As a specific calcium antagonist, Adalat's main action is to relax arterial smooth muscle both in the coronary and peripheral circulation.

In angina pectoris Adalat capsules relax peripheral arteries so reducing the load of the left ventricle. Additionally Adalat dilates submaximally both clear and atherosclerotic coronary arteries, thus protecting the heart against coronary artery spasm and improving perfusion to the ischaemic myocardium.

Adalat capsules reduce the frequency of painful attacks and the ischaemic ECG changes irrespective of the relative contribution from coronary artery spasm or atherosclerosis. In normotensive individuals Adalat has little or no effect on blood pressure.

In hypertension Adalat Retard twice daily provides smooth 24 hour control of raised blood pressure. Adalat Retard causes a reduction in blood pressure such that the percentage lowering of blood pressure is directly related to its initial height.

In long-term treatment, none of these formulations have been shown to cause serious adverse reactions. Metabolic disturbance, failure of ejaculation, increased incidence of Raynaud's phenomenon and bronchospasm associated with other anti-anginal and anti-hypertensive agents have not been observed.

Product licence numbers

Adalat	PL0010/0021
Adalat 5	PL0010/0079
Adalat Retard	PL0010/0078

ALRHEUMAT*

Presentation Opaque 'off-white' hard gelatin capsules

each containing 50 mg ketoprofen. Suppositories each containing 100 mg ketoprofen.

Uses Alrheumat is recommended for the management of the rheumatic diseases: rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, sero-negative (non-rheumatoid) arthropathies, non-articular rheumatism and soft tissue rheumatism.

Dosage and administration Alrheumat capsules are administered orally and should be taken with food. Dosage is usually 1 capsule (50 mg) three times daily. This dosage may be increased to 1 capsule four times daily or decreased to 1 capsule twice daily depending on the weight and clinical condition of the patient and the severity of the disease. As an alternative to oral therapy, one suppository should be inserted in the morning and before retiring. For the relief of night pain and morning stiffness, one suppository should be inserted before retiring. Combined oral and rectal therapy: one suppository should be inserted before retiring, supplemented during the day with Alrheumat capsules as needed, up to a maximum daily dosage of 200 mg ketoprofen. Paediatric usage has not been established.

Contra-indications, warnings, etc

Contra-indications: Ketoprofen should not be given to patients known to be sensitive to aspirin or to other non-steroidal anti-inflammatory agents which are prostaglandin inhibitors. In such patients, and in those with a history of bronchial asthma or allergic disease, severe broncho-spasm may be precipitated.

Ketoprofen should not be given to patients with active peptic ulceration.

The suppositories should not be used in patients with any inflammatory conditions of the rectum or anus.

Side-effects: Occasional gastro-intestinal disturbances occur and in some such cases a reduction in dosage has been helpful. In common with most other anti-inflammatory agents, there have been very rare reports of gastro-intestinal haemorrhage. Skin rashes have been rare.

Precautions: Patients with a history of peptic ulcer or chronic dyspepsia should be carefully monitored. Care should also be taken in patients with a history of impaired hepatic function. Alrheumat, in common with other propionic acid derivatives, exhibits moderate plasma protein binding. Patients receiving anticoagulants, hydantoins and protein-bound sulphonamides must therefore be closely monitored. The required dose of these drugs may well be beneficially reduced if taken concurrently with Alrheumat.

No embryotoxic or teratogenic effects have been reported, but, on principle, caution should be exercised when prescribing any new medication during pregnancy and lactation.

Pharmaceutical precautions The suppositories should be stored in a cool place.

Legal category POM.

Package quantities Alrheumat Capsules are available in blister strips of 10 packed in boxes of 100 and 500 capsules. Alrheumat suppositories available in blister strips of 10. Packed in boxes of 50.

Further information Nil.

Product licence numbers

R Capsules 0010/0025
Suppositories 0010/0066

BAYCARON*

Presentation A white scored tablet 7 mm × 2 mm, one side scored L/1, the reverse side with the Bayer cross, containing 25 mg mefruside.

Uses Baycaron is a diuretic agent and is intended for the treatment of hypertension and oedema.

Dosage and administration Baycaron is best taken with a little fluid as a single morning dose.

Oedema: Initially for 10–14 days, 25–50 mg every morning increasing if necessary to 75–100 mg to obtain the desired response. Daily doses in excess of 100 mg usually do not further increase diuresis.

For maintenance, and for long-term therapy, 25 mg each morning.

Alternate day dosage may also be used.

Hypertension: Initially for 10–14 days, 25–50 mg, then a maintenance dose of 25 mg each morning. Alternate day dosage may also be used.

Contra-indications, warnings, etc

Contra-indications: Severe hypokalaemia and hepatic coma.

Side-effects: Occasionally with daily doses up to 100 mg dyspepsia and nausea are encountered initially, but usually subside on continuing treatment. Patients with known sulphonamide sensitivity may show allergic reactions to Baycaron.

Overdosage: There is no special antidote or other action to be taken, since an adverse reaction is unlikely.

Precautions: As with other diuretics, during long-term treatment with Baycaron, potassium supplements may be necessary, especially for patients with impaired liver function, or for those also receiving cardiac glycosides. No teratogenic effect has been shown to be related to the use of Baycaron in animals or following its use in toxemia of pregnancy, but the benefits of the preparation should be weighed against the possible risks in the first trimester of pregnancy.

Pharmaceutical precautions There are no special precautions or requirements regarding the storage of Baycaron.

Legal category POM.

Package quantities Bottles of 150 tablets.

Further information Nil.

Product licence number 0010/5903.

BAYOLIN*

Presentation A white cream. Each 100 g cream contains heparinoid 'Bayer' 5,000 HDBu., glycoester of monosalicylic acid 10 g, benzyl nicotinate 2.5 g.

Uses Bayolin is a rubefacient used to treat all forms of muscular rheumatism, muscular stiffness due to exertion, lumbago, lumbar and cervical syndrome, local therapy of pains in muscles and joints due to rheumatic polyarthritis, arthroses and spondylosis deformans.

Dosage and administration Topical application two or three times daily, the cream being massaged gently into the affected area until absorbed.

Contra-indications, warnings, etc **Side-effects:** Occasionally a skin reaction to the nicotinic acid component of Bayolin may be seen.

Precautions: Bayolin is very well tolerated, but like any other rubefacient it can be very painful if it is allowed to get into the eyes, or come into contact with mucous membranes. It is advisable for the hands to be washed after application.

Pharmaceutical precautions There are no special requirements for storage or other precautions to be taken.

Legal category P.

Package quantities Bayolin Cream is available in 35 g tubes.

Further information Nil.

Product licence number 0010/5907.

BAYPEN*

Presentation Vials containing 0.5 g, 1 g, 2 g mezlocillin as mezlocillin sodium monohydrate. Infusion vials containing 5 g mezlocillin as mezlocillin sodium monohydrate. Baypen infusion sets containing 3 × 5 g mezlocillin, 3 × 50 ml Water for Injections and 3 transfer needles.

Uses Mezlocillin is a broad spectrum antibiotic indicated for the treatment of infections caused by sensitive organisms and prophylaxis of post-operative sepsis following abdominal surgery and vaginal hysterectomy.

The following Gram-positive and Gram-negative pathogens are sensitive to mezlocillin: *Escherichia coli*, species of the *Klebsiella-Enterobacter-Serratia* group, *Proteus* spp. (indole-positive and indole-negative), *Providencia* spp., *Citrobacter* spp., *Pseudomonas aeruginosa*, *Salmonella* spp. and *Shigella* spp., enterococci, staphylococci (penicillin sensitive), *Corynebacteria* and *Clostridium* spp. as well as *Bacteroidaceae*, in particular *Bacteroides fragilis*, *Haemophilus influenzae*, gonococci, meningococci, pneumococci and streptococci are particularly sensitive.

Mezlocillin is, therefore, indicated for the treatment of the following systemic and/or local infections in which the above-named organisms have been detected or are suspected: Septicaemia, infections of the urogenital tract (including gonorrhoea), respiratory and biliary tracts, meningitis, bone and soft tissue infections, peritonitis, infected wounds and burns, proven or suspected infections in patients with impaired or suppressed immunological status.

Mezlocillin may be administered concomitantly with an aminoglycoside antibiotic or with beta-lactamase stable isoxazolyl penicillins since there is evidence of synergy.

An aminoglycoside should not be mixed in the same syringe or intravenous fluid container as mezlocillin.

Dosage and administration Mezlocillin is normally given by the intravenous route but may be given intramuscularly if required.

Intravenous administration: Mezlocillin is prepared for injection by shaking the powder with a suitable volume of Water for Injections for 30–60 seconds until completely dissolved to make a 10% solution, i.e. 0.5 g in 5 ml, 1 g in 10 ml, 2 g in 20 ml and 5 g in 50 ml. A 10% aqueous solution is isotonic.

It is recommended that the 5 g strength is given by infusion over 15–20 minutes; all other strengths by bolus

injection over two to four minutes depending on the volume.

Intramuscular administration: Mezlocillin may be administered by the IM route if required as an alternative to the IV route (e.g. patients with poor veins). A single dose should not exceed 2 g, each 1 g of powder requiring 3.5 ml of water for injection to achieve complete solution.

Adults:

1. **Patients with normal renal function:** Life-threatening infections and infections due to unidentified organisms or *Pseudomonas* strains should be treated with 5 g, IV, six to eight hourly, by infusion over 15–20 minutes.

Non life-threatening infections due to sensitive organisms, and biliary and urinary tract infections, should be treated with 2 g, IV, six to eight hourly, as a bolus injection over two to four minutes.

If required, an intramuscular injection of 0.5–2 g may be given by deep injection into the buttocks in these cases.

For the treatment of acute gonorrhoea the dose is a single IM injection of 1 g.

Prophylactic dosage: 2.0 g i.v. to be given pre-operatively followed by two injections of 2.0 g post-operatively at eight hourly intervals.

2. **Patients with renal insufficiency:** These patients should receive the appropriate doses outlined above but at intervals of only 12 hours. Monitoring of the serum levels is recommended to ensure that adequate and constant levels are maintained.

Children: In the dosage schedule below the individual dose for premature babies and neonates is based on 75 mg/kg twice daily as a prolonged IV infusion and for infants and older children 3 × 75 mg/kg as bolus injection or short transfusion (IV).

Children over six years old, over 20 kg body weight: 1.5 g eight hourly.

Children two to six years old, 13–20 kg body weight: 1–1.5 g eight hourly.

Children one to two years old, 10–13 kg body weight: 0.75–1 g eight hourly.

Infants over three months, 5–10 kg body weight: 0.4–0.75 g eight hourly.

Infants up to three months, 3–5 kg body weight: 0.2–0.4 g eight hourly.

Infants and premature babies, below 3 kg body weight: 75 mg/kg body weight 12 hourly corresponding to 0.2 g 12 hourly.

Duration of treatment: The duration of treatment depends upon the severity of the case and also the clinical response and bacteriological findings. In principle, treatment should be carried out for at least three days after disappearance of clinical symptoms. Duration of treatment is usually 7–10 days.

Contra-indications, warnings, etc

Contra-indications: Penicillin hypersensitivity.

As with all new drugs mezlocillin should not be used during the first three months of pregnancy.

Side-effects: As for other penicillins.

Pharmaceutical precautions Mezlocillin should not be stored in temperatures exceeding 25°C.

Mezlocillin should be freshly prepared prior to administration, any unused solution being discarded.

Mezlocillin should be administered separately unless compatibility is proven.

Mezlocillin is compatible with dextrose 5% and 10%,

laevulose 5%, Ringer's Solution and physiological saline during the period of administration.

Legal category POM.

Package quantities Vials containing 0.5 g, 1 g, 2 g in boxes of 5 vials.

Vials of 5 g: single vials.

Baypen Infusion Packs of 3 × 5 g.

Further information Sodium content:

Each 5.0 g vial contains	9.27 mEq sodium (213.1 mg)
Each 2.0 g vial contains	3.71 mEq sodium (85.2 mg)
Each 1.0 g vial contains	1.85 mEq sodium (42.6 mg)
Each 0.5 g vial contains	0.93 mEq sodium (21.3 mg)

Product licence number 0010/0070

CANESTEN®

Presentation

- 1. Cream:** A white cream containing 1.0% clotrimazole.
- 2. Atomiser Spray:** A clear solution containing 1.0% clotrimazole in 30% isopropanol. The spray is produced by an atomiser and contains no propellant.
- 3. Solution:** A clear solution containing 1.0% clotrimazole in polyethylene glycol 400.
- 4. Powder:** A white powder containing 1.0% clotrimazole.
- 5. Vaginal Tablets:** White convex tablets, measuring 25 mm × 6.5 mm × 10 mm, 100 mg tablet marked 'BAYER' on one side and 'AD' on the other. 200 mg tablet marked 'BAYER' on one side and 'F9' on the other.

500 mg tablet (Canesten 1) marked 'Bayer' on one side and 'MU' on the other.

5. Vaginal Cream: A white cream containing 2.0% clotrimazole.

7. Duopak: A combination pack comprising 6 Canesten vaginal tablets (each containing 100 mg clotrimazole) plus a 20 g tube of Canesten cream (containing 1.0% clotrimazole).

indications Clotrimazole is a broad spectrum anti-fungal. It also exhibits activity against *Trichomonas*, *Streptococci* and *Bacteroides*. It has no effect on *Lactobacilli*:

- 1. Cream:** All fungal skin infections due to dermatophytes (e.g. *Trichophyton* species), yeasts (e.g. *Candida* species), moulds and other fungi. These include ringworm (tinea) infections, athlete's foot, paronychia, pityriasis versicolor, erythrasma, intertrigo, fungal nappy rash, candida vulvitis and candida balanitis.
- 2. Atomiser Spray:** As Canesten cream, recommended on infections covering large and/or hairy areas.
- 3. Solution:** The solution is particularly suitable for use on hairy skin and in fungal infections of the outer ear (otitis externa).
- 4. Powder:** As an adjunct to treatment with cream or atomiser spray and as a prophylactic against re-infection, particularly in infections such as athlete's foot. The powder should be applied to the lesions simultaneously and dusted inside articles of clothing in contact with infected areas.

5. Vaginal Tablets: Candida vaginitis and mixed vaginal infections where trichomonas is present or suspected. Canesten is not recommended as sole treatment for pure trichomoniasis, except in cases where systemic therapy is contra-indicated.

6. Vaginal Cream: As for (5) above.

7. Duopak: Vaginal tablets for candida vaginitis; cream for associated vulvitis and to treat the sexual partner to prevent re-infection.

Dosage and administration

1. Cream: Canesten cream should be thinly and evenly applied to the affected area two to three times daily, and rubbed in gently.

Treatment should be continued for at least one month, or for at least two weeks after the disappearance of all signs of infection (to prevent relapse).

If the feet are infected, they should be thoroughly washed and dried, especially between the toes, before applying the cream.

2. Atomiser Spray: As per Canesten cream.

3. Solution: as per Canesten cream.

4. Powder: Sprinkle on to the affected areas two to three times daily after using the cream or atomiser spray. The powder may also be dusted inside articles of clothing and footwear which are in contact with the infected area.

5. Vaginal Tablets 100 mg: Two vaginal tablets should be inserted daily, preferably at night, for three consecutive days. Alternatively, 1 vaginal tablet daily for six days may be given.

Vaginal Tablets 200 mg: One vaginal tablet should be inserted daily, preferably at night for three consecutive days.

Vaginal tablet 500 mg: (Canesten 1). The single tablet should be inserted at night.

Using the applicator provided, each vaginal tablet should be inserted as deeply as is comfortable into the vagina. This is best achieved when lying back with the legs bent up.

6. Vaginal Cream: insert one filled applicator (5 g) intravaginally twice daily for three consecutive days or once daily for six consecutive days preferably at night.

7. Duopak: 100 mg vaginal tablets as in 5, above. The cream should be applied night and morning to the vulva and surrounding area and/or to the sexual partner's penis to prevent re-infection.

Contra-indications, warnings, etc

Contra-indications: None known.

Side-effects: Rarely patients may experience local mild burning or irritation immediately after applying cream or atomiser spray or after inserting the vaginal tablet. Very rarely, the patient may find this irritation intolerable and stop treatment.

Precautions: Canesten atomiser spray should not be used near a naked flame, should not be allowed to come into contact with the eyes, ears or mucous membranes and should not be inhaled.

Pharmaceutical precautions Storage:

Cream – none.

Atomiser Spray – none.

Solution – none.

Powder – none.

Vaginal Tablets – none.

Vaginal Cream – none.

Duopak – none.

Legal category

Cream P.
Atomiser Spray P.
Solution P.
Powder P.
Vaginal Tablets POM.
Vaginal Cream POM.
Duopak POM.

Package quantities

1. *Cream*: Each tube contains 20 g or 50 g.
2. *Atomiser Spray*: Each bottle contains 40 ml.
3. *Solution*: Each dropper bottle contains 20 ml.
4. *Powder*: Each pack contains 30 g.
5. *Vaginal Tablets*: 6 × 100 mg vaginal tablets packed in a blister strip. 3 × 200 mg vaginal tablets packed in a blister strip. 1 × 500 mg vaginal tablet packed in foil.

An applicator and patient instructions are included.

6. *Vaginal Cream*: Each tube contains 35 g and is supplied with 6 disposable applicators and a patient instruction leaflet.

7. *Duopak*: Each box contains 6 × 100 mg vaginal tablets packed in a blister strip plus a 20 g tube of cream. An applicator for the vaginal tablets and patient instructions are included.

Further information Nil.**Product licence numbers**

Cream	0010/0016
Atomiser Spray	0010/0060
Solution	0010/0082
Powder	0010/0067
Vaginal Tablets 100 mg	0010/0015
Vaginal Tablets 200 mg	0010/0072
Vaginal Tablet 500 mg	0010/0083
Vaginal Cream	0010/0077
Duopak	0010/0016 & 0010/0015

FABAHISTIN*

Presentation *Tablets*: orange-coloured sugar-coated tablets measuring approximately 8.5 mm × 5.5 mm, each tablet containing 50 mg mebhydrolin base.

Suspension: An orange-coloured suspension in a 100 ml glass bottle, each 5 ml suspension containing 50 mg mebhydrolin as mebhydrolin napadisylate.

Uses Fabahistin is an antihistamine recommended for the treatment of hay fever, urticaria, rhinitis and all other allergic disorders.

Dosage and administration Oral administration as follows:

Adults: 1 or 2 × 50 mg tablets three times a day.

Children: Over 10 years: 1 or 2 × 50 mg tablets three times a day.

Under 10 years: 1–4 × 5 ml spoonfuls of suspension daily, according to age, in divided doses after meals.

Contra-indications, warnings, etc

Contra-indications: None known.

Side-effects: Very rarely cases of granulocytopenia or agranulocytosis associated with the use of mebhydrolin have been reported.

Overdosage: No symptoms have been reported in a patient receiving 140 × 50 mg tablets.

Precautions: The substance may cause drowsiness. If affected, do not drive or operate machinery. Avoid alcoholic drinks.

No embryotoxic or teratogenic effects have been reported, but, on principle, caution should be exercised when prescribing any new medication during pregnancy and lactation.

Pharmaceutical precautions There are no special requirements for storage.

The suspension should not be diluted with water, but a suitable suspending agent should be used such as tragacanth. Suspensions to be stored for long periods should be diluted with a suspending agent containing methyl hydroxybenzoate BP 0.07 g, sodium carboxymethyl cellulose 0.5 g in 100 ml Purified Water BP.

Legal category P.

Package quantities Strip packs of 20 tablets. Bottles of 250 tablets. Bottles of 100 ml suspension.

Further information Nil.**Product licence numbers**

Tablets	0010/5913
Suspension	0010/5915

LASONIL*

Presentation *Ointment*: A yellow-tinged transparent soft ointment contained in aluminium tubes. Each 100 g ointment contains heparinoid 'Bayer' 5,000 HDBu., hyaluronidase 15,000 i.u.

Uses Lasonil is a preparation containing heparinoid and hyaluronidase, which counteracts inflammation, promotes resorption of local oedema and extravasated blood, and locally delays blood clotting.

Ointment: Traumatic conditions: bruises, sprains, soft tissue injuries.

Varicose conditions: thrombophlebitis, superficial thrombosis, varicose ulcers.

Haemorrhoids.

Dosage and administration *Ointment*: *Traumatic conditions*: Unless otherwise directed, apply thickly and gently massage into the affected area two to three times daily.

Varicose conditions: In varicose ulcers Lasonil should be applied around the ulcer and gently massaged into the skin.

In thrombophlebitis and superficial thrombosis Lasonil should be massaged gently into the affected area three to five times daily.

Haemorrhoids: Apply night and morning, and after defaecation, to the anal region and inject a small quantity into the anal canal through the applicator.

There is no special dosage for children.

Contra-indications, warnings, etc *Contra-indications*: None.

Side-effects: None.

Precautions: Lasonil should not be applied to open or infected wounds.

Pharmaceutical precautions There are no special precautions or requirements regarding the storage, etc of Lasonil.

Legal category P.

Package quantities *Ointment*: Aluminium tubes containing 14 g and 40 g Lasonil.

Further information Nil.

Product licence number 0010/5914.

OSPOLOT®

Presentation *Tablets*: White lacquer-coated convex tablets 50 mg marked with Bayer Cross on one side and C4 on the other. 200 mg marked with the Bayer Cross on one side and the Letters 'F' and 'S' divided by a score mark on the other.

Suspension: A yellow/orange suspension contained in 100 ml and 500 ml glass bottles, each 5 ml of suspension containing 50 mg sulthiame.

Uses Ospolot is an anticonvulsant recommended for the treatment of grand mal, temporal lobe epilepsy, Jacksonian seizures, myoclonic attacks, hyperkinetic behaviour and disturbed behaviour associated with epilepsy, mental subnormality and psychiatric disorders.

Dosage and administration Oral administration as follows:

Adults: **Initial**: 100 mg twice daily.

Optimum: 200 mg three times daily.

Children: According to body weight:

Initial: 3–5 mg/kg daily in equal divided doses.

Optimum: 10–15 mg/kg daily in equal divided doses.

Contra-indications, warnings, etc

Contra-indications: None known, but caution should be exercised in patients with a history of renal disease.

Side-effects: These are usually mild and subside after 8–14 days. Paraesthesia of the extremities and face is the commonest. A usually transient hyperpnoea sometimes occurs unassociated with biochemical or cardiovascular changes. Gastric disturbances, headaches and vertigo have also been reported.

Where Ospolot is used in combination with phenytoin, it has been shown that there is a rise in phenytoin serum levels. This fact should be borne in mind when using this combination.

Overdosage: Crystalluria and renal damage are the main risks of overdosage with Ospolot. Alkaline fluid should therefore be administered, both orally and by intravenous infusion. Symptoms of overdosage are vomiting, severe headache, vertigo, ataxia and hyperventilation. Catatonia may develop; patients remain conscious.

Pharmaceutical precautions There are no special requirements for storage.

The suspension should not be diluted with water, but a suitable suspending agent should be used such as tragacanth. Suspensions to be stored for long periods should be diluted with a suspending agent containing methyl hydroxybenzoate BP 0.07 g, sodium carboxymethyl cellulose 1.0 g in 100 ml Purified Water BP.

Legal category POM.

Package quantities Bottles of 50 and 250 scored and lacquered tablets of 200 mg.

Bottles of 250 lacquered tablets of 50 mg.

Bottles of 500 ml suspension 50 mg/5 ml.

Further information Nil.

Product licence numbers

Tablets 200 mg 0010/5924

Tablets 50 mg 0010/5908
Suspension 0010/5909

SECUROPEN®

Presentation Vials containing 0.5 g, 1.0 g, 2.0 g azlocillin as azlocillin monosodium. Infusion vials containing 5.0 g as azlocillin monosodium.

Securopen infusion set containing 3 × 5 g azlocillin, 3 × 50 ml Water for Injections and 3 transfer needles.

Uses Azlocillin is a broad spectrum antibiotic with especially significant anti-pseudomonal activity. In addition to *Pseudomonas* strains the spectrum of activity of azlocillin includes the following Gram-negative and Gram-positive pathogens: *Escherichia coli*, *Klebsiella Enterobacter Serratia* group, *Proteus* (indole-positive and indole-negative), *Providencia*, *Citrobacter*, *Salmonella* and *Shigella*, enterococci, staphylococci (penicillin sensitive), *Haemophilus influenzae*, gonococci, meningococci, pneumococci, streptococci and *Corynebacterium* spp. The spectrum also includes the anaerobic organisms *Clostridia* and *Bacteroides species*, including *Bacteroides fragilis*.

Azlocillin is specifically indicated for the treatment of infections due to *Pseudomonas* strains especially those of the respiratory and urinary tracts and for septicæmia. Also for infections in other areas due to this organism.

Azlocillin may be administered concomitantly with an aminoglycoside or with beta-lactamase stable isoxazolyl-penicillins, since there is evidence of synergy with these groups.

Dosage and administration *Adult Dosage*: **Patients with normal renal function**: Life-threatening infections 5.0 g every 8 hours. In non life-threatening and urinary tract infections 2.0 g every 8 hours.

Patients with severely impaired renal function: i.e. with a serum creatinine above 2 mg% or with creatinine clearance less than 30 ml/minute, the unit dose should be as above but at 12 hourly intervals.

Patients on haemodialysis: Azlocillin is dialysable. On non-dialysing days, patients receive the recommended unit dose of azlocillin twice daily. Before each dialysis an additional unit dose should be given to compensate for the amount of azlocillin removed by dialysis.

Children's Dosage:

Children 1–14 years	: 3 × 75 mg/kg bodyweight/day
Infants > 7 days–1 year	: 3 × 100 mg/kg bodyweight/day
Neonates < 7 days	: 2 × 100 mg/kg bodyweight/day
Premature babies	: 2 × 50 mg/kg bodyweight/day

From this the following dosages can be derived:

Children 6–14 years (20–40 kg bodyweight)	1.5–3.0 g 3 × daily
Children 2–6 years (13–20 kg bodyweight)	1.0–1.5 g 3 × daily
Children 1–2 years (10–13 kg bodyweight)	0.75–1.0 g 3 × daily
Infants 7 days–1 year (about 3–10 kg bodyweight)	0.3–1.0 g 3 × daily
Neonates 7 days (about 3 kg bodyweight)	0.3 g 2 × daily

Premature babies up to 2.5 kg bodyweight	2.5 kg bodyweight: 125 mg 2 × daily
	2.0 kg bodyweight: 100 mg 2 × daily
	1.5 kg bodyweight: 75 mg 2 × daily.

Duration of Treatment: The duration of treatment depends upon the severity of the case and also the clinical and bacteriological course of the disease. In principle, treatment should be maintained for at least 3 days after fever or clinical symptoms have disappeared. This on average requires 7–10 days therapy.

Administration: Azlocillin is administered intravenously as a 10% solution in Water for Injections. For doses of 2.0 g or less it is administered as a bolus injection and for higher doses as an infusion over 20–30 minutes. Aminoglycosides, when given concomitantly, should not be mixed in the same syringe or infusion fluid as azlocillin.

Combination Therapy: In patients already receiving intravenous infusion therapy with other drugs, azlocillin should be infused during the intervening periods or as a parallel infusion. In order to achieve higher initial concentrations in the serum and tissues, part of the dose – up to half – may be injected slowly through the tubing of the existing infusion. Azlocillin solution is compatible with glucose solution (5% and 10%), laevulose solution (5%), Ringer's solution and physiological saline. Supplementary drugs should be injected through the drip tubing and not introduced into the bag or bottle. Injectable tetracycline derivatives, for example, have proved to be incompatible. Before administering special, rarely used solutions or drugs the compatibility of the individual components must be ascertained; precipitation, cloudiness or discolouration indicates possible incompatibility.

Stability in other infusions: Azlocillin is stable in the common infusion fluids provided the solution has been freshly prepared. If azlocillin must be prepared before administration it may be kept as the 10% solution at room temperature for 6 hours without loss of efficacy.

Contra-indications, warnings, etc

Contra-indications: A history of allergy to other penicillins and cephalosporins. Securopen is inactivated by β -lactamases (penicillinases). As with all new drugs Securopen should not be used during the first 3 months of pregnancy.

Side-effects: Uncommon and typical for other injectable penicillins.

Toxicity and treatment of overdose: There have been no reports of toxic effects or overdosage.

Pharmaceutical precautions *Storage:* The shelf life is 4 years when stored below 25°C and expiry date is printed on the packaging. Azlocillin should not be stored in temperatures exceeding 25°C.

Dilution: Azlocillin should be freshly prepared immediately before administration by shaking the powder with a suitable volume of Water for Injections until completely dissolved to make a 10% solution – that is, 0.5 g in 5 ml, 1.0 g in 10 ml, 2.0 g in 20 ml and 5.0 g in 50 ml. Any unused solution should be discarded. Azlocillin is stable in 5% and 10% dextrose solution, laevulose 5%, Ringer's solution and physiological saline.

Legal category POM.

Package quantities 0.5 g, 1.0 g, 2.0 g vials packed in boxes of 5.
5.0 g vial packed singly.
Securopen infusion pack of 3 × 5 g.

Further information

Sodium content:	
Each 5.0 g vial contains	10.84 mEq sodium (249.1 mg)
Each 2.0 g vial contains	4.33 mEq sodium (99.6 mg)
Each 1.0 g vial contains	2.17 mEq sodium (49.8 mg)
Each 0.5 g vial contains	1.08 mEq sodium (24.9 mg)

Product licence number 0010/0075

TRASYLOL®

Presentation A colourless ampoule containing a solution of aprotinin for injection, each 5 ml ampoule containing 100,000 kallikrein inactivator units (KIU) and each 10 ml ampoule containing 200,000 KIU.

Uses Trasylol is a broad-spectrum protease inhibitor. Its indications are as follows:

Traumatic, haemorrhagic, pancreatogenic, endotoxin shock and fat-embolism syndrome.

Acute pancreatitis.

Prophylaxis in upper abdominal surgery.

Hyperfibrinolytic haemorrhage.

Dosage and administration *Traumatic, haemorrhagic, pancreatogenic, endotoxin shock and fat-embolism syndrome:* An initial 500,000 KIU should be administered immediately by slow i.v. injection (at a rate not exceeding 5 ml/min.) followed by 200,000 KIU four-hourly by i.v. infusion. It may be necessary to continue this dosage for three days or longer, depending on the clinical picture.

Acute pancreatitis: As above.

Prophylaxis in upper abdominal surgery: 200,000 KIU should be administered by slow i.v. injection immediately before commencing the operation. During the day of the operation, as well as during the first and second post-operative days, 200,000 KIU should be administered four-hourly by slow i.v. injection or continuous i.v. infusion.

Hyperfibrinolytic haemorrhage: Up to 500,000 KIU should be administered by slow i.v. injection within the first 30 minutes; subsequently 200,000 KIU four-hourly should be given by continuous i.v. infusion until haemostasis has definitely been achieved. In disseminated intravascular coagulation with secondary hyperfibrinolysis (consumption coagulopathy) higher dosages up to 1,000,000 KIU or more may be required. In fibrinogen deficiency substitution may be necessary.

The dose for children should be calculated in proportion to the adult dose on the basis of body weight.

Contra-indications, warnings, etc

Contra-indications: There are no contra-indications.

Side-effects: Trasylol is very well tolerated, even in high dosage. Local or general reactions are very rare (less than 0.1%). However, being a polypeptide, care should be exercised in treating patients intermittently or those who have previously received Trasylol, since an anaphylactic reaction can occur.

Trasylol is incompatible with most corticosteroids and nutrient solutions containing amino-acids or fat emulsions.

Overdosage: There is no special antidote or other action to be taken.

Pharmaceutical precautions Trasylol is very stable when stored in sealed ampoules at room temperature. Opened ampoules, however, quickly lose activity if bacterial contamination is not prevented.

Legal category POM.

Package quantities Trasylol is supplied in strengths of 100,000 KIU per 5 ml ampoule and 200,000 KIU per 10 ml ampoule in boxes of 5 and 25 ampoules.

Further information Nil.

Product licence number 0010/5900.

YOMESAN*

Presentation Yellowish tablets measuring 13 mm x 4 mm, each tablet containing 500 mg niclosamide BP. One side marked FE, the reverse side with the Bayer cross. The tablets are flavoured with vanilla.

Uses An anthelmintic for treatment of tapeworm infections:

<i>Taenia saginata</i>	(beef tapeworm)
<i>Taenia solium</i>	(pork tapeworm)
<i>Diphyllobothrium latum</i>	(fish tapeworm)
<i>Hymenolepis nana</i>	(dwarf tapeworm)

It has no effect in cysticercosis and echinococcosis due to cestode larvae (cysticerci) lodging in extra intestinal tissues.

Dosage and administration *Taenia saginata*, *Taenia solium*, *Diphyllobothrium latum*.

<i>Adults and children over 6 years:</i>	4 tablets
<i>Children 2 to 6 years:</i>	2 tablets
<i>Children under 2 years:</i>	1 tablet

In *Taenia solium* the tablets should be taken as a single dose after a light breakfast but in the case of *Taenia saginata* and *Diphyllobothrium latum* the dose may be divided, half being taken after breakfast and the remainder one hour later.

An aperient should be administered two hours later and in the case of *Taenia solium* a drastic purge should be given.

If reinfection occurs repeat treatment.

Infection due to *Hymenolepis nana* should be treated for 7 days:

First day:

<i>Adults and children over 6 years:</i>	4 tablets
<i>Children from 2 to 6 years:</i>	2 tablet
<i>Children under 2 years:</i>	1 tablets

The subsequent 6 days:

<i>Adults and children over 6 years:</i>	2 tablets
<i>Children from 2 to 6 years:</i>	1 tablet
<i>Children under 2 years:</i>	1/2 tablets

It is important that the tablets are chewed thoroughly before washing down with water. In the case of small children the tablets should be ground up before administration.

Contra-indications, warnings, etc

Contra-indications: there are no known contra-indications.

Side-effects: limited to occasional gastrointestinal upsets, light headedness and pruritus.

Overdosage: Yomesan is not absorbed and no cases of overdosage have occurred.

Use in Pregnancy: In common with most drugs it is wise to avoid treatment in the first trimester of pregnancy. Healthy children have been born to women treated with Yomesan in the first trimester of pregnancy.

Experimental studies in rats showed no embryotoxic or teratogenic effects.

Warning: In infections with *Taenia solium* there is always a danger of cysticercosis. A drastic purge is therefore recommended after treatment to eject the lower segment of the tapeworm containing mature eggs.

The hands should be thoroughly scrubbed after defaecation not only on the treatment day but for several days afterwards to avoid reinfection.

The consumption of alcohol during treatment must be avoided.

Pharmaceutical precautions The tablets are light sensitive and should only be stored in the original foil.

Legal category P.

Package quantities Packs of 4 tablets of 0.5 g.

Further information Unless the tapeworm is expelled by a drastic purgative, residual parts of it may be eliminated with the stools during the next two or three days. Thereafter, neither tapeworm segments nor ova should be present in the stools. In re-infection with *Taenia saginata* and *Taenia solium* new tapeworm segments or ova should only appear after three months.

In infections with *Hymenolepis nana* the follow-up period is only 14 days as surviving scolices regenerate very rapidly to sexually mature tapeworms and accordingly, after approx. 10 days, ova are eliminated with the stools.

Product licence number 0010/5910.

*Trade Mark

Beecham Research Laboratories
Great West Road
Brentford
Middlesex TW8 9BD



AMPICLOX* INJECTION

Presentation *Ampiclox Injection*: Vials containing 250 mg ampicillin as Ampicillin Sodium BP with 250 mg cloxacillin as Cloxacillin Sodium BP.

Uses Ampiclox is indicated for the immediate treatment of severe infections before the infecting organism is identified, and for mixed staphylococcal and Gram-negative infections.

Typical indications include: Bronchopneumonia, post-influenzal pneumonia and other severe respiratory infections. Post-operative chest and wound infections. Septic abortions and infections during the puerperium. Septicaemia. Infections in patients receiving immunosuppressive drugs. Prophylaxis in major surgery.

Dosage and administration *Adult dosage: Intramuscular/Intravenous*: 1–2 vials four to six hourly.

Children's dosage: Up to 2 years: $\frac{1}{4}$ adult dose.†
2–10 years: $\frac{1}{2}$ adult dose.

Administration: Intramuscular: Dissolve vial contents in 1.5 ml Water for Injections BP.

Intravenous: Dissolve vial contents in 10 ml Water for Injections BP and administer slowly (three to four minutes). Ampiclox may also be added to infusion fluids or injected, suitably diluted, into the drip tube over a period of three to four minutes.

Dosage may be further increased where necessary.

Contra-indications, warnings, etc

Contra-indications: Penicillin hypersensitivity; ocular administration.

Side-effects: As with other penicillins. An erythematous rash may occasionally occur, as with ampicillin. The incidence of this rash is particularly high in patients with infectious mononucleosis. If a rash is reported it is advisable to discontinue treatment.

Pharmaceutical precautions Ampiclox should be stored in a cool, dry place. Solutions for injection should be used immediately.

Ampiclox may be added to most intravenous fluids but should not be mixed with blood products or other proteinaceous fluids (e.g. protein hydrolysates). In intravenous solutions containing dextrose or other carbohydrates, Ampiclox should be infused within two hours.

Legal category POM.

Package quantities *Ampiclox Injection*: Boxes of 10.

Further information Nil.

Product licence number 0038/5003.

† Ampiclox Neonatal (regd) is recommended for the treatment of infections in neonates and premature babies.

**AMPICLOX* NEONATAL INJECTION
AMPICLOX* NEONATAL SUSPENSION**

Presentation *Ampiclox Neonatal Injection*: Vials containing 50 mg ampicillin as Ampicillin Sodium BP with 25 mg cloxacillin as Cloxacillin Sodium BP.

Ampiclox Neonatal Suspension: Bottles containing powder for the preparation of 10 ml suspension. When reconstituted each 0.6 ml dose contains 60 mg ampicillin as Ampicillin Trihydrate BP with 30 mg cloxacillin as Cloxacillin Sodium BP. A pipette to measure the 0.6 ml dose is provided.

Uses Ampiclox Neonatal is indicated for the prophylaxis or treatment of infections in premature babies or neonates, particularly:

Suspected or confirmed infections.

Babies born of mothers with infected liquor or whose membranes ruptured more than 48 hours before delivery.

Babies requiring certain surgical procedures carrying risk of infection such as exchange transfusions.

Babies born with respiratory distress necessitating endotracheal procedures, when subsequent infection is a possible hazard.

Babies following difficult delivery, when inhalation of much liquor, mucus or meconium has occurred.

Dosage and administration *Dosage: Oral*: 0.6 ml suspension (90 mg) every four hours.

Intramuscular/Intravenous: 1 vial (75 mg) three times a day.

Administration: Ampiclox Neonatal Injection:

Intramuscular: Dissolve vial contents in 0.5 ml Water for Injections BP.

Intravenous: Dissolve vial contents in 2 ml Water for Injections BP and administer slowly (three to four minutes). Ampiclox Neonatal may also be added to infusion fluids or injected, suitably diluted, into the drip tube over a period of three to four minutes.

Contra-indications, warnings, etc

Contra-indications: Penicillin-hypersensitivity; ocular administration.

Caution should be observed when administering Ampiclox Neonatal to babies whose mothers are hypersensitive to penicillin.

Side-effects: As with other penicillins. An erythematous rash may occasionally occur, as with ampicillin. The incidence of this rash is particularly high in patients with infectious mononucleosis. If a rash is reported it is advisable to discontinue treatment.

Pharmaceutical precautions Ampiclox Neonatal should be stored in a cool, dry place.

Solutions for injection should be used immediately. Ampiclox Neonatal may be added to most intravenous fluids but should not be mixed with blood products or other proteinaceous fluids (e.g. protein hydrolysates). In intravenous solutions containing dextrose or other

carbohydrates, Ampiclox Neonatal should be infused within two hours.

Ampiclox Neonatal Suspension, once dispensed, should be kept in a refrigerator and used within five days.

Legal category POM.

Package quantities *Ampiclox Neonatal Injection:* boxes of 10.

mpiclox Neonatal Suspension: 10 ml bottles.

Further information Ampiclox Neonatal Suspension sugar-free to minimise the risks of diarrhoea in the newborn.

If tube feeding is necessary the suspension can easily be passed down a Ryle's tube.

Product licence numbers

mpiclox Neonatal Injection 0038/5001

mpiclox Neonatal Suspension 0038/5009

ANXON* CAPSULES ▼

Presentation Anxon Capsules: Dark pink/light pink capsules, in two sizes containing 15 mg or 30 mg citalopram overprinted with product name Anxon and its strength.

Uses *Action:* Anxon is a benzodiazepine and shares the general characteristics of this group of products.

Indications: Anxon is indicated for the treatment of anxiety, tension, irritability and similar stress related symptoms. Anxon also possesses muscle-relaxant properties and may be used in the management of spasticity associated with conditions such as spinal cord trauma, cerebrovascular accident and multiple sclerosis.

Dosage and administration *Usual Adult Dosage:* for most patients it is recommended that treatment should commence with a single dose of 30 mg, taken before retiring.

The effective dosage is usually in the range 15–60 mg per day, taken either as a single dose before retiring or in divided doses. When treating elderly or debilitated patients (e.g. those with cerebral disorders or cardio-respiratory insufficiency), a reduced dosage should be used initially until tolerance and efficacy have been assessed.

Patients undergoing therapy with centrally active products should be periodically reviewed.

Children: Insufficient data are available to recommend the administration of Anxon to children.

Contra-indications, warnings, etc

Precautions: The usual precautions when prescribing products of the benzodiazepine group should be observed.

Anxon may potentiate other centrally acting drugs such as alcohol, tranquillisers, anti-depressants, hypnotics, analgesics and anaesthetics.

Patients should be warned to exercise care when driving or operating heavy machinery, since drowsiness and modification of their reactions may occur depending on dosage and individual sensitivity.

Use cannot be recommended during pregnancy, labour or lactation.

Side-effects: Anxon is well tolerated; in comparative studies the overall incidence of side-effects was no greater than that observed with placebo.

As with other benzodiazepines daytime drowsiness has been reported.

Overdosage: Symptoms of overdosage may include drowsiness and ataxia, with coma in severe cases. The toxicity of the benzodiazepine group of drugs is very low, however, and symptomatic treatment only is required. Gastric lavage may be useful if performed soon after ingestion.

Pharmaceutical precautions Anxon capsules should be stored in well closed containers in a cool place.

Legal category POM.

Package quantities

Anxon Capsules: 15 mg – packs of 100.

30 mg – packs of 100.

Further information Anxon is particularly appropriate for those patients for whom a simple once daily dosage and a low incidence of side-effects are important considerations.

Product licence numbers

Anxon Capsules 15 mg 0038/0252

Anxon Capsules 30 mg 0038/0253

AUGMENTIN* TABLETS ▼

AUGMENTIN* DISPERSIBLE TABLETS ▼

Presentation *Augmentin Tablets:* White oval film coated tablets engraved 'AUGMENTIN' on one side. Each tablet contains potassium clavulanate equivalent to 125 mg clavulanic acid with amoxycillin trihydrate equivalent to 250 mg amoxycillin.

Augmentin Dispersible Tablets: White round tablets engraved 'AUGMENTIN'. Each tablet contains potassium clavulanate equivalent to 125 mg clavulanic acid with amoxycillin trihydrate equivalent to 250 mg amoxycillin.

Uses Augmentin is an antibiotic agent with a notably broad spectrum of activity against the commonly occurring bacterial pathogens in general practice and hospital. The novel action of clavulanate extends the spectrum of amoxycillin to embrace a wider range of organisms, including many resistant to other β -lactam antibiotics.

Augmentin is indicated for the short term oral treatment of common bacterial infections such as:

Upper Respiratory Tract Infections (including ENT) e.g. tonsillitis, sinusitis, otitis media.

Lower Respiratory Tract Infections e.g. acute and chronic bronchitis, lobar and bronchopneumonia.

Genito-urinary Tract Infections e.g. cystitis, urethritis, pyelonephritis, septic abortion, puerperal sepsis.

Other Infections e.g. skin and soft tissue infections, intra-abdominal sepsis, osteomyelitis.

Augmentin is bactericidal to a wide range of organisms including:

Gram-positive

Aerobes:

Streptococcus faecalis

Streptococcus pneumoniae

Streptococcus pyogenes

Streptococcus viridans

Staphylococcus aureus

Corynebacterium species

Bacillus anthracis

Listeria monocytogenes

Anaerobes:

Clostridium species
 Peptococcus species
 Peptostreptococcus

Gram-negative**Aerobes:**

Haemophilus influenzae
 Escherichia coli
 Proteus mirabilis
 Proteus vulgaris
 Klebsiella species
 Salmonella species
 Shigella species
 Bordetella pertussis
 Brucella species
 Neisseria gonorrhoeae
 Neisseria meningitidis
 Vibrio cholerae
 Pasteurella septica

Anaerobes:

Bacteroides spp.

Dosage and administration *Dosage: Adults and Children over 12 years:* One Augmentin or Augmentin Dispersible tablet (375 mg) three times a day. In severe infections this may be increased to two tablets three times a day. Treatment with Augmentin should not be extended beyond 14 days without review.

At present there is insufficient clinical evidence to permit a firm dosage recommendation to be made for younger children.

Administration: The absorption of Augmentin is unaffected by food.

Dispersible tablets should be stirred into a little water before taking.

Contra-indications, warnings, etc

Contra-indication: Penicillin hypersensitivity.

Precautions: A number of studies at high dosages have shown Augmentin to be free from teratogenicity in animals; however, its safety in human pregnancy has not yet been established.

Renal impairment delays the excretion of clavulanate and amoxycillin but unless impairment is severe enough to require dialysis, no reduction of dosage is necessary. Each 375 mg tablet contains 0.63 m.mol of potassium.

Side-effects: Side-effects, as with amoxycillin, are uncommon and mainly of a mild and transitory nature.

Diarrhoea, indigestion, nausea, vomiting and candidiasis have been reported. Nausea, although uncommon, is more often associated with higher dosages. If gastrointestinal side-effects occur they may be reduced by taking Augmentin at the start of meals.

Urticarial and erythematous rashes sometimes occur but their incidence has been particularly low in clinical trials. Erythematous rashes have been associated with glandular fever in a few patients receiving amoxycillin. Treatment should be discontinued if either type of rash appears.

Pharmaceutical precautions Augmentin preparations should be stored in a dry place.

Bottles of Augmentin tablets should be kept tightly closed and the tablets should be dispensed in moisture-proof containers.

Legal category POM

Package quantities *Augmentin tablets:* Bottles of 30 and 100.

Augmentin Dispersible tablets: Foil wrapped in cartons of 30 and 90.

Further information Augmentin is a novel concept in antibiotic therapy.

Resistance to many antibiotics is caused by bacteria enzymes which destroy the antibiotic before it can act on the pathogen. The clavulanate in Augmentin anticipates this defence mechanism by blocking the β -lactamase enzymes, thus rendering the organisms sensitive to amoxycillin's rapid bactericidal effect at concentration readily attainable in the body. Clavulanate by itself has little antibacterial activity; however, in association with amoxycillin as Augmentin it produces a novel antibiotic agent of broad spectrum with wide application in hospital and general practice.

The pharmacokinetics of the two components of Augmentin are closely matched. Peak serum levels of both occur about 1 hour after oral administration. Both clavulanate and amoxycillin have low levels of serum binding; about 70% remains free in the serum.

Doubling the dosage of Augmentin approximately doubles the serum levels achieved.

Product licence numbers

Augmentin Tablets	0038/0270
Augmentin Dispersible Tablets	0038/0272

BROXIL* CAPSULES**BROXIL* TABLETS****BROXIL* SYRUP**

Presentation *Broxil Capsules* (Phenethicillin Capsules BP): Black and ivory capsules overprinted 'Broxil' containing 250 mg phenethicillin as Phenethicillin Potassium BP.

Broxil Tablets (Phenethicillin Tablets BP): Yellow scored tablets engraved 'Broxil', containing 250 mg phenethicillin as Phenethicillin Potassium BP.

Broxil Syrup (Phenethicillin Elixir BP): Bottles containing powder for the preparation of 100 ml syrup.

When reconstituted each 5 ml contains 125 mg phenethicillin as Phenethicillin Potassium BP.

Uses Broxil is indicated for the oral treatment of infections caused by sensitive organisms. Typical indications include:

Ear, nose and throat infections: Tonsillitis, pharyngitis, sinusitis, laryngitis, otitis media, 'Strep' throat, dental abscess.

Respiratory tract infections: Acute bronchitis and lobar pneumonia.

Skin and soft tissue infections.

Dosage and administration *Adults:* 250 mg orally four times a day.

Children 2 to 10: $\frac{1}{2}$ adult dose.

Children under 2: $\frac{1}{4}$ adult dose.

Broxil should be given half to one hour before meals. Dosage may be doubled where necessary. Broxil Syrup may be diluted with Syrup BP.

Contra-indications, warnings, etc

Contra-indication: Penicillin hypersensitivity.

Side-effects: As with other penicillins.

Pharmaceutical precautions Broxil should be stored in a cool, dry place.

Broxil Syrup when dispensed should be stored in a cool place and used within seven days.

Legal category POM.

Package quantities *Broxil Capsules and Tablets:* 100 capsules of 100.

Broxil Syrup: 100 ml bottles.

Further information Nil.

Product licence numbers

Broxil Capsules 0038/5023
Broxil Tablets 0038/5020
Broxil Syrup 0038/0094

CELBININ* INJECTION

Presentation *Celbenin Injection* (Methicillin Injection BP 1973): Vials containing 1 g Methicillin Sodium BP 973.

Uses Celbenin is indicated for the treatment of infections suspected or confirmed to be caused by penicillinase-producing staphylococci.

Typical indications include: Respiratory tract infections. Skin and soft tissue infections. Osteomyelitis and septic arthritis. Staphylococcal urinary tract infections. Endocarditis. Meningitis.† Septicaemia.

Dosage and administration *Usual adult dosage:* Intramuscular: 1 g four to six hourly.

Intravenous: 1 g four to six hourly.

All recommended dosages are a guide only. In severe infections systemic dosages may be increased.

Intra-articular: 500 mg to 1 g once daily.

Intrapleural: 500 mg to 1 g once daily.

Subconjunctival: 500 mg once daily.

By nebuliser: 500 mg four times a day.

Usual children's dosage: 2–10 years: $\frac{1}{2}$ adult dose.

Under 2 years: $\frac{1}{4}$ adult dose.

Administration: *Intramuscular:* Dissolve 1 g in 1.5 ml Water for Injections BP.

Intravenous: Dissolve 1 g in 20 ml Water for Injections BP and give by slow injection (three to four minutes).

Celbenin may also be added to infusion fluids or injected, suitably diluted, into the drip tube over a period of three to four minutes. Infusion bottles containing Celbenin should be changed every five hours.

Intra-articular: Dissolve 1 g in 5 ml Water for Injections BP or 0.5% lignocaine hydrochloride solution.

Intrapleural: Dissolve 1 g in 10 ml Water for Injections BP.

Subconjunctival: Dissolve 0.5 g in 0.5–0.75 ml of sterile water.

Nebuliser Solution: Dissolve 500 mg in 5 ml sterile water and administer by a suitable nebuliser.

Contra-indications, warnings, etc

Contra-indications: Penicillin hypersensitivity.

Side-effects: As with other penicillins.

Pharmaceutical precautions Celbenin should be kept in a cool, dry place.

Solutions should be used within 30 minutes of preparation.

Celbenin may be added to most intravenous fluids but should not be mixed with blood products or other proteinaceous fluids (e.g. protein hydrolysates).

Legal category POM.

Package quantities Celbenin vials are supplied in boxes of 10.

Further information Nil.

Product licence number 0038/5024.

FLOXAPEN* CAPSULES FLOXAPEN* SYRUP FLOXAPEN* INJECTION

Presentation *Floxapen Capsules* (Flucloxacillin Capsules BP): Black and caramel capsules overprinted 'Floxapen', containing 250 mg or 500 mg flucloxacillin as Flucloxacillin Sodium BP.

Floxapen Syrup (Flucloxacillin Elixir BP): Bottles containing powder for the preparation of 100 ml syrup. When reconstituted each 5 ml contains 125 mg flucloxacillin, as Flucloxacillin Sodium BP.

Floxapen Vials for Injection (Flucloxacillin Injection BP): Each vial contains 250 mg, 500 mg or 1 g flucloxacillin as Flucloxacillin Sodium BP.

Uses Floxapen is indicated for the treatment of infections due to Gram-positive organisms, including infections caused by penicillinase-producing staphylococci.

Typical indications include:

Skin and soft tissue infections: Boils. Abscesses. Carbuncles. Furunculosis. Cellulitis. Infected wounds. Infected burns. Protection for skin grafts. Otitis media and externa.

Infected skin conditions: e.g. ulcer, eczema and acne.

Respiratory tract infections: Pneumonia. Lung abscess. Empyema. Sinusitis. Pharyngitis. Tonsillitis. Quinsy.

Other infections caused by Floxapen-sensitive organisms: Osteomyelitis. Enteritis. Endocarditis. Urinary tract infection. Meningitis.† Septicaemia.

Dosage and administration *Usual adult dosage – Oral:* 250 mg four times a day.

Intramuscular: 250 mg four times a day.

Intravenous: 250–500 mg four times a day.

Systemic dosages may be doubled where necessary; oral doses should be administered a half to one hour before meals.

Intrapleural: 250 mg once daily.

By nebuliser: 125–250 mg four times a day.

Intra-articular: 250–500 mg once daily.

Usual children's dosage: 2–10 years: $\frac{1}{2}$ adult dose.

Under 2 years: $\frac{1}{4}$ adult dose.

Administration – Intramuscular: Dissolve 250 mg vial contents in 1.5 ml Water for Injections BP or 500 mg vial contents in 2 ml Water for Injections BP.

Intravenous: Dissolve 250–500 mg in 5–10 ml or 1 g in 15–20 ml Water for Injections BP. Administer by slow intravenous injection (three to four minutes). Floxapen may also be added to infusion fluids or injected, suitably diluted, into the drip tube over a period of three to four minutes.

† *Intrathecal:* An intrathecal preparation and further information may be obtained from the Company's Medical Department.

Intrathecal: Consult the Company's Medical Department.

Intrapleural: Dissolve 250 mg in 5–10 ml Water for Injections BP.

Intra-articular: Dissolve 250–500 mg in up to 5 ml Water for Injections BP or 0.5% lignocaine hydrochloride solution.

Nebuliser Solution: Dissolve 125–250 mg of the vial contents in 3 ml sterile water.

Contra-indications, warnings, etc

Contra-indications: Penicillin hypersensitivity; ocular administration.

Side-effects: As with other penicillins.

Pharmaceutical precautions Floxapen should be stored in a cool, dry place.

Floxapen Syrup when dispensed should be stored in a cool place and used within seven days; it may be diluted with Syrup BP.

Solutions for IM and direct IV injection should normally be administered within 30 minutes of preparation. However, aqueous solutions of Floxapen retain their activity for up to 24 hours at room temperature (25°C) and for up to 72 hours in the refrigerator (5°C). If storage for this increased period is necessary, reconstitution should be carried out under appropriate aseptic conditions.

Floxapen may be added to most intravenous fluids but should not be mixed with blood products or other proteinaceous fluids (e.g. protein hydrolysates).

Legal category POM.

Package quantities *Capsules 250 mg:* Canisters of 20 and 100; bottles of 500.

Capsules 500 mg: bottles of 100.

Syrup 125 mg: 100 ml bottles.

Vials 250 mg, 500 mg: Boxes of 10.

Vials 1 g: Boxes of 5

Further information Floxapen has the same spectrum of activity as the earlier antistaphylococcal penicillins methicillin and cloxacillin against Gram-positive organisms, including penicillinase-producing strains. However, following oral administration Floxapen gives blood levels comparable with those achieved by intramuscular injection.

Product licence numbers

Floxapen Capsules 250 mg	0038/5055
Floxapen Capsules 500 mg	0038/5056
Floxapen Syrup	0038/5058
Floxapen Vials 500 mg	0038/5052
Floxapen Vials 1 g	0038/5053

MAGNAPEN* CAPSULES

MAGNAPEN* SYRUP

MAGNAPEN* INJECTION

Presentation *Magnapen Capsules:* Black and turquoise capsules overprinted 'Magnapen', containing 250 mg ampicillin as Ampicillin Trihydrate BP with 250 mg flucloxacillin as Flucloxacillin Sodium BP.

Magnapen Vials for Injection: 500 mg Vial: containing 250 mg ampicillin as Ampicillin Sodium BP with 250 mg flucloxacillin as Flucloxacillin Sodium BP.

1 g Vial: containing 500 mg ampicillin as Ampicillin Sodium BP with 500 mg flucloxacillin as Flucloxacillin Sodium BP.

Magnapen Syrup: Bottles containing powder for the preparation of 100 ml suspension. When reconstituted

each 5 ml contains 125 mg ampicillin as Ampicillin Trihydrate BP with 125 mg flucloxacillin as Flucloxacillin Sodium BP.

Uses Magnapen is indicated for the treatment of severe infections where the causative organism is unknown, and for mixed infections involving 'resistant' staphylococci. Typical indications include:

In general practice: Chest infections, ENT infections, skin and soft tissue infections, and patients with an underlying pathology which makes them more susceptible to infection.

In hospital (prior to laboratory results being available): Severe respiratory infections. Post-operative chest and wound infections. Septic abortion; puerperal fever. Septicaemia. Prophylaxis in major surgery. Infections in patients receiving immuno-suppressive therapy.

Magnapen's spectrum also makes it suitable for the treatment of many mixed infections, particularly those where penicillinase-producing staphylococci are suspected or confirmed.

Dosage and administration *Oral: Adult:* 1 capsule or 10 ml syrup four times a day.

Children: Under 10 years: 5 ml syrup four times a day.†

Intramuscular/Intravenous: Adult: 500 mg four times a day.

2–10 years: $\frac{1}{2}$ adult dose. *Under 2 years:* $\frac{1}{4}$ adult dose.†

Dosage for adults and children may be doubled where necessary. Oral doses should be given a half to one hour before meals.

Administration: *Intramuscular:* 500 mg Vial: contents should be dissolved in 1.5 ml Water for Injections BP. 1 g Vial: contents should be dissolved in 2.0 ml Water for Injections BP.

Intravenous: Dissolve 500 mg Vial in 10 ml Water for Injections BP. Dissolve 1 g Vial in 20 ml Water for Injections BP. Administer by slow intravenous injector (3–4 minutes). Magnapen injection may be added to infusion fluids or injected, suitably diluted into the drip tube over a period of 3–4 minutes.

Contra-indications, warnings, etc

Contra-indications: Penicillin hypersensitivity; ocular administration.

Side-effects: As with other penicillins. An erythematous rash may occasionally occur, as with ampicillin. The incidence of this rash is particularly high in patients with infectious mononucleosis. If a rash is reported it is advisable to discontinue treatment.

Pharmaceutical precautions Magnapen should be stored in a cool, dry place.

Magnapen Syrup, when dispensed, should be stored in a cool place and used within seven days. It may be diluted with Syrup BP.

Magnapen solutions for injection should be used immediately.

Magnapen may be added to most intravenous fluid; but should not be mixed with blood products or other proteinaceous fluids (e.g. protein hydrolysates). In intravenous solutions containing dextrose or other carbohydrates, Magnapen should be infused within two hours.

† Ampiclox* Neonatal is recommended for the treatment of infections in neonates and premature babies.

Legal category POM.

Package quantities *Magnapen Capsules*: Canisters of 20 and 100.

Magnapen Syrup: 100 ml bottles.

Magnapen Injections: Boxes of 10 vials.

Further information Infections encountered in medical practice can be of mixed bacteriology, often including penicillinase-producing strains. Magnapen provides the broad spectrum of activity which should be considered when dealing with such infections.

Product licence numbers

Magnapen Capsules 0038/0090

Magnapen Syrup 0038/0120

Magnapen Vials 500 mg 0038/0089

Magnapen Vials 1 g 0038/0089

MAXOLON* TABLETS**MAXOLON* SYRUP****MAXOLON* PAEDIATRIC LIQUID****MAXOLON* INJECTION**

Presentation *Maxolon Tablets*: (Metoclopramide tablets BP): Small, white, scored tablets, engraved Maxolon. Each tablet contains Metoclopramide Hydrochloride BP equivalent to 10 mg of the anhydrous substance.

Maxolon Syrup: Clear yellow lemon/lime solution. Each 5 ml dose contains Metoclopramide Hydrochloride BP equivalent to 5 mg of the anhydrous substance.

Maxolon Paediatric Liquid: Clear, yellow, lemon/lime flavoured solution, in a bottle with a 1 ml pipette. Each 5 ml contains Metoclopramide Hydrochloride BP equivalent to 1 mg of the anhydrous substance.

Maxolon Ampoules (Metoclopramide Injection BP): Clear, colourless solution. Each 2 ml ampoule contains Metoclopramide Hydrochloride BP equivalent to 10 mg of the anhydrous substance.

Uses *Digestive disorders*: Maxolon restores normal co-ordination and tone to the upper digestive tract and relieves symptoms of gastro-duodenal dysfunction including:

Dyspepsia. Flatulence. Heartburn. Regurgitation of bile. Sickness. Pain. – associated with such conditions as:

peptic ulcer. Reflux oesophagitis. Gastritis. Duodenitis. Hiatal hernia. Cholelithiasis and post-cholecystectomy dyspepsia.

Nausea and vomiting: Maxolon is indicated for the treatment of nausea and vomiting associated with:

Gastro-intestinal disorders. Cyclical vomiting. Intolerance to essential drugs including digitalis, antibacterial and cytotoxic drugs. Congestive heart failure. Deep X-ray or cobalt therapy. Post-anaesthetic vomiting.

Migraine: Maxolon relieves symptoms of nausea and vomiting, and overcomes gastric stasis associated with attacks of migraine. This improvement in gastric emptying assists the absorption of concurrently administered oral anti-migraine therapy (e.g. paracetamol) which may otherwise be impaired in such patients.

Post-operative conditions: Post-operative gastric hypomotility. Post-vagotomy syndrome. Maxolon promotes normal gastric emptying and restores motility in vagotomised patients, and where post-operative symptoms suggest gastro-duodenal dysfunction.

Diagnostic procedures: Radiology. Duodenal intubation.

Maxolon speeds up the passage of a barium meal by decreasing gastric emptying time, co-ordinating peristalsis and dilating the duodenal bulb. Maxolon also facilitates duodenal intubation procedures.

Dosage and administration Total daily dosage of Maxolon, especially for children and young adults, should not normally exceed 0.5 mg/kg bodyweight.

Medical indications:**Oral:****Adults:**

Young adults 15–20 years

10 mg three times daily
5–10 mg three times daily, commencing at the lower dosage.

Children

Maxolon should only be used after careful examination to avoid masking an underlying disorder, e.g. cerebral irritation. The following dosage recommendations should be strictly adhered to if side-effects of the dystonic type are to be avoided.

Accurate dosage is facilitated by the use of the paediatric liquid. Tablets should not be used in children under the age of 15: more accurate dosing can be obtained using the liquid presentations for the younger age groups.

5–14 years: 2½–5 mg three times daily.

3–5 years 2 mg two to three times daily.

1–3 years 1 mg two to three times daily.

Under 1 year 1 mg twice daily.

Treatment of children should commence at the lower dosage.

IM or IV:

Maxolon may be administered at the dosages stated above.

Diagnostic indications:

A single dose of Maxolon may be given 5–10 minutes before the examination.

Adults (over 15 years) 10–20 mg

Children 5–14 years 2½–5 mg

3–5 years 2 mg

Under 3 years 1 mg

Contra-indications, warnings, etc There are no absolute contra-indications to the use of Maxolon.

If vomiting persists the patient should be re-assessed to exclude the possibility of an underlying disorder, e.g. cerebral irritation.

Various extrapyramidal reactions to Maxolon, usually of the dystonic type, have been reported. The incidence of these reactions in children and young adults may be increased if daily dosages higher than 0.5 mg/kg body weight are administered. Reactions include: spasm of the facial muscles, trismus, rhythmic protrusion of the tongue, a bulbar type of speech, spasm of extra-ocular muscles including oculogyric crises, unnatural positioning of the head and shoulders and opisthotonos. There

may be a generalised increase in muscle tone. The majority of reactions occur within 36 hours of starting treatment and the effects usually disappear within 24 hours of withdrawal of the drug. Should treatment of a reaction be required, an anticholinergic anti-Parkinsonian drug or a benzodiazepine may be used. Since extrapyramidal symptoms may occur with both Maxolon and phenothiazines, care should be exercised in the event of both drugs being prescribed concurrently.

Raised serum prolactin levels have been observed during metoclopramide therapy; this effect is similar to that noted with many other compounds.

Maxolon's action on the gastro-intestinal tract is antagonised by anticholinergics.

Although animal tests in several mammalian species have shown no teratogenic effects, treatment with Maxolon is not advised during the first trimester of pregnancy.

Following operations such as pyloroplasty or gut anastomosis Maxolon therapy should be withheld for three or four days as vigorous muscular contractions may not help healing.

Pharmaceutical precautions Maxolon Syrup must be protected from light and should be dispensed into amber glass containers. It may be diluted with Purified Water BP but should not be stored diluted for long periods.

Both Syrup and Paediatric Liquid should be stored in a cool place, and the Paediatric Liquid, once dispensed, should be used within 14 days.

If ampoules are removed from their carton, they should be stored away from light. If inadvertent exposure occurs, ampoules showing a yellow discoloration must be discarded.

Legal category POM.

Package quantities *Tablets:* Canisters of 100 and 500.

Syrup: Bottles of 200 ml and 1 litre.

Paediatric Liquid: 15 ml bottles with 1 ml pipette.

Ampoules: Boxes of 10.

Further information Maxolon's action is closely associated with parasympathetic nervous control of the upper gastro-intestinal tract, where it has the effect of encouraging normal peristaltic action. This provides for a fundamental approach to the treatment of those conditions where disturbed gastro-intestinal motility is a common underlying factor.

The absorption of any concurrently administered oral medication may be modified by the normalising effect of Maxolon.

The IV use of Maxolon 'High Dose' (100 mg in 20 ml) in the treatment of nausea and vomiting associated with cytotoxic drugs is the subject of a separate Data Sheet available from the Company.

Product licence numbers

Maxolon Tablets	0038/5041
Maxolon Syrup	0038/5040
Maxolon Paediatric Liquid	0038/0095
Maxolon Ampoules	0038/0098

ORBENIN* CAPSULES ORBENIN* SYRUP ORBENIN* INJECTION

Presentation *Orbenin Capsules* (Cloxacillin Capsules BP): Orange and black capsules overprinted 'Orbenin',

containing 250 mg or 500 mg cloxacillin as Cloxacillin Sodium BP.

Orbenin Syrup (Cloxacillin Elixir BP): Bottles containing powder for the preparation of 100 ml syrup.

When reconstituted each 5 ml contains 125 mg cloxacillin as Cloxacillin Sodium BP.

Orbenin Vials for Injection (Cloxacillin Injection BP): Each vial contains 250 mg, 500 mg or 1 g cloxacillin as Cloxacillin Sodium BP.

Uses Orbenin is indicated for the treatment of infections caused by Gram-positive organisms, including infections caused by penicillinase-producing staphylococci.

Typical indications include:

Skin and soft tissue infections: Boils. Abscesses. Carbuncles. Furunculosis. Cellulitis. Infected wounds. Infected burns. Protection for skin grafts. Otitis media and externa.

Infected skin conditions, e.g. ulcer, eczema and acne.

Respiratory tract infections: Pneumonia. Lung abscess. Empyema. Sinusitis. Pharyngitis. Tonsillitis. Quinsy.

Other infections caused by Orbenin-sensitive organisms: Osteomyelitis. Enteritis. Endocarditis. Urinary tract infection. Meningitis.† Septicaemia.

Dosage and administration *Usual adult dosage:*

Oral: 500 mg four times a day.

Intramuscular: 250 mg four to six hourly.

Intravenous: 500 mg four to six hourly.

Systemic dosages may be doubled where necessary: oral dosages should be administered half to one hour before meals.

Intrapleural: 500 mg once daily.

Intra-articular: 500 mg once daily.

By nebuliser: 125–250 mg four times a day.

Usual children's dosage:

2–10 years: $\frac{1}{2}$ adult dose.

Under 2 years: $\frac{1}{4}$ adult dose.

Administration: Intramuscular: Dissolve 250 mg in 1.5 ml Water for Injections BP.

Intravenous: Dissolve 500 mg in 10 ml or 1 g in 15–20 ml Water for Injections BP. Administer by slow intravenous injection (three to four minutes). Orbenin may also be added to infusion fluids or injected, suitably diluted, into the drip tube over a period of three to four minutes.

Intrapleural: Dissolve 500 mg in 5–10 ml Water for Injections BP.

Intra-articular: Dissolve 500 mg in up to 5 ml Water for Injections BP or 0.5% lignocaine hydrochloride solution.

Nebuliser Solution: Dissolve 125–250 mg of the vial contents in 3 ml sterile water and administer by a suitable nebuliser.

Contra-indications, warnings, etc

Contra-indications: Penicillin hypersensitivity; ocular administration.

Side-effects: As with other penicillins.

Pharmaceutical precautions Orbenin should be stored in a cool, dry place.

Orbenin Syrup when dispensed should be stored in a cool place and used within seven days: it may be diluted with Syrup BP.

Solutions for IM and direct IV injection should normally be administered within 30 minutes of preparation.

† *Intrathecal:* An intrathecal preparation and further information may be obtained from the Company's Medical Department.

however, aqueous solutions of Orbenin retain their activity for up to 24 hours at room temperature (25°C) and for up to 72 hours in the refrigerator (5°C). If storage or this increased period is necessary, reconstitution should be carried out under appropriate aseptic conditions.

Orbenin may be added to most intravenous fluids but should not be mixed with blood products or other proteinaceous fluids (e.g. protein hydrolysates).

Legal category POM.

Package quantities Capsules 250 mg or 500 mg: Canisters of 50 and 250.

Vials 250 mg or 500 mg: Boxes of 10.

Vials 1 g: Box of 100.

Syrup: 100 ml bottles.

Further information Nil.

Product licence numbers

Orbenin Capsules 250 mg	0038/5028
Orbenin Capsules 500 mg	0038/5029
Orbenin Vials for Injection 250 mg	0038/5025
Orbenin Vials for Injection 500 mg	0038/5026
Orbenin Vials for Injection 1 g	0038/5027
Orbenin Syrup	0038/0128

'ARAMAX' ▼

Presentation *Paramax Tablets*: White, round scored tablets, engraved 'Paramax' on one side.

Paramax Sachets: Sachets containing effervescent powder.

Each tablet or sachet contains 500 mg Paracetamol BP with Metoclopramide Hydrochloride BP equivalent to 5 mg of the anhydrous substance.

Uses *Indications*: Paramax is indicated for the symptomatic treatment of migraine.

Action: Paracetamol relieves pain. More rapid absorption; promoted by the action of metoclopramide which also relieves gastric stasis and overcomes nausea and vomiting.

Dosage and administration For oral administration only.

Paramax should be taken at the first warning of an attack. If symptoms persist, further doses may be taken at four-hourly intervals. Total dosage in any 24-hour period should not exceed the quantity stated.

Usual Recommended Dosage (Tablets or Sachets)

	Initial dose at first warning of attack	Maximum dosage in any 24-hour period
Adults	2	6
Young Adults (15–20 years)	1 or 2	5
Adolescents (12–14 years)	1	3

Children: A presentation of Paramax suitable for the treatment of children under 12 years of age is not available.

Note: Total daily dosage of metoclopramide should not exceed 0.5 mg/kg body weight.

Paramax Sachets: The contents should be emptied into about $\frac{1}{4}$ of a tumbler of water and stirred before taking.

Contra-indications, warnings, etc There are no absolute contra-indications to the use of Paramax.

If vomiting persists the patient should be re-assessed to exclude the possibility of an underlying disorder, e.g. cerebral irritation.

Various extra-pyramidal reactions to metoclopramide, usually of the dystonic type, have been reported. The incidence of these reactions may be increased if the metoclopramide dosage exceeds 0.5 mg/kg body weight/day. Reactions include: spasm of the facial muscles, trismus, rhythmic protrusion of the tongue, a bulbar type of speech, spasm of extra-ocular muscles, including oculogyric crises, unnatural positioning of the head and shoulders and opisthotonos. There may be a generalised increase in muscle tone. The majority of reactions occur within 36 hours of starting treatment and the effects usually disappear within 24 hours of withdrawal of the drug. Should treatment of a reaction be required, a benzodiazepine or an anticholinergic anti-Parkinson drug may be used.

Care should be exercised in the event of Paramax being prescribed concurrently with a phenothiazine since extra-pyramidal symptoms may occur with both products. The action of metoclopramide on the gastrointestinal tract is antagonised by anticholinergics.

Raised serum prolactin levels have been observed during metoclopramide therapy; this effect is similar to that noted with many other compounds.

There is no evidence that metoclopramide by itself has teratogenic effects; however, treatment with Paramax is not advised during the first trimester of pregnancy.

As with other paracetamol-containing products, an overdose of Paramax can be toxic to the liver. Overdosage should be treated by gastric lavage with appropriate supportive measures. Intravenous N-acetylcysteine or oral methionine if administered within 10 hours of paracetamol overdosage appears to exert a protective effect on the liver.

Pharmaceutical precautions Protect tablets from light. Store sachets in a dry place.

Legal category POM.

Package quantities *Paramax tablets*: bottles of 100. *Paramax sachets*: cartons of 30.

Further information An acute attack of migraine is frequently characterised by impaired absorption of analgesics even when abdominal symptoms are absent. The beneficial effect of Paramax on delayed gastric emptying, nausea and vomiting contrasts with the gastric stasis which may occur following administration of phenothiazine or antihistamine antiemetics.

Product licence numbers

Paramax Tablets 0038/0256

Paramax Sachets 0038/0257

PAYNOCIL*

Presentation *Appearance*: Flat, circular, white, scored tablet embossed on one side with the product name PAYNOCIL.

Active ingredients: Each tablet contains:

Aspirin (acetylsalicylic acid)	600 mg
Glycine (aminoacetic acid)	300 mg

Uses *Principal action*: Aspirin is an analgesic, and antipyretic.

The glycine content allows the tablet to disperse instantly on the tongue and be rapidly distributed into the stomach in the finest glycine-coated particles; the risk of gastric irritation is therefore minimised.

Uses: Pain and Febrile conditions in which aspirin is indicated.

Rheumatoid Arthritis and other rheumatic conditions in which high and sustained dosage with plain aspirin tablets may increase the risk of intolerance.

Dosage and administration Paynocil should be taken orally. It can be taken without water as the lemon flavoured glycine coating of the particles masks the unpleasant taste of aspirin.

Adult dosage using Paynocil Tablets: As Paynocil contains 600 mg aspirin per tablet it is twice the strength of Aspirin Tablets BP and in equivalent dosage is twice as rapidly absorbed.

Analgesic/antipyretic: 1 tablet, every four to six hours if required.

In Rheumatoid Arthritis: for the treatment of early and recurrent rheumatoid arthritis, it is recommended that 2–3 tablets should be taken three times a day for two to three weeks. When the patient responds, the dosage should be reduced to 1–2 tablets three times a day as a maintenance dose.

Do not exceed the stated dose.

Contra-indications, warnings, etc

Contra-indications: Paynocil should not be given when aspirin is contra-indicated: e.g. hypersensitivity, peptic ulceration, haemophilia.

Warnings and precautions: Aspirin may enhance the effects of anti-coagulants, inhibit the action of uricosurics and precipitate attacks of asthma in susceptible individuals. As aspirin is a prostaglandin inhibitor and may affect blood clotting, therapy should ideally be withheld at term and during labour.

Side-effects: Aspirin may induce gastro-intestinal haemorrhage (occasionally severe). Gastric irritation, however, is minimised with Paynocil as the aspirin particles are coated with glycine.

Overdosage: Irrespective of the reported time interval since ingestion, gastric aspiration and lavage should be performed. Blood must be taken for plasma salicylate estimation. Forced alkaline diuresis may be needed.

Pharmaceutical precautions Store in a cool, dry place.

Legal category P.

Package quantities 18 tablets in foil strips of 6; 240 tablets in foil strips of 6.

Further information Paynocil is rapidly absorbed and well tolerated. It is easy to take because of its palatable lemon flavour.

Product licence number 0038/5081.

PENBRITIN* CAPSULES
PENBRITIN* SYRUP
PENBRITIN* SYRUP FORTE
PENBRITIN* PAEDIATRIC SUSPENSION
PENBRITIN* PAEDIATRIC TABLETS
PENBRITIN* INJECTION

Presentation *Penbritin Capsules* (Ampicillin Capsules BP): black and red capsules overprinted 'Penbritin', containing 250 mg or 500 mg ampicillin as Ampicillin Trihydrate BP.

Penbritin Syrup (Ampicillin Mixture BP): Bottles containing powder for the preparation of 100 ml cream coloured suspension. When reconstituted each 5 ml contains 125 mg ampicillin as Ampicillin Trihydrate BP.

Penbritin Syrup Forte (Strong Ampicillin Mixture BP) Bottles containing powder for the preparation of 100 ml cream-coloured suspension. When reconstituted each 5 ml contains 250 mg ampicillin as Ampicillin Trihydrate BP.

Penbritin Paediatric Suspension: Bottles containing powder for the preparation of 25 ml pink-coloured suspension. When reconstituted each 1.25 ml contains 125 mg ampicillin as Ampicillin Trihydrate BP. A pipette to measure the 1.25 ml dose is provided.

Penbritin Paediatric Tablets (Ampicillin Tablets BPC) Flavoured, off-white, scored tablets engraved 'Penbritin' Each tablet contains 125 mg ampicillin as Ampicillin Trihydrate BP.

Penbritin Vials for Injection (Ampicillin Sodium BP for Injection): Each vial contains 250 mg or 500 mg ampicillin as Ampicillin Sodium BP.

Uses Penbritin is a broad-spectrum penicillin, indicated for the treatment of a wide range of bacterial infection caused by most commonly occurring pathogens.

Typical indications include: Ear, nose and throat infections. Bronchitis. Pneumonia. Urinary tract infections. Gonorrhoea. Gynaecological infections. Septicaemia. Peritonitis. Endocarditis. Meningitis. Enteric fever. Gastro-intestinal infections. Or any other infection caused by Penbritin-sensitive organisms.

Penbritin is also indicated for the prevention of surgical infections by extraperitoneal application to wounds.

Dosage and administration *Usual adult dosage* (Oral except where stated):

Ear, nose and throat infections: 250 mg four times a day.
Bronchitis: Routine therapy: 250 mg four times a day.

High-dosage therapy: 1 g four times a day.
Pneumonia: 500 mg four times a day.

Urinary tract infections: 500 mg three times a day.
Gonorrhoea: 2 g orally with 1 g probenecid as a single dose. Repeated doses are recommended for the treatment of females.

Gastro-intestinal infections: 500–750 mg three to four times daily.

Enteric: Acute: 1–2 g four times a day for two weeks.

Carriers: 1–2 g four times a day for four to twelve weeks.

Septicaemia, endocarditis, osteomyelitis: 500 mg four to six times a day i.m. or i.v. for one to six weeks.

Peritonitis, intra-abdominal sepsis: 500 mg four times a day i.m. or i.v.

Meningitis: Adult dosage: 2 g six-hourly i.v. for two days. 500 mg to 1 g six-hourly i.m. from third day onwards. *Children's dosage:* 150 mg/kg daily i.v. for two days in divided doses. 100 mg/kg daily in divided doses from third day onwards. (Intrathecal therapy may be given concurrently – see below.)

Usual children's dosage (under 10 years): $\frac{1}{2}$ adult routine dosage.

All recommended dosages are a guide only. In severe infections dosages may be increased, or Penbritin given by injection. Oral doses of Penbritin should be taken half an hour before meals.

Administration: *Oral:* Capsules, Syrups, Paediatric Suspension or Paediatric Tablets.

Intramuscular: Dissolve 250 mg or 500 mg in 1.5 ml Water for Injections BP.

Intravenous: 250 mg dissolved in 5 ml or 500 mg in 10 ml Water for Injections BP given by slow injection (three to four minutes). Penbritin may also be added to infusion fluids or injected, suitably diluted, into the drip tube over a period of three to four minutes.

Intraperitoneal: At least 500 mg per 10 ml Water for Injections BP daily.

Intrapleural: 500 mg daily in 5–10 ml Water for Injections BP.

Intra-articular: 500 mg daily, dissolved in up to 5 ml Water for Injections BP or 0.5% procaine hydrochloride solution.

Intrathecal: An intrathecal preparation and further information may be obtained from the Company's Medical Department.

Local use in surgery: 1 g sterile powder sprinkled into the wound extraperitoneally or into muscle layers to prevent wound infection post-operatively.

Contra-indications, warnings, etc

Contra-indications: Penicillin hypersensitivity.

Side-effects: Side-effects, as with other penicillins, are rare and usually of a mild, transitory nature. Two types of rashes have been observed: an urticarial rash which is usually indicative of true penicillin hypersensitivity and an erythematous rash which is generally specific to ampicillin. The incidence of this erythematous rash is particularly high in patients with infectious mononucleosis. If a rash is reported it is advisable to discontinue treatment.

Pharmaceutical precautions Penbritin should be stored in a cool dry place.

Penbritin Syrup and Suspension, when dispensed, should be stored in a cool place and used within seven days: the syrups may be diluted with Syrup BP.

Penbritin solutions for injection should be used immediately.

Penbritin may be added to most intravenous fluids but should not be mixed with blood products or other proteinaceous fluids (e.g. protein hydrolysates). In intravenous solutions containing dextrose or other carbohydrates, Penbritin should be infused within one hour of preparation.

Legal category POM.

Package quantities *Penbritin Capsules* 250 mg: Canisters of 20, 100 and 500.

Penbritin Capsules 500 mg: Canisters of 20 and 100.

Penbritin Vials for Injection 250 mg, 500 mg: Boxes of 10.

Penbritin Syrup and Syrup Forte: 100 ml bottles.

Penbritin Paediatric Suspension: Bottles of 25 ml.

Penbritin Paediatric Tablets: Canisters of 100.

Further information Nil.

Product licence numbers

Penbritin Capsules 250 mg	0038/5074
Penbritin Capsules 500 mg	0038/5075
Penbritin Vials for Injection 250 mg	0038/5060
Penbritin Vials for Injection 500 mg	0038/5061
Penbritin Syrup	0038/5067
Penbritin Syrup Forte	0038/5068
Penbritin Paediatric Suspension	0038/5066
Penbritin Paediatric Tablets	0038/5072

PYOPEN* INJECTION PYOPEN* INFUSION

Presentation *Pyopen 1 g Vial:* Vials containing 1 g carbenicillin as Carbenicillin Sodium BP.

Pyopen 5 g Vial: Vials containing 5 g carbenicillin as Carbenicillin Sodium BP.

Pyopen Infusion: Infusion bottles containing 5 g carbenicillin as Carbenicillin Sodium BP.

Uses Pyopen is indicated primarily for the treatment of infections caused by sensitive *Pseudomonas* and *Proteus* species.

At recommended dosages, Pyopen is also effective against a wide range of other Gram-negative and Gram-positive bacteria, including: *Escherichia coli*, *Haemophilus influenzae*, *Bacteroides fragilis* and other anaerobes, *Clostridium* spp., *Staphylococcus aureus* (penicillin sensitive), *Streptococcus* spp.

Typical indications include: General Systemic Infections, Respiratory Tract Infections, Septicaemia, Urinary Tract Infections, Post-surgical Infections, Intra-abdominal sepsis, Endocarditis, Meningitis, Infected Burns, Infected Wounds.

In life-threatening infections, consideration should be given to the synergistic effects of Pyopen and a parenteral aminoglycoside; they should be given separately, at recommended dosages.

Dosage and administration *Dosage:* See table below.

Preparation 1 gram vial: *Intramuscular:* Add 2 ml Water for Injections BP to the contents of the vial and shake vigorously.

Intravenous: Add 5 ml Water for Injections BP to the contents of the vial and shake vigorously. Dilute to 20 ml.

5 gram vial (50 ml): *Intravenous injection:* Add at least 20 ml Water for Injections BP to the contents of the 5 g vial and shake vigorously.

Intravenous infusion: Add 20 ml Water for Injections BP to the contents of the 5 g vial, shake vigorously and add to a suitable volume of infusion fluid (approximately 100–150 ml).

5 g vials are not suitable for multidose use.

Infusion pack: See detailed instructions contained in Package Enclosure Leaflet.

Administration: *Intramuscular:* Pyopen should be given every six hours.

Intravenous: Pyopen should be given every four to six hours by slow injection (three to four minutes) or by rapid infusion over 30–40 minutes (i.e. at a rate of approximately 50 drips per minute). Infusion over longer periods may result in sub-therapeutic serum concentrations.

Higher and more prolonged serum concentrations may be achieved with concurrent oral administration of probenecid (1 g three times a day in adults); however, caution should be exercised in the administration of probenecid to patients with impaired renal function.

† *Intrathecal:* An intrathecal preparation and further information may be obtained from the Company's Medical Department.

Pyopen may be administered by other routes in conjunction with systemic therapy.

Intra-articular: Add 2–4 ml Water for Injections BP or

† Intrathecal therapy: see 'Administration'

Dosage of Pyopen

<i>Infection</i>	<i>Organism</i>	
	<i>Pseudomonas</i>	<i>Proteus spp.</i>
Adult		
Respiratory tract infections Chronic urinary tract infections Infected wounds and burns	5 g i.v. four to six-hourly	2 g i.m. six-hourly
Systemic infections Septicaemia, endocarditis, meningitis†		
Acute uncomplicated urinary tract infections		
Paediatric (daily dosage per kg body weight: to be administered in divided doses 4–8 hourly)		
Respiratory tract infections Chronic urinary tract infections Infected wounds and burns	250–400 mg i.v.	100 mg i.m.
Systemic infections Septicaemia, endocarditis, meningitis†		
Acute uncomplicated urinary tract infections		

† Intrathecal therapy: see 'Administration'.

0.5% lignocaine solution to the contents of a 1 g vial. 500 mg to 1 g is a suitable dosage.

Intrapleural: Add 5 ml Water for Injections BP to the contents of a 1 g vial. Dilute to 10 ml. This dosage is normally given once daily.

Nebuliser Solution: Dissolve 250–500 mg Pyopen powder in 3–5 ml of water and administer four times daily by a suitable nebuliser.

Subconjunctival: A 25% solution (125 mg in Lignocaine and Adrenaline Injection BP) is recommended.

Local irrigation: A 0.2% solution of Pyopen should be used.

Contra-indications, warnings, etc

Contra-indication: Penicillin hypersensitivity.

Side-effects: Side-effects are uncommon and typical of other injectable penicillins. If pain at the intramuscular injection site is troublesome, the vial contents may be dissolved in 0.5% lignocaine hydrochloride solution. In rare cases, spontaneous skin and mucous membrane haemorrhages due to interference with normal clotting mechanisms have been reported.

Precautions: Except in cases of renal impairment, recommended dosages should never be reduced. Administration at less than full dosage may permit the multiplication of resistant strains, especially of *Pseudomonas*. Where renal function is impaired, Pyopen dosage may be reduced. However, monitoring is advisable in these cases to ensure that adequate serum antibiotic concentrations are achieved. In treating patients on sodium restriction it should be noted that each 1 g vial of Pyopen contains 5.4 mmol sodium (approx. 124 mg), and each 5 g vial contains 27.1 mmol sodium.

When Pyopen is used with an aminoglycoside the usual dosage should be adopted; concurrent therapy is not an opportunity to secure dosage reduction unless indicated for other reasons – for instance renal failure.

If Pyopen is prescribed with a parenteral aminoglycoside, the compounds should be administered separately.

Pharmaceutical precautions *Stability and storage:* Pyopen is unstable to heat and is very hygroscopic. The

vials of dry powder should be stored in a refrigerator at 5°C.

Solutions for IM and direct IV injection should normally be administered within 30 minutes of preparation. However, aqueous solutions of Pyopen retain their activity for up to 24 hours at room temperature (25°C) and for up to 72 hours in the refrigerator (5°C). If storage for this increased period is necessary, reconstitution should be carried out under appropriate aseptic conditions. Details of the stability of Pyopen in various fluids are given in the Package Enclosure Leaflet.

Compatibility: Pyopen is compatible with intravenous solutions in general use except: proteinaceous fluids (e.g. protein hydrolysates), blood and plasma.

Legal category POM.

Package quantities

Pyopen 1 g Vials: Cartons of 10.

Pyopen 5 g Vials: Cartons of 6 (50 ml vials).

Pyopen Infusion: 5 g infusion bottle, with diluent and transfer needle, in packs of 6.

Further information Pyopen continues to be effective in patients with lowered host defences.

Product licence numbers

Pyopen 1 g Vials 0038/5035

Pyopen 5 g Vials 0038/5037

Pyopen Infusion 0038/5037

Water for Injections BP 0038/0118

TALPEN*

Presentation *Talpen Tablets:* Red film coated tablets, engraved Talpen on one side. Each tablet contains 250 mg of the ampicillin ester, talampicillin hydrochloride.

Talpen Syrup: Bottles containing powder for the preparation of 100 ml suspension. When reconstituted each 5 ml contains talampicillin napsylate (167 mg) equivalent to 125 mg talampicillin hydrochloride.

Talpen Syrup Forte: Bottles containing powder for the preparation of 100 ml suspension. When reconstituted each 5 ml contains talampicillin napsylate (334 mg) equivalent to 250 mg talampicillin hydrochloride.

Uses Following oral administration, Talpen is particularly well absorbed and rapidly hydrolysed to give high blood levels of ampicillin. Talpen is indicated for the oral treatment of a wide range of bacterial infections caused by commonly occurring pathogens, for example:

Gram-positive: Penicillin sensitive *Staph. aureus*, *Strep. pyogenes*, *Strep. faecalis*, *Strep. viridans*, *Strep. pneumoniae*, *Clostridium species*, *Bacillus anthracis*, *Corynebacterium diphtheriae*.

Gram-negative: *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Escherichia coli*, *Haemophilus influenzae*, *Bordetella pertussis*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonellae* (other), *Shigella species*, *Brucella species*, *Proteus mirabilis*.

Typical indications include: Acute and chronic bronchitis; Pneumonia; Ear, nose and throat infections; Gynaecological infections; Urinary tract infections; Skin and soft tissue infections; Gonorrhoea.

Dosage and administration *Usual adult oral dosage:* †One Talpen tablet or 5 ml Talpen Syrup Forte, three times a day.

Gonorrhoea: 1.5–2 g talampicillin hydrochloride as a single dose, is recommended.

Usual children's oral dosage: (2–10 years) †5 ml Talpen Syrup, three times a day. (Under two years) the equivalent of 3–7 mg talampicillin hydrochloride per kilogram body weight, three times a day. (Talpen Syrup may be diluted with Syrup BP.)

Total ampicillin availability following oral administration of Talpen is unaffected by food.

Contra-indications, warnings, etc

Contra-indication: Penicillin hypersensitivity.

Precaution: Talpen is not recommended for patients with severe renal or hepatic impairment.

Side-effects: As with other penicillins. These are rare and usually of a mild and transitory nature. An erythematous rash may occasionally occur. The incidence of this rash is particularly high in patients with infectious mononucleosis. Controlled clinical trials have shown that the incidence of diarrhoea as a side-effect is significantly lower following the administration of Talpen than following oral ampicillin.

Pharmaceutical precautions Talpen should be stored in tightly closed containers and kept in a cool dry place. Talpen Syrup and Syrup Forte should be used within seven days of dispensing, and should be kept in a cool place, preferably a refrigerator.

Legal category POM.

Package quantities *Talpen Tablets:* Bottles of 100 and 500.

Talpen Syrup: Bottles of 100 ml.

Talpen Syrup Forte: Bottles of 100 ml.

Further information Following oral administration of 250 mg Talpen, ampicillin peak serum concentrations are twice those obtained from 250 mg ampicillin capsules and are usually achieved in half the time. This excellent absorption is further reflected in urinary recovery studies.

Each 250 mg of talampicillin hydrochloride is chemically equivalent to 169 mg of ampicillin.

Product licence numbers

Talpen Tablets 0038/0209

Talpen Syrup 0038/0243

Talpen Syrup Forte 0038/0245

TICAR* ▼

Presentation *Ticar 1 g vial:* Vials containing 1 g ticarcillin as the disodium salt.

Ticar 3 g vial: Vials containing 3 g ticarcillin as the disodium salt.

Ticar 5 g vial: Vials containing 5 g ticarcillin as the disodium salt.

Ticar infusion: Infusion bottles containing 5 g ticarcillin as the disodium salt.

Uses Ticar is an injectable broad-spectrum penicillin indicated for the treatment of a wide range of bacterial infections. Sensitive organisms include:

Streptococcus species
Staphylococcus aureus (penicillin sensitive)
Clostridium species
Bacteroides species and other anaerobes
Pseudomonas species
Proteus species
E. coli
Haemophilus influenzae

Typical indications include:

General Systemic Infections
Respiratory Tract Infections
Septicaemia
Urinary Tract Infections
Peritonitis, intra-abdominal sepsis
Endocarditis
Infected burns
Infected wounds
Post-surgical infections

Ticar acts synergistically with aminoglycosides against *Pseudomonas* and other organisms. When Ticar is prescribed concurrently with an aminoglycoside the two products should be administered separately, at recommended dosages.

Dosage and administration *Dosage: Adults:* The normal recommended daily dosage is 15–20 g administered in divided doses, usually at 4–8 hourly intervals.

For the treatment of acute uncomplicated urinary tract infections the normal recommended daily dosage is 3–4 g in divided doses, usually at 4–8 hourly intervals.

Children: The normal recommended dosage for children is 200–300 mg/kg/day in divided doses, usually at 4–8 hourly intervals.

For acute uncomplicated urinary tract infections the recommended dosage is 50–100 mg/kg/day in divided doses, usually at 4–8 hourly intervals.

Abnormal Renal Function: If renal function is impaired as indicated by urea or creatinine levels monitoring of antibiotic serum levels is advised and a reduction in dosage may need to be considered. In renal failure an appropriate adult dose would be 2 g every 8–12 hours. In such cases the serum half life may be as long as 13 hours compared with 70 minutes in normal subjects. (Corresponding reductions in dosage should be considered for children.)

† Dosage may be doubled in severe infections.

Haemodialysis removes Ticar from the blood stream therefore a supplementary 2 g dose is recommended midway through the dialysis period.

Peritoneal dialysis removes Ticar at a slower rate than haemodialysis therefore a dosage of 2 g 8 hourly is recommended.

Preparation: 1 gram vial: Intramuscular – Add 2 ml Water for Injections BP and shake vigorously.

Intravenous – Add 5 ml Water for Injections BP and shake vigorously. Dilute to 20 ml.

3 gram vial: Intravenous injection: Add 20 ml Water for Injections BP and shake vigorously.

Intravenous infusion: Add 20 ml Water for Injections BP shake vigorously and add to a suitable volume of infusion fluid (approximately 100 ml).

5 gram vial: Intravenous injection: Add 20 ml Water for Injections BP and shake vigorously.

Intravenous infusion: Add 20 ml Water for Injections BP shake vigorously and add to a suitable volume of infusion fluid (approximately 100–150 ml).

Water for Injections BP is the preferred diluent for intravenous infusion of Ticar. Alternatively, the antibiotic may be infused in 5% dextrose solution. (The use of 0.9% sodium chloride solution as diluent will add to the sodium load of ticarcillin and is, therefore, not usually recommended). The use of these appropriate diluents, when Ticar is given intravenously, will reduce the possibility of phlebitis.

Infusion pack: See detailed instructions on Package Enclosure Leaflet.

Reconstituted solutions of Ticar are normally a pale straw colour.

Heat is generated when Ticar dissolves. Ticar vials may therefore become warm during preparation of solutions for injection.

Ticar vials are not suitable for multi-dose use.

Administration: When administered intravenously Ticar should be given by slow injection (three to four minutes) or by infusion over e.g. 30–40 minutes (i.e. at a rate of approximately 50 drops per minute). Infusion over long periods may result in subtherapeutic concentrations.

Higher and more prolonged serum concentrations may be achieved with concurrent oral administration of probenecid (1 g three times a day in adults); however, caution should be exercised in the administration of probenecid to patients with impaired renal function.

Other routes of administration: Insufficient clinical information is available to assess fully the value of Ticar by the following routes of administration. In life-threatening infections, however, the following dosage guidelines may be helpful. In all cases systemic Ticar therapy, at full dosage, should also be administered.

Nebuliser solution: Dissolve 500 mg Ticar powder in 3–5 ml water (or smaller volume if required). Administer this dosage three to four times daily by a suitable nebuliser.

Intra-articular: Add 2–4 ml Water for Injections BP or 0.5% lignocaine solution to the contents of a 1 g vial. 500 mg to 1 g is a suitable dosage.

Intrapleural: Add 5 ml Water for Injections BP to the contents of a 1 g vial. Dilute to 10–20 ml. This dosage is normally given once daily.

Local irrigation: A 0.2% solution of Ticar may be used.

Intrathecal: Further information may be obtained from the Company's Medical Department.

Contra-indications, warnings, etc

Contra-indication: Penicillin hypersensitivity.

Side-effects: Side-effects are uncommon and typical of other injectable penicillins. If pain at the intramuscular injection site is troublesome the vial contents may be dissolved in 0.5% lignocaine hydrochloride solution. In rare cases spontaneous skin and mucous membrane haemorrhages due to interference with normal clotting mechanisms have been reported.

Precautions: Use of Ticar at less than recommended dosages may permit multiplication of resistant strains of bacteria especially of *Pseudomonas*. For patients with abnormal renal function see 'Dosage and Administration'. In treating patients on sodium restriction it should be noted that each 1 g vial of Ticar contains 5.3 mmol of sodium (approx.) each 3 g vial contains 16.0 mmol of sodium (approx.) and each 5 g vial contains 26.7 mmol of sodium (approx.)

Pharmaceutical precautions *Stability and storage:* Vials of Ticar powder should be stored at room temperature (25°C or below).

Solutions for IM and direct IV injection should normally be administered within 30 minutes of preparation. However, aqueous solutions of Ticar retain their activity for up to 24 hours at room temperature (25°C) and for up to 72 hours in the refrigerator (5°C). If storage for this increased period is necessary, reconstitution should be carried out under appropriate aseptic conditions. Details of the stability of Ticar in various fluids are given in the Package Enclosure Leaflet.

Compatibility: Ticar is compatible with intravenous solutions in general use except:

Proteinaceous fluids (e.g. protein hydrolysates)
Blood and plasma
Intravenous lipids

If Ticar is prescribed concurrently with an aminoglycoside the antibiotics should not be mixed in the syringe or intravenous fluid container because loss of activity of the aminoglycoside can occur under these conditions.

Legal category POM.

Package quantities Ticar 1 g vials: Cartons of 10.

Ticar 3 g vials: Cartons of 6.

Ticar 5 g vials: Cartons of 4.

Ticar infusion: 5 g infusion bottle with diluent and transfer needle, in packs of 4.

Further information Ticar has proved to be particularly valuable in the treatment of patients with lowered host defences.

Synergy has been observed between Ticar and aminoglycosides, such as gentamicin, tobramycin and amikacin, against *Pseudomonas* and other organisms. When Ticar is used with an aminoglycoside the usual recommended dosages of both products should be used. Concurrent therapy is not an opportunity to secure dosage reduction unless indicated for other reasons – for example renal failure. (See manufacturers' literature for details of aminoglycoside prescribing information.)

As with other penicillins, Ticar is eliminated by glomerular filtration and tubular secretion. It is not highly bound to serum protein (approximately 45%) and is excreted unchanged in high concentrations in the urine.

Ticar can be detected in tissues and interstitial fluid following parenteral administration. Penetration into the cerebrospinal fluid, bile and pleural fluid has been demonstrated.

Product licence numbers

1 g vial	0038/0084
3 g vial	0038/0084
5 g vial	0038/0084
5 g infusion	0038/0084
Water for Injections BP	0038/0118

UTICILLIN* TABLETS

Presentation Oval, white tablets, engraved 'Uticillin'. Each Uticillin Tablet contains 500 mg carfecillin sodium.

Uses Uticillin is indicated for the treatment of acute and chronic infections of the upper and lower urinary tract when these are caused by sensitive organisms, including *Escherichia coli*, *Proteus* spp. and *Strep. faecalis*. Uticillin is of particular value in the treatment of *Pseudomonas* urinary tract infections.

Typical indications include: Cystitis. Pyelonephritis. Asymptomatic bacteriuria.

Dosage and administration *Adults*: Simple urinary tract infections – 1 tablet (500 mg) three times a day.

Complicated and recurrent urinary tract infections – 2 tablets (1 g) three times a day.

Children: 2–10 years: $\frac{1}{2}$ adult dose.

Children's dosage should be in the range 30–60 mg/kg daily in 3 divided doses.

Contra-indications, warnings, etc

Contra-indication: Penicillin hypersensitivity.

Side-effects: As with other penicillins.

Precaution: In mild and moderate degrees of renal impairment, the normal dosage recommendations should be followed. In patients with severe renal failure (creatinine clearance of 10 ml/min or less) carfecillin is not recommended; in such patients the levels of carbenicillin in the urine may be insufficient for therapeutic efficacy.

Pharmaceutical precautions Uticillin should be stored in a cool, dry place.

Legal category POM.

Package quantities Bottles of 30.

Further information *Pharmacology*: Following oral administration, Uticillin is rapidly absorbed in the body and hydrolysed to carbenicillin, producing high concentrations in the urine.

Product licence number 0038/0155.

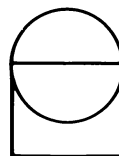
*Trade Mark

Bencard

Great West Road

Brentford

Middlesex TW8 9BD



ALAVAC-P*

Presentation Alavac-P vaccine contains alum-precipitated extracts from aqueous pyridine solutions or twelve varieties of common grass pollens: (Bent, Brome, Cocksfoot, Crested Dogtail, False Oat, Fescue, Meadow Foxtail, Meadow Grass, Rye Grass, Timothy, Vernal and Yorkshire Fog).

The vaccine consists of a set of three multidose vials in graded concentrations as follows:

Vial Number	Concentration
1. (Green Label)	250 Noon units per ml.
2. (Buff Label)	2,500 Noon units per ml.
3. (Red Label)	25,000 Noon units per ml.

The aluminium hydroxide content is not more than 3 mg/ml and the preparation is preserved with Phenol BP 0.5% w/v.

Uses Indicated for the treatment of classical hayfever and pollen asthma, to give long-term protection whenever grass pollens are considered to be the sole or predominant cause.

Alavac-P is formulated from the pollens of twelve common grasses which are responsible for the majority of classical hayfever and pollen asthma cases and provides a convenient and effective preventive treatment.

Dosage and administration Please note that the section on 'Contra-Indications, Warnings, Etc.' must be studied before Alavac-P is administered.

Adrenaline Injection BP (Adrenaline 1 in 1,000) should always be kept at hand when giving any desensitising vaccine.

The administration procedures shown in the leaflet included with each course of Alavac-P should be carefully followed.

Alavac-P may be given to adults and children aged 5 years and over in accordance with the provisions given below.

Injections should be given at intervals of 7-14 days.

The vial should be shaken thoroughly immediately before withdrawing a dose.

Sterile syringes should always be used for the withdrawal of doses. Since each vial is used more than once, aseptic precautions must be sufficient to avoid the risk of microbial contamination.

Injections should be given slowly by the subcutaneous route. Do not inject into a blood vessel or intramuscularly. Do not rub the site of injection.

Treatment should be given pre-seasonally. The course should normally be started by mid-March (in the UK) to ensure completion before the onset of the grass pollen season. For continued clinical improvement it is recommended that a course should be given in each of three successive years.

Dosage schemes:

Adults

The dosage scheme should be selected according to the patient's previous history of asthma and severity of allergic symptoms as outlined below. When in doubt, treatment should be commenced at the lowest dosage.

Patient Classification

Very sensitive	Moderately sensitive	Mildly sensitive
Severe symptoms of allergy (e.g. eczema) or any history of asthma	Moderate symptoms of allergy with no history of asthma	Mild symptoms of allergy with no history of asthma

Children

Children aged 5-14 years: treat according to the child's dosage scheme shown below. However, in the presence of a history of asthma or severe symptoms, consultant advice should be sought.

Children under five: consultant advice should be sought.

Recommended dosage schemes

Not to be used during the grass pollen season.

Commence with the No. 1 (Green label) vial then proceed to the No. 2 (Buff label) vial and the No. 3 (Red label) vial as indicated in the scheme below.

If a reaction occurs during treatment, dosage should be reduced: see 'Adjustment of Dosage'.

Adults:

Vial number	Very sensitive adult patients	Moderately sensitive adult patients	Mildly sensitive adult patients
	dosage (ml)	dosage (ml)	dosage (ml)
1. Green label	0.1 0.2 0.4 0.8	0.2 0.5	0.5
2. Buff label	0.15 0.3 0.6	0.1 0.2 0.4 0.8	0.1 0.3 0.7
3. Red label	0.1 0.2	0.15 0.25 0.4	0.15 0.3 0.5 1.0

Children:

Vial Number	Dosage for children aged 5–14 years (ml)	Children under five
1. Green label	0.1 0.2 0.4 0.8	Children under five: consultant advice should be sought
2. Buff label	0.15 0.3 0.6	
3. Red label	0.1 0.2	

Extended treatment: when time is available before the onset of the pollen season and there is sufficient vaccine, it may be beneficial to repeat the top treatment dose at fortnightly intervals, the final dose being given two weeks before the pollen season is expected to start.

Contra-indications, warnings, etc

Contra-indications: Patients suffering from febrile conditions or an acute attack of asthma should not be given an injection until 24 hours after the condition has subsided.

It is advisable to avoid use during pregnancy, especially in the first trimester.

Precautions: Children under five: consultant advice should be sought.

Patients should be warned not to eat a heavy meal immediately before an injection is due to be given.

In very sensitive patients, it is advantageous to give an antihistamine tablet about one hour before each injection.

Injections should be given slowly by the subcutaneous route. Do not inject into a blood vessel or intramuscularly. Do not rub the site of injection.

Adrenaline Injection BP (Adrenaline 1 in 1,000) should always be kept at hand when giving any desensitising vaccine.

All patients should be instructed to remain under observation in the surgery for at least 20 minutes after each injection and advised to contact the doctor immediately in the unlikely event of a delayed reaction.

The patient should not take any strenuous physical exercise for several hours following the injection.

Note: A patient must not be transferred from Alavac-P to an aqueous vaccine unless a complete course of the aqueous vaccine is to be given, commencing with the lowest strength (No. 1) vial.

Reactions: (see also 'Adjustment of Dosage'):

Local reactions, such as slight swelling or irritation, can sometimes occur and may require symptomatic treatment if they persist.

Mild systemic reactions such as rhinitis or urticaria may be treated with antihistamines orally, or by injection if necessary. In mild bronchospasm, a sympathomimetic bronchodilator such as salbutamol and possibly an anti-inflammatory steroid should be given. If required, 0.5 ml Adrenaline Injection BP (1 in 1,000) may be given subcutaneously.

Severe systemic reactions may occasionally arise in the form of typical allergic symptoms; anaphylaxis is rare.

Treatment of anaphylaxis:

Anaphylactic shock: characterised by bronchospasm,

laryngeal oedema, urticaria and shock. Immediate attention should be given as follows:

1. The patient should be laid down and treated immediately.

2. 0.5 ml† Adrenaline Injection BP (Adrenaline 1 in 1,000) should be given intramuscularly close to the vaccine injection site. This should be repeated to a total of 2 ml† over 15 minutes if necessary. In extreme cases, 0.5 ml† Adrenaline (1 in 10,000) can be given by slow intravenous injection.

3. If bronchospasm persists, 10–20 ml† of Aminophylline Injection BP (250 mg per 10 ml) should be given by slow intravenous injection at a rate of 2 ml† per minute.

4. In addition, 200–400 mg† of Hydrocortisone Injection BP should be given intravenously. This is to combat persistent bronchospasm which can occur 6–8 hours after the initial collapse.

5. Full supportive measures should be available and employed if necessary and patients should be closely monitored for at least 24 hours after recovery.

Adjustment of Dosage (in the event of the occurrence of a reaction):

Reaction to the first injection:

Moderately sensitive or mildly sensitive adult dosage scheme: The patient should be transferred to the very sensitive adult dosage scheme.

Very sensitive adult dosage scheme and children: return the complete course to Bencard. An appropriate course of Alavac-S containing grass pollens together with a Special Dilution Vial (No. 0 – Black label, 1/10th dilution of the No. 1 vial) will be supplied free of charge. Treatment should recommence from the Special Dilution Vial according to the dosage scheme issued with it; the normal dosage scheme should then be continued, but no attempt should be made to exceed the maximum tolerated dose.

Reaction to subsequent injections:

Local

Mild reaction: Reduce the dose by one step.

Severe reaction: Reduce the dose by two steps.

Systemic

Mild reaction: Reduce the dose by two steps.

Severe reaction: Treatment should be discontinued.

Except in cases where a severe systemic reaction has occurred, the course may be continued with caution up to the top dose quoted, or to the highest dose tolerated without significant reaction.

Pharmaceutical precautions Alavac-P must be stored in a refrigerator (2–8°C). It must not be frozen. Vaccine left over from an Alavac-P course must not be used the following year.

Legal category POM.

Package quantities Each course of treatment consists of a set of three multidose vials of vaccine in graded concentrations. Ready assembled disposable syringes with attached needles and an instruction leaflet are included with each set.

Further information Alavac-P is formulated from the pollens of twelve common grasses responsible for classical hayfever and pollen asthma and offers a fundamental alternative to symptomatic treatment. Alavac-P may be prescribed from case history and clinical symptoms alone, providing these reveal marked seasonality corresponding with the grass pollen season. Risk of

† All dosages should be reduced as required for children.

reaction is reduced because of the slow release of active material into the system.

Alavac-P may be prescribed on NHS form FP10 and is available for immediate supply from stock.

The Bencard Medical Department will be pleased to advise on any aspect of treatment.

Product licence number 0038/5085.

ALAVAC-S*

Presentation Each course of Alavac-S is a desensitising vaccine, specially prepared for an individual patient, from extracts of specific allergens, in accordance with the information obtained from the patient during case history investigations and subsequent skin tests. The vaccine comprises alum-adsorbed extracts of specific allergens precipitated from aqueous pyridine solutions. Each course is presented as three multidosed vials of allergen concentrate in graded concentrations. The No. 1 and No. 2 vials are 1/100th and 1/10th dilutions respectively of the No. 3 vial.

Special Dilution Vials (No. 0, Black label, 1/10th dilution of the No. 1 vial) are available on request to initiate treatment of highly sensitive patients.

The No. 3 vial is also available in a larger size for physicians practising maintenance therapy with courses which do not contain pollen allergens (see Dosage and Administration).

For the best clinical results with Alavac-S, no more than 4 allergens should normally be included (with a maximum of 6) in any one course.

If the patient is sensitive to more than 6 allergens, those which can be avoided without undue inconvenience, or are of little clinical significance, should be omitted and the patient given advice on avoidance; otherwise two separate vaccines will be prepared.

The aluminium hydroxide content is not more than 3 mg/ml and the preparation is preserved with Phenol BP 0.5% w/v.

The adsorbed allergen extracts available for inclusion in Alavac-S are:

Dusts: Hay dust, House dust, Straw dust, Mixed threshings (barley, maize, oats and wheat).

Epithelials: Mixed feathers, Cat fur, Rabbit fur, Cow hair, Dog hair, Horse hair, Human hair, Sheep wool.

Fabrics: Cotton flock, Kapok.

House Dust Mite: *Dermatophagoides pteronyssinus*.

Fungi: *Alternaria alternata*, *Aspergillus fumigatus*, *Aspergillus niger*, *Candida albicans*, *Cladosporium herbarum*, *Fusarium spp.*, *Merulius lacrymans*, *Neurospora sitophila*, *Penicillium notatum*, *Rhizopus nigricans*, *Sporobolomyces roseus*, *Trichophyton (T. mentagrophytes and T. rubrum)*.

Pollens: Available individually:

Elder (*Sambucus nigra*), Hazel (*Corylus spp.*), Maize (*Zea mays*), Nettle (*Urtica dioica*), Plantain (*Plantago lanceolata*), Poplar (*Populus spp.*), Rye, Cultivated (*Secale cereale*), Silver Birch (*Betula spp.*).

Available as standard groups.

Group B2-Grass pollens containing:

Bent, Brome, Cocksfoot, Crested Dogtail, False Oat, Meadow Fescue, Meadow Foxtail, Meadow Grass, Rye Grass, Timothy, Vernal, Yorkshire Fog.

Group B3-Tree pollens containing:

Alder, Ash, Beech, Birch, Elm, Hazel, Oak, Plane, Poplar, Willow.

Group B5-Weed and Shrub pollens containing:

Heather, Nettle, Plantain, Fat Hen, Mugwort, Orache.

The allergens used in the preparation of Alavac-S correspond with those available as Bencard Skin Testing Solutions. Alavac vaccines themselves are unsuitable for skin testing.

Uses To provide fundamental treatment for a wide variety of common allergic conditions such as asthma, perennial rhinitis, hay fever and some skin conditions.

Dosage and administration Please note that the section on 'Contra-Indications, Warnings, Etc.' must be studied before Alavac-S is administered.

Adrenaline Injection BP (Adrenaline 1 in 1,000) should always be kept at hand when giving any desensitising vaccine.

The administration procedures shown in the leaflet included with each course of Alavac-S should be carefully followed.

Alavac-S may be given to adults and children aged 5 years and over in accordance with the guidelines given below.

Children under five: consultant advice should be sought.

Injections should be given at intervals of 7–14 days unless otherwise stated.

The vial should be shaken thoroughly immediately before withdrawing a dose.

Sterile syringes should always be used for the withdrawal of doses. Since each vial is used more than once, aseptic precautions must be sufficient to avoid the risk of microbial contamination.

Injections should be given slowly by the subcutaneous route. Do not inject into a blood vessel or intramuscularly. Do not rub the site of injection.

Adults

The dosage scheme should be selected according to the patient's previous history of asthma and severity of allergic symptoms as outlined below. When in doubt, treatment should be commenced at the lowest dosage.

Patient Classification

Very sensitive	Moderately sensitive	Mildly sensitive
Severe symptoms of allergy (e.g. eczema) or any history of asthma	Moderate symptoms of allergy with no history of asthma	Mild symptoms of allergy with no history of asthma

Children

Children aged 5–14 years: treat according to the children's dosage scheme shown below. However, in the presence of a history of asthma or severe symptoms, consultant advice should be sought.

Children under five: consultant advice should be sought.

Alavac-S: Dosage recommendations for vaccines which contain pollen allergens:

Treatment should be given pre-seasonally. The course should be timed to end before the usual date of onset of the patient's seasonal symptoms (e.g. in the UK, by mid-May for grass pollen sensitivity and by the end of March for tree pollen sensitivity). For continued clinical improvement it is recommended that a course should be given in each of three successive years.

Recommended dosage schemes for vaccines which contain pollen allergens

Not to be used during the pollen season.

Commence with the No. 1 (Green label) vial then proceed to the No. 2 (Buff label) vial and the No. 3 (Red label) vial as indicated in the schemes below.

If a reaction occurs during treatment, dosage should be reduced: see 'Adjustment of Dosage'.

Adults:

Vial Number	Very sensitive adult patients	Moderately sensitive adult patients	Mildly sensitive adult patients
	dosage (ml)	dosage (ml)	dosage (ml)
1. Green label	0.1 0.2 0.4 0.8	0.2 0.5	0.5
2. Buff label	0.15 0.3 0.6	0.1 0.2 0.4 0.8	0.1 0.3 0.7
3. Red label	0.1 0.2	0.15 0.25 0.4	0.15 0.3 0.5 1.0

Children:

Vial Number	Dosage for children aged 5–14 years (ml)	Children under five
1. Green label	0.1 0.2 0.4 0.8	Children under five: consultant advice should be sought.
2. Buff label	0.15 0.3 0.6	
3. Red label	0.1 0.2	

Surplus vaccine must not be used the following season.

Extended treatment: when time is available before the onset of the pollen season and there is sufficient vaccine, it may be beneficial to repeat the top treatment dose at fortnightly intervals, the final dose being given two weeks before the pollen season is expected to start.

Alavac-S: Recommended dosage schemes for vaccines which do not contain pollen allergens (Initial course)
Courses may be given at any time of year.

Commence with the No. 1 (Green label) vial then proceed to the No. 2 (Buff label) vial and the No. 3 (Red label) vial as indicated in the schemes below.

If a reaction occurs during treatment, dosage should be reduced: see 'Adjustment of Dosage'.

Adults

Vial Number	Very sensitive adult patients	Moderately sensitive adult patients	Mildly sensitive adult patients
	dosage (ml)	dosage (ml)	dosage (ml)
1. Green label	0.25 0.5 1.0	0.5 1.0	
2. Buff label	0.2 0.4 0.8	0.2 0.4 0.8	0.1 0.2 0.4 0.8
3. Red label	0.15 0.25	0.15 0.3 0.6	0.15 0.3 0.6

Maintenance treatment following the initial course is recommended.

Children

Vial Number	Dosage for children aged 5–14 years (ml)	Children under five
1. Green label	0.25 0.5 1.0	Children under five: consultant advice should be sought.
2. Buff label	0.2 0.4 0.8	
3. Red label	0.15 0.25	

Maintenance treatment following the initial course is recommended.

Maintenance therapy: (for use only with vaccines which do not contain pollens)

Maintenance therapy, which consists of a series of boosting injections, is recommended particularly for patients with perennial symptoms provided that the initial treatment course has been well tolerated.

Maintenance therapy should commence between 1 and 2 weeks after completion of the initial course, and should follow the dosage scheme below. Treatment may be continued at the discretion of the physician, with review at appropriate intervals.

N.B. Maintenance therapy is not suitable for use with pollen-containing vaccines.

Recommended maintenance dosage schemes for vaccines which do NOT contain pollen allergens.

Injections should be given from vial No. 3.

If a reaction occurs during treatment, dosage should be reduced: see 'Adjustment of Dosage'.

N.B. Care should be taken when administering the first injection from a new No. 3 vial, as in a very few cases a local or general reaction may occur.

If a period of five to eight weeks has elapsed since the last injection, from the previous No. 3 vial, the first two doses from the new No. 3 vial should be modified according to the following recommendations:

Adults: Maintenance Dosage Scheme (Using No. 3 vial supplied with Initial Course).

Injection Number	Interval since previous injection	Dosage (ml) from No. 3 Vial (use maximum tolerated dose if lower)		Duration
		very sensitive adults	moderately or mildly sensitive adults	
First	1–2 weeks after completion of Initial Course	0.25	0.6	Maintenance therapy may be continued at the discretion of the physician, with review at appropriate intervals.
2nd	1–2 weeks	0.25	0.6	
3rd	2 weeks	0.25	0.6	
4th	2 weeks	0.25	0.6	
5th and subsequent	4 weeks	0.25	0.6	

Children: (aged 5–14 years) Maintenance Dosage Scheme (Using No. 3 vial supplied with Initial Course).*

Injection Number	Interval since previous injection	Dosage (ml) from No. 3 vial (use maximum tolerated dose if lower)	Duration
First	1–2 weeks after completion of Initial Course	0.25	Maintenance therapy may be continued at the discretion of the physician, with review at appropriate intervals.
2nd	1–2 weeks	0.25	
3rd	2 weeks	0.25	
4th	2 weeks	0.25	
5th and subsequent	4 weeks	0.25	

* Children under five: consultant advice should be sought.

- for very sensitive adults and for children the first dose should be 0.05 ml and the second dose 0.15 ml
 - for moderately or mildly sensitive adults the first dose should be 0.15 ml and the second dose 0.3 ml
- given at an interval of 7–14 days.

Maintenance treatment should then be continued as shown in the above tables.

If more than eight weeks have elapsed since the previous injection, it is advisable not to attempt maintenance therapy but to re-start with a complete initial course, commencing with the lowest strength (No. 1 Green label) vial.

This regimen is unsuitable for use with pollen-containing vaccines.

Contra-indications, warnings, etc

Contra-indications: Patients suffering from febrile conditions or an acute attack of asthma should not be given an injection until 24 hours after the condition has subsided.

It is advisable to avoid use during pregnancy, especially in the first trimester.

Precautions: Children under five: consultant advice should be sought.

Patients should be warned not to eat a heavy meal immediately before an injection is due to be given.

In very sensitive patients it is advantageous to give an antihistamine tablet about one hour before each injection.

Injections should be given slowly by the subcutaneous route. Do not inject into a blood vessel or intramuscularly. Do not rub the site of injection.

Adrenaline Injection BP (Adrenaline 1 in 1,000) should always be kept at hand when giving any desensitising vaccine.

All patients should be instructed to remain under observation in the surgery for at least 20 minutes after each injection and advised to contact the doctor immediately in the unlikely event of a delayed reaction. The patient should not take any strenuous physical exercise for several hours following the injection.

Note: A patient must not be transferred from Alavac-S to an aqueous vaccine unless a complete course of the aqueous vaccine is to be given, commencing with the lowest strength (No. 1 Green label) vial.

Reactions (see also 'Adjustment of Dosage'):

Local reactions, such as slight swelling or irritation, can sometimes occur and may require symptomatic treatment if they persist.

Mild systemic reactions such as rhinitis or urticaria may be treated with antihistamines orally, or by injection if necessary. In mild bronchospasm, a sympathomimetic bronchodilator such as salbutamol and possibly an anti-inflammatory steroid should be given. If required, 0.5 ml

Adrenaline Injection BP (Adrenaline 1 in 1,000) may be given subcutaneously.

Severe systemic reactions may occasionally arise in the form of typical allergic symptoms; anaphylaxis is rare.

Treatment of anaphylaxis:

Anaphylactic shock: characterised by bronchospasm, laryngeal oedema, urticaria and shock. Immediate attention should be given as follows:

1. The patient should be laid down and treated immediately.
2. 0.5 ml† Adrenaline Injection BP (Adrenaline 1 in 1,000) should be given intramuscularly close to the vaccine injection site. This should be repeated to a total of 2 ml† over 15 minutes if necessary. In extreme cases, 0.5 ml† Adrenaline (1 in 10,000) can be given by slow intravenous injection.
3. If bronchospasm persists, 10–20 ml† of Aminophylline Injection BP (250 mg per 10 ml) should be given by slow intravenous injection at a rate of 2 ml† per minute.
4. In addition, 200–400 mg† of Hydrocortisone Injection BP should be given intravenously. This is to combat persistent bronchospasm which can occur 6–8 hours after the initial collapse.
5. Full supportive measures should be available and employed if necessary and patients should be closely monitored for at least 24 hours after recovery.

Adjustment of Dosage (in the event of the occurrence of a reaction):

Reaction to the first injection

Moderately sensitive or mildly sensitive adult dosage scheme: The patient should be transferred to the very sensitive adult dosage scheme.

Very sensitive adult dosage scheme and children: return the complete course to Bencard. A Special Dilution Vial (No. 0 – Black label, 1/10th dilution of the No. 1 vial) will be prepared free of charge and returned with a new complete course.

Treatment should recommence from the dilute vial according to the dosage scheme issued with it; the normal dosage scheme should then be continued, but no attempt should be made to exceed the maximum tolerated dose.

Reaction to subsequent injections:

Local

Mild reaction: Reduce the dose by one step.

Severe reaction: Reduce the dose by two steps.

Systemic

Mild reaction: Reduce the dose by two steps.

Severe reaction: Treatment should be discontinued.

Except in cases where a severe systemic reaction has occurred, the course may be continued with caution up to the top dose quoted, or to the highest dose tolerated without significant reaction.

Pharmaceutical precautions Alavac-S must be stored in a refrigerator (2–8°C). It must not be frozen.

Surplus vaccine from courses of Alavac-S containing pollen allergens must not be used the following year.

Vaccine left over from the No. 3 vial of courses which do not contain pollen allergens may be used for maintenance therapy (see Maintenance therapy for vaccines which do not contain pollen allergens).

Legal category POM.

Package quantities Each course of treatment consists of a set of three multidose vials of vaccine in graded

concentrations. Ready-assembled disposable syringes with attached needles and an instruction leaflet are included with each set. The No. 3 vial is also available in a larger size for maintenance therapy with Alavac-S vaccines which do not contain pollen allergens (see Dosage and Administration).

Normal delivery time for a complete course or a single vial is about two weeks to allow for individual formulation and sterility testing.

Further information Ordering procedure: FP10 forms (or other prescriptions) should be taken to a chemist who will arrange the supply of the vaccine. The prescription should be accompanied by the following information:

When available, a Skin Test Reaction Chart or a list of the allergens to be included in the vaccine with a note of the patient's sensitivity to each one, or, the reference number of a previous course.

Patient's name

Patient's date of birth and/or age

The Bencard Medical Department will be pleased to advise on any aspect of treatment.

Product licence number 0038/5086.

AMOXIL* CAPSULES

AMOXIL* DISPERSIBLE TABLETS ▼

AMOXIL* SYRUP 125 mg

AMOXIL* SYRUP FORTE 250 mg

AMOXIL* SACHETS 3 g ▼

AMOXIL* PAEDIATRIC SUSPENSION

AMOXIL* INJECTION ▼

Presentation *Amoxil Capsules:* (Amoxycillin Capsules BP) Maroon and gold capsules overprinted 'Amoxil 250', each providing 250 mg amoxycillin.

Maroon and gold capsules overprinted 'Amoxil 500', each providing 500 mg amoxycillin.

Amoxil Dispersible Tablets: Flat, white circular tablets, engraved 'Amoxil 500', each providing 500 mg amoxycillin.

Amoxil Syrups: (Amoxycillin Mixture BP) Citrus flavoured syrup, providing 125 mg or 250 mg amoxycillin per 5 ml.

Presented as powder in bottles for preparing 100 ml.

Amoxil 3 g Sachet: Each sachet provides 3 g amoxycillin for reconstitution in approximately one third of a glass of water.

Amoxil Paediatric Suspension. Citrus flavoured suspension, providing 125 mg amoxycillin per 1.25 ml (measured by the pipette supplied).

Presented as powder in bottles for preparing 20 ml.

Amoxil Vials for Injection: Each vial provides 250 mg, 500 mg or 1 g amoxycillin. Presented as powder for reconstitution.

The amoxycillin content per dose unit is present as the trihydrate in Amoxil oral preparations and as the sodium salt in Amoxil injections.

Uses *Treatment of Infection:* Amoxil is a broad spectrum antibiotic indicated for the treatment of commonly-occurring bacterial infections such as:

Upper Respiratory Infections

Otitis media

Acute and Chronic Bronchitis

Lobar and Bronchopneumonia

Cystitis, Urethritis, Pyelonephritis

† All dosages should be reduced as required for children.

Bacteriuria in pregnancy
Gynaecological infections including puerperal sepsis and septic abortion
Gonorrhoea
Peritonitis
Intra abdominal sepsis
Septicaemia
Bacterial endocarditis
Typhoid and Paratyphoid fever
Skin and Soft Tissue Infections
Osteomyelitis

In children with urinary tract infection the need for investigation should be considered.

Oral prophylaxis of endocarditis: Amoxil may be used for the prevention of bacteraemia, associated with procedures such as dental extraction in patients at risk of developing bacterial endocarditis.

The wide range of organisms sensitive to Amoxil's bactericidal action include.

<i>Gram-positive</i>	<i>Gram-negative</i>
Streptococcus faecalis	Haemophilus influenzae
Streptococcus pneumoniae	Escherichia coli
Streptococcus pyogenes	Proteus mirabilis
Streptococcus viridans	Salmonella species
Staphylococcus aureus (penicillin-sensitive)	Shigella species
Clostridium species	Bordetella pertussis
Corynebacterium species	Brucella species
Bacillus anthracis	Neisseria gonorrhoeae
Listeria monocytogenes	Neisseria meningitidis
	Vibrio cholerae
	Pasteurella septica

Dosage and administration *Treatment of Infection:*

Adult dosage: Oral.

Standard adult dosage: 250 mg three times daily, increasing to 500 mg three times daily for more severe infections.

High dosage therapy (maximum recommended oral dosage 6 g daily in divided doses): A dosage of 3 g twice daily is recommended in appropriate cases for the treatment of severe or recurrent purulent infection of the respiratory tract.

Short course therapy: Simple acute urinary tract infection: two 3 g doses with 10–12 hours between the doses. Gonorrhoea: single 3 g dose.

Adult dosage: Injectable: 500 mg IM eight hourly (or more frequently if necessary) in moderate infections. 1 g IV six hourly in severe infections.

Children's dosage (up to 10 years of age): Oral: 125 mg three times daily, increasing to 250 mg three times daily for more severe infections.

Injectable 50–100 mg/kg body weight a day, in divided doses.

Parenteral therapy is indicated if the oral route is considered impracticable or unsuitable, and particularly for the urgent treatment of severe infection.

In renal impairment the excretion of the antibiotic will be delayed and depending on the degree of impairment it may be necessary to reduce the total daily dosage.

Oral prophylaxis of endocarditis: Adults and children over 10 years: A single 3 g dose about one hour before the procedure from which bacteraemia may arise.

N.B. Oral prophylaxis is generally inappropriate for patients who require a general anaesthetic. Prophylaxis with parenteral antibiotics may also be considered more appropriate for patients with prosthetic heart valves or pacemakers.

Children under 10 years: Half adult dosage.

Administration: Oral: Using capsules, dispersible tablets, syrups, 3 g sachets or paediatric suspension.

Intramuscular: 250 mg: Add 1.5 ml Water for Injections BP and shake vigorously.

500 mg: Add 2.5 ml Water for Injections BP and shake vigorously.

A transient pink colouration or slight opalescence may appear during reconstitution. Reconstituted solutions are normally a pale straw colour.

If pain is experienced on intramuscular injection, a sterile 1% solution of lignocaine hydrochloride or 0.5% solution of procaine hydrochloride may be used in place of Water for Injections.

Intravenous: Dissolve 250 mg in 5.0 ml Water for Injections BP.

Dissolve 500 mg in 10 ml Water for Injections BP.

Dissolve 1 g in 20 ml Water for Injections BP.

Amoxil injection, suitably diluted, may be injected directly into a vein or drip tube, taking 3–4 minutes – or added to infusion fluids, as recommended in the package enclosure leaflet, and infused over a period of ½–1 hour.

Contra-indications, warnings, etc Amoxil is a penicillin and should not be given to penicillin-hypersensitive patients.

Side-effects: Side-effects, as with other penicillins, are usually of a mild and transitory nature; they may include diarrhoea, indigestion, or occasionally rash, either urticarial or erythematous. An urticarial rash suggests penicillin hypersensitivity and the erythematous type rash may arise if Amoxil is administered to patients with glandular fever. In either case treatment should be discontinued. Since Amoxil is a penicillin, problems of overdosage are unlikely to be encountered.

Pharmaceutical precautions Prior to use, oral presentations of Amoxil should be stored in a dry place. Amoxil injections should be stored in a cool, dry place. Once dispensed, Amoxil syrups and paediatric suspension should be used within the periods stated on the labels. Any remaining syrup or suspension should be discarded.

Amoxil Injections should be prepared immediately before use. Their stability in various infusion fluids is given in the package enclosure leaflet. They should not be mixed with blood products, other proteinaceous fluids such as protein hydrolysates, or with intravenous lipid emulsions.

Legal category POM.

Package quantities Amoxil Capsules: 250 mg packs of 100 and 500. 500 mg packs of 100.

Amoxil Dispersible Tablets: 500 mg packs of 30.

Amoxil Syrups: 125 mg and 250 mg per 5 ml: 100 ml bottles.

Amoxil 3 g Sachet: Packs of 2 and 10.

Amoxil Paediatric Suspension: 125 mg per 1.25 ml: 20 ml bottles with pipette.

Amoxil Vials for Injection: 250 mg, 500 mg and 1 g: packs of 10, 10 and 5 respectively.

Further information Amoxil is well absorbed by the oral and parenteral routes. Oral administration, usually at convenient t.d.s. dosage, produces high serum levels independent of the time at which food is taken. Amoxil gives good penetration into bronchial secretions and high urinary concentrations of unchanged antibiotic. It is rapidly bactericidal and possesses the safety of the penicillins.

Sucrose content: Amoxil Syrup 3.1 g per 5 ml; Syrup Forte 2.9 g per 5 ml; Paediatric Suspension 0.6 g per 1.25 ml; Sachet 19 g. (Amoxil Capsules and Dispersible Tablets are sugar-free.)

Product licence numbers

Amoxil Capsules 250 mg	0038/0103
Amoxil Capsules 500 mg	0038/0105
Amoxil Dispersible Tablets 500 mg	0038/0277
Amoxil Syrup 125 mg per 5 ml	0038/0108
Amoxil Syrup Forte 250 mg per 5 ml	0038/0109
Amoxil 3 g Sachet	0038/0238
Amoxil Paediatric Suspension	0038/0107
Amoxil Vials for Injection 250 mg	0038/0221
Amoxil Vials for Injection 500 mg	0038/0222
Amoxil Vials for Injection 1 g	0038/0225

**ASERBINE* CREAM
ASERBINE* SOLUTION**

Presentation *Aserbine Cream:* White cream in a tube.

Aserbine Solution: Clear colourless liquid in a polythene bottle.

Aserbine is prepared from:

	<i>Aserbine cream %</i>	<i>Aserbine solution %</i>
Propylene glycol	1.7	40.0
Malic acid	0.36	2.25
Benzoic acid	0.024	0.15
Salicylic acid	0.006	0.0375

Uses *Principal action:* Aserbine is a desloughing and cleansing agent which does not affect living tissue and has antibacterial properties to guard against wound infection.

Uses:

- Whenever the presence of slough delays healing:
 - Chronic skin ulcers:
 - Venous (varicose) ulcers and other benign chronic ulcers; Trophic ulcers including pressure sores.
 - Burns.
 - Traumatic injuries:
 - Crushed limb injuries; multiple lesions.
 - Surgical procedures where slough may be a problem:
 - Preparation for skin grafting; mastectomies; amputations; post-surgical incisions.
- Cleansing:
 - Wounds and abrasions where coagulum, debris, dirt and grit, etc. are a problem.

Administration Aserbine is suitable for both adults and children and should be applied topically.

For desloughing: Aserbine Cream should be applied liberally to the wound surface and before each new application the wound should be washed with Aserbine Solution so that the loose slough and cream from the previous application are removed.

Dressing the wound twice daily has been found to produce the best results; however, more frequent dressings may be made if necessary.

Aserbine Solution may also be applied as a wet dressing which should be kept constantly moist.

For cleansing: Both Aserbine Cream and Solution have proved of value as cleansing agents in casualty work for the removal of coagulum, debris, dirt, grit, etc. from wounds and abrasions.

Contra-indications, warnings, etc

Contra-indications: None.

Warning: For external use only.

Precautions: Care should be taken to avoid contact with the eyes because of Aserbine's low pH.

As Aserbine Cream contains 0.015% hexachlorophane it should not be administered except on medical advice, to a child under two years of age.

Overdosage: Not applicable.

Side-effects: Mild pyrexia, partially due to the absorption of protein products of slough breakdown from the wound, has been reported in severely burned patients. Irritation of the hypersensitive skin surrounding the wound may occur in a few patients. In these cases, Aserbine should be kept away from the growing epithelium at the periphery of the wound.

Occasionally a mild urticarial rash has been seen a small distance around the treated area. The discomfort was slight and readily controlled by antihistamines.

Pharmaceutical precautions Prolonged contact of Aserbine Solution with metallic surfaces is inadvisable.

Legal category GSL.

Package quantities *Aserbine Cream:* 100 g tube. *Aserbine Solution:* 500 ml bottle.

Further information The acid pH of Aserbine Cream and Solution is such that, when applied to a wound, it causes maximum differential swelling between the living protein of healthy tissues and the dead protein of slough, leading to the separation of the dead tissue (desloughing). The wound surface is cleared from the presence of slough and debris without affecting the living tissue so that uninterrupted normal healing can proceed. Aserbine also has antibacterial properties which guard against wound infection.

Dressings with Aserbine Cream are non-adherent, odourless and do not stain the skin, clothing, etc.

Product licence numbers

Aserbine Cream 0038/5089
Aserbine Solution 0038/5090

BENCARD* SKIN TESTING SOLUTIONS

Presentation Bencard Skin Testing Solutions for the diagnosis of allergy are available for over 200 allergens. Prick testing is the generally recommended method. The full range of extracts is available for inclusion in SDV (specific desensitising vaccines).

The more common allergens (marked † in the list of allergens below) are also available for inclusion in Alavac-S vaccines.

Prick tests: Aqueous allergen extracts containing 50% glycerin, 6% sodium chloride (with the exception of mould extracts, which contain < 1% sodium chloride) and 0.5% phenol as a preservative. Supplied in polythene-stoppered vials containing approximately 2 ml of solution, sufficient for about 100 individual tests.

Intradermal tests: When these are requested they will be supplied as aqueous allergen extracts in dilute phosphate buffer with 0.5% phenol as a preservative. Supplied in vials containing approximately 2 ml of sterile solution, sufficient for about 30 individual tests.

Form and appearance: The colours of individual skin testing solutions vary depending on the characteristics of the raw material involved, e.g. pollens tend to be

yellowish whilst dusts and moulds, in particular, are shades of brown.

Availability: Bencard Skin Testing Solutions are available either individually from the list specified below or as Kits (Series I and Series II) containing selections of the most important allergens.

STANDARD GROUPS OF ALLERGENS

(all allergens contained in these groups are also available individually)

† **B2 Grass pollens:** Bent; Brome; Cocksfoot; Dogstail (Crested); False oat (Oat grass); Fescue (Meadow); Foxtail (Meadow); Meadow grass; Rye grass; Timothy; Vernal (Sweet); Yorkshire fog.

† **B3 Tree pollens:** Alder; Ash; Beech; † Birch, Silver; Elm; † Hazel; Oak; Plane; † Poplar; Willow.

† **B5 Weed and shrub pollens:** Heather; † Nettle; † Plantain; Fat Hen; Mugwort; Orache.

INDIVIDUAL ALLERGENS

Dusts: Flax Dust and Fibre; † Hay; † House; † Straw; † Threshings (bran); Mixed (Barley, Maize, Oats, Wheat); Threshings (bran), Wheat.

Epithelial (feathers, fur, hair and danders): Feathers: Budgerigar; Canary; Chicken; Goose; † Mixed; Pigeon.

Fur: † Cat; Mixed (fine); (Beaver, Fox, Mink, Musquash, Squirrel); † Rabbit.

Hair: Camel; † Cow; † Dog; Goat; Guinea Pig; Hamster; † Horse; † Human; Mouse; Rat.

Pig bristle.

† Sheep wool.

Fabrics: Acrilan; † Cotton flock; Hessian (Jute); † Kapok; Linen; Nylon; Rayon; Silk; Terylene; White wool.

Flowers and foliage (mixed): Chrysanthemum (*C. morifolium*); Geranium (*Pelargonium* spp.); Grass cuttings; Primula (*Primula* spp.).

Woods (sawdust): Beech (*Fagus sylvatica*); Birch (*Betula* spp.); Cedar of Lebanon (*Cedrus libani*); Cedar, Western Red (*Thuja plicata*); Deal; (*Pinus sylvestris*); Douglas Fir (*Pseudotsuga douglasii*); Hemlock (*Tsuga heterophylla*); Iroko (*Chlorophora* spp.); Makore (*Mimusops beckelii*); Mahogany (*Khaya ivorensis*); Oak (*Quercus* spp.); Obeche (*Triplochiton scleroxylon*); Pine, Parana (*Araucaria brasiliana*); Ramin (*Gonyostylus* spp.); Teak (*Tectona grandis*).

(FOODS)

Cereals (Grain, Flour, Bread): Flour, Mixed (Plain, Self-raising and Wholewheat); Plain; Rye; Wholewheat.

Grain: Barley; Maize; Oat, Rice; Rye; Wheat.

Dairy products: Cheese, Mixed (Cheddar and Dutch); Egg Whole; Milk (Cow).

Drinks: Coffee; Tea.

Fish: Cod; Herring; Plaice; Sardine.

Shellfish: Crab; Lobster; Mussel; Oyster; Shrimp.

Fruits: Apple; Banana; Grapes (Mixed black and white); Lemon; Orange; Strawberry; Tomato.

Meats: Beef-veal; Mutton-lamb; Pork-bacon.

Nuts: Mixed (Almond, Brazil, Chestnut, Hazel and Walnut).

Vegetables: Beans, Mixed (Broad, Haricot and Runner); Cabbage; Carrot; Mushroom; Onion; Pea; Potato (New); Spinach.

Unclassified: Chocolate; Mustard; Yeast (Mixed); Yeast (Bakers).

(MICRO-ORGANISMS)

House dust mite: *Dermatophagoides farinae* (culinae); † *Dermatophagoides pteronyssinus*.

Bacteria: *Corynebacterium hofmannii*; *Escherichia coli* (*B. coli*); *Haemophilus influenzae*; *Klebsiella pneumoniae*; (*Friedlander's bacillus*); *Neisseria catarrhalis*; *Pseudomonas aeruginosa*; (*B. pyocyaneus*); *Staphylococcus aureus*; *Staphylococcus albus*; *Streptococcus Lancefield Group C*; *Streptococcus Lancefield Group G*; *Streptococcus pneumoniae* Type 1; *Streptococcus viridans*.

Fungi (moulds and yeasts): † *Alternaria alternata*; *Aspergillus amstelodami*; † *Aspergillus fumigatus*; † *Aspergillus niger*; *Aspergillus terreus*; *Botrytis cinerea*; † *Candida albicans*; *Chaetomium globosum*; † *Cladosporium herbarum*; *Epicoccum purpurascens*; † *Fusarium* spp.; † *Merulius lacrymans* (Dry rot); *Mucor mucedo*; *Mucor racemosus*; *Mucor spinosus*; † *Neurospora sitophila*; *Paecilomyces marquandii* (*Spicaria violacea*); † *Penicillium notatum*; *Phoma betae*; *Pullularia pullulans*; † *Rhizopus nigricans*; † *Sporobolomyces roseus*; † *Trichophyton (T. mentagrophytes and T. rubrum)*; *Trichophyton mentagrophytes (interdigitale)*; *Trichophyton rubrum*; *Trichophyton verrucosum*; *Ustilago*.

Insects: Bee (*Apis mellifera*); Flour beetle (*Tribolium confusum*); Mosquito (*Culex* spp.); Wasp (*Vespula* spp.).

(POLLENS)

Flower pollens: Aster (*Callistephus chinensis*); Bluebell (*Endymion non-scriptus*); Chrysanthemum (*C. morifolium koreanum*); Daffodil (*Narcissus* spp.); Dahlia (*Dahlia* spp.); Goldenrod (*Solidago canadensis*); Lupin (*Lupinus polyphyllus*); Marguerite, (*Chrysanthemum leucanthemum*); Michaelmas Daisy (*Aster novi-belgii*); Tulip (*Tulipa* spp.); Wallflower (*Cheiranthus cheiri*).

Grass pollens: Bent (*Agrostis tenuis*); Bermuda (*Cynodon dactylon*); Brome (*Bromus* spp.); Cocksfoot (*Dactylis glomerata*); Couch (*Agropyron repens*); Dogstail, Crested (*Cynosurus cristatus*); False Oat (*Arrhenatherum elatius*); Fescue, Meadow (*Festuca pratensis*); Foxtail, Meadow (*Alopecurus pratensis*); † Maize (*Zea mays*); Meadow Grass (*Poa pratensis/trivialis*); Oat, Cultivated (*Avena sativa*); Oat, Wild (*Avena fatua*); † Rye, Cultivated (*Secale cereale*); Rye-grass (*Lolium perenne/multiflorum*); Timothy (*Phleum pratense*); Vernal, Sweet (*Anthoxanthum odoratum*); Wheat, Cultivated (*Triticum* spp.); Yorkshire Fog (*Holcus lanatus*).

Shrub and tree pollens: Acacia, False (*Robinia pseudo-acacia*); Alder (*Alnus* spp.); Ash (*Fraxinus* spp.); Beech (*Fagus* spp.); † Birch, Silver (*Betula* spp.); † Elder (*Sambucus nigra*); Elm (*Ulmus* spp.); Hawthorn (*Crataegus* spp.); † Hazel (*Corylus* spp.); Heather (*Calluna vulgaris*); Horse-chestnut (*Aesculus* spp.); Laburnum (*L. anagyroides*); Lilac (*Syringa vulgaris*); Lime (*Tilia europea/cordata*); Mezquit (*Prosopis* spp.); Mock Orange (*Philadelphus* spp.); Oak, Common (*Quercus* spp.); Pine, Austrian (*Pinus nigra*); Pine Scots (*Pinus sylvestris*); Plane (*Platanus* spp.); † Poplar (*Populus* spp.); Privet (*Ligustrum* spp.); Rose (*Rosa* spp.); Sycamore (*Acer* spp.); Willow (*Salix* spp.).

Weed and miscellaneous pollens: Buttercup (*Ranunculus* spp.); Clover (*Trifolium* spp.); Dandelion (*Taraxacum* spp.); Fat Hen (*Chenopodium* spp.); Mugwort (*Artemisia vulgaris*); † Nettle (*Urtica dioica*); Orache (*Atriplex* spp.); † Plantain (*Plantago lanceolata*); Ragweed, Common or Short (*Ambrosia elatior*); Ragwort (*Senecio jacobaea*); Sorrel (*Rumex acetosa*); Willow-

herb, Rosebay (*Chamaenerion angustifolium*); Worm-wood (*Artemisia absinthium*).

SERIES I AND SERIES II KITS

The most important allergens are supplied as Series I, and the next important as Series II kits. Both kits are supplied complete with control solution, prick test instruments, Bencard Case History Charts and Skin Test Reaction Charts.

The contents are listed below:

Series I (20 prick test solutions): †House dust mite (*D. pteronyssinus*); †House dust; †Feathers; †Horse hair and dander; †Cat fur; †Dog hair; †Sheep wool; †Human hair and dandruff; †Rabbit fur; †Cotton flock; †B2 Grass pollens; †B3 Tree pollens; †B5 Weed and shrub pollens; †Hay dust; †Straw dust; †*Cladosporium herbarum*; †*Alternaria alternata*; †Plantain pollen; †Nettle pollen; †Birch pollen.

Series II (19 prick test solutions): †Cow dander; †Kapk; †*Aspergillus niger*; †*Neurospora sitophila*; †*Rhizopus nigricans*; †*Penicillium notatum*; †*Fusarium* spp.; †*Sporobolomyces roseus*; †Dry rot; †*Aspergillus fumigatus*; †Mixed threshings; †*Staph. aureus*; †Hazel pollen; Whole egg; Wheat grain; Milk; Chocolate; Cod; Lobster.

Allergens marked † in the above lists are available for inclusion in both Alavac-S and SDV vaccines.

All other allergens listed are available for inclusion in SDV only.

Bencard tries to ensure that all allergens are immediately available from stock; however, in view of the large range, this may not always be possible.

The Bencard list of allergens is continually being reviewed to reflect current practice and demand.

Uses Bencard Skin Testing Solutions are used to confirm the significance of the most likely causative allergens indicated by case history and to establish their relative importance in allergic conditions.

Dosage and administration Prick testing solutions must not be used for intradermal testing.

Recommended technique for skin testing:

1. **General information:** Adrenaline Injection BP (1 in 1000) and other supportive measures must always be kept at hand when skin testing with any allergens.

Antihistamines and other drugs which are likely to suppress the immediate Type 1 reaction should be discontinued 48 hours prior to testing.

The flexor aspect of the forearm is a convenient site for testing. Clean the skin with soap and water if necessary – do not sterilize with organic solvents or strong antiseptics.

A ball point pen may be used to mark the skin (with suitable symbols) adjacent to planned test sites to identify the allergen and control solutions used.

Since each vial is used more than once, aseptic precautions must be sufficient to avoid the risk of microbial contamination.

2. **Prick testing:** Using the applicator attached to the vial cap, place one drop of the control solution on the skin.

In the same way, place one drop of each prick test solution required at about 3 cm intervals along the arm.

Hold the prick test instrument supplied almost parallel to the skin with its tip in the drop of control solution. Push until the tip just enters the superficial skin layer taking care not to draw blood. Raise the tip slightly and then withdraw the instrument.

Repeat the procedure with each test solution, either rinsing the prick test instrument in carbol saline and wiping it between each test, or using a fresh prick test instrument.

Carefully wipe any excess test solution away using a fresh piece of sterile cotton wool for each test.

3. **Intradermal testing:** Clean the rubber cap of the testing solution vial with sterile saline or 0.5% phenol solution. Do not use spirit or other strong antiseptics.

Using a tuberculin syringe with a short bevel needle, inject 0.01 to 0.02 ml of control solution intradermally. It is important to inject into the skin and not beneath it. This will raise a small bleb.

In the same way, inject 0.01 to 0.02 ml of each intradermal test required at about 3 cm intervals along the arm.

Use either a fresh syringe or clean the syringe and needle after each test by three times drawing into it and ejecting sterile saline or 0.5% phenol solution. The three washes are best drawn from three separate beakers (which should be used in the same order after each test) and each wash discarded into a fourth beaker.

4. **Interpretation of Skin Test Reactions:** Examine reactions approximately fifteen minutes after testing. Assess the strength of each reaction by the degree of erythema and the area of the weal formed. Weal size may be measured with a Bencard Skin Test Reaction Gauge. Record the strength of each reaction relative to the control on a Bencard Skin Test Reaction Chart as follows:

Prick testing

- No weal. Erythema absent or less than 1 mm diameter.
- + Weal absent or very slight. Erythema present, not more than 3 mm diameter.
- + + Weal not more than 3 mm diameter, with associated erythema.
- + + + Weal between 3 mm and 5 mm diameter, with erythema.
- + + + + Any larger reaction, possibly with pseudopodia.

Intradermal testing

- No increase in the size of bleb since injection. No erythema.
- + An increase in the size of bleb to a weal not more than 5 mm diameter, with associated erythema.
- + + Weal between 5 mm and 8 mm diameter, with associated erythema.
- + + + Weal between 8 mm and 12 mm diameter, with erythema.
- + + + + Any larger reaction, possibly with pseudopodia.

Small positive skin test reactions no greater than that of the control solution should be ignored.

Contra-indications, warnings, etc

Prick testing solutions must not be used for intradermal testing.

Precautions: Although the likelihood of a systemic reaction is very low, Adrenaline Injection BP (1 in 1000) and other supportive measures must always be kept at hand.

Treatment of anaphylaxis: Anaphylactic shock: characterised by bronchospasm, laryngeal oedema, urticaria and shock. Immediate attention should be given as follows:

1. The patient should be laid down and treated immediately.
2. 0.5 ml Adrenaline Injection BP (Adrenaline 1 in 1,000) should be given intramuscularly close to the vaccine injection site. This should be repeated to a total of 2 ml over 15 minutes if necessary. In extreme cases, 0.5 ml Adrenaline (1 in 10,000) can be given by slow intravenous injection.
3. If bronchospasm persists, 10–20 ml of Aminophylline Injection BP (250 mg per 10 ml) should be given by slow intravenous injection at a rate of 2 ml per minute.
4. In addition, 200–400 mg of Hydrocortisone Injection BP should be given intravenously. This is to combat persistent bronchospasm which can occur 6–8 hours after the initial collapse.
5. Full supportive measures should be available and employed if necessary and patients should be closely monitored for at least 24 hours after recovery.

Pharmaceutical precautions Bencard skin testing solutions should be stored between 2 and 8°C. Do not freeze.

Legal category POM.

Package quantities Prick and Intradermal Testing Solutions are prepared in 2ml multidose vials available individually or in Series I and II Skin Testing Kits.

Further information Nil.

Product licence number 0038/5000.

FERRAPLEX B* TABLETS

Presentation *Appearance:* Red, capsule shaped sugar-coated tablets.

Active ingredients. Each Ferraplex B tablet contains

Dried ferrous sulphate	167 mg
Copper carbonate	0.4 mg
Ascorbic acid (vitamin C)	8 mg
Thiamine hydrochloride (vitamin B ₁)	0.5 mg
Riboflavin (vitamin B ₂)	1 mg
Nicotinamide	5 mg
Dried brewers yeast	292 mg

Uses *Principal action:* Ferraplex B provides a therapeutic quantity of easily assimilable ferrous iron with other haemopoietic factors needed for maximum absorption and utilisation of iron so that haemoglobin levels are rapidly increased and maintained.

Uses: Iron deficiency anaemias associated with pregnancy and lactation, haemorrhage and menorrhagia, childhood and adolescence, old age and debility, febrile states.

Dosage and administration Ferraplex B should be taken orally.

Adults: One or two tablets three times daily, during or after meals.

Children (under 15 years of age): Reduced dosage as indicated by age and weight.

Contra-indications, warnings, etc

Contra-indications: Nil.

† All dosages should be reduced as required for children.

Warnings and precautions: Young children should not have access to iron preparations especially in the form of sugar-coated tablets, as excessive doses may be dangerous.

Side-effects: Side-effects occasionally have been reported, usually in the form of gastro-intestinal disturbances at the beginning of therapy. These upsets are usually short-lived if the dose is reduced and then gradually increased.

Overdosage: In the event of overdosage, the patient should be referred to hospital, where desferrioxamine may be administered, if required, to reduce plasma iron levels. For full details please refer to the desferrioxamine data sheet.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities 250 tablets.

Further information *Iron:* Oral iron is best given in the form of inorganic ferrous salts and ferrous sulphate is one of the most stable and most easily utilised.

Copper: Copper in minute amounts promotes the utilisation of iron for the synthesis of haemoglobin appearing to act as a catalyst.

Vitamin C: Ascorbic acid influences both the absorption and utilisation of iron.

Vitamin B Complex: Members of the B complex – provided in Ferraplex B by dried brewers yeast with added thiamine hydrochloride, riboflavin and nicotinamide – have an essential role as co-enzymes in haemopoiesis.

Product licence number 0038/5088.

JUVEL* TABLETS JUVEL* ELIXIR

Presentation *Juvel Tablets:* Bright yellow, sugar-coated tablets overprinted in black with the product name JUVEL.

Juvel Elixir: Lemon-flavoured elixir.

Active ingredients

	Tablet	5 ml elixir
Vitamin A	5,000 units	4,000 units
Vitamin D ₂	500 units	400 units
Vitamin B ₁ (Thiamine hydrochloride)	2.5 mg	2 mg
Vitamin B ₂ (Riboflavin)	2.5 mg	2 mg
Vitamin B ₆ (Pyridoxine hydrochloride)	2.5 mg	2 mg
Nicotinamide	50 mg	40 mg
Vitamin C	50 mg	40 mg

Uses *Principal action:* Juvel is a balanced multivitamin dietary supplement.

Uses: As a course of multivitamin therapy, in the elderly on restricted diets; in patients on imposed dietary regimes; when impaired absorption is suspected; or when nutritional demand is greater than normal, during periods of rapid growth in childhood or adolescence and during pregnancy and lactation.

Dosage and administration For oral administration only.

Adults: 1 tablet or one 5 ml spoonful of elixir daily.
Children: over 2 years: One 5 ml spoonful of elixir daily.
Children under 2 years: 2.5 ml of elixir daily.
 (Syrup BP is a suitable diluent.)

Contra-indications, warnings, etc

Contra-indications: None at the recommended dosage.

Precautions: Care should be exercised when Juvel is co-prescribed with levodopa therapy in Parkinson's Disease since pyridoxine may antagonise the therapy.

Side-effects: None reported.

Overdosage: Prolonged ingestion of massive doses of vitamins A and D can lead to hypervitaminosis states. Symptoms include dry rough skin, painful joint swellings, anorexia and vomiting, but these disappear on withholding the vitamins.

Pharmaceutical precautions

Store in a cool place.
 The elixir should be protected from strong light and be well shaken before dispensing into amber glass containers.

Syrup BP is a suitable diluent.

Legal category

Tablets P.

Elixir GSL.

Package quantities

Tablets: 100.

Elixir: 200 ml, 1 litre.

Further information Vitamin A is required for normal epithelial growth; vitamins of the B complex for normal intracellular carbohydrate metabolism, particularly in the brain; vitamin C for the maintenance of collagen, tissue repair and blood formation; and vitamin D for metabolism of calcium and phosphorus.

Product licence numbers

Tablets 0038/5112

Elixir 0038/5111

MIGEN*

Presentation Migen contains tyrosine-adsorbed glycerinated extract of house dust mite (*Dermatophagoides pteronyssinus*).

Initial course: Six unit-dose syringes prefilled with 0.5 ml of vaccine in graded concentrations as follows:

Syringe no.	Dose: Noon Units
1	4
2	10
3	25
4	60
5	150
6	400

Maintenance course: Six unit-dose syringes prefilled with 0.5 ml of vaccine at the top dose concentration of 400 Noon units.

The tyrosine content is 4.0% w/v; with Phenol BP as a preservative.

The *D. pteronyssinus* extract is adsorbed on to tyrosine, a naturally occurring amino acid, to ensure slow release of the active material, giving a prolonged and efficient desensitising effect.

Uses Indicated for the treatment of asthma and perennial rhinitis for patients in whom house dust mite is implicated as the principal allergen.

Dosage and administration Please note that the section on 'Contra-indications, warnings, etc.' must be studied before Migen is administered.

Adrenaline Injection BP (Adrenaline 1 in 1,000) should always be kept at hand when giving any desensitising vaccine.

The administration procedures shown in the leaflet included with each course of Migen should be carefully followed.

Migen may be given to adults and children of six years and over.

Injections should be given at intervals of 7–14 days.

Migen must be removed from the refrigerator 2–3 hours before use.

The syringe should be shaken thoroughly immediately prior to giving the injection.

Injections should be given slowly by the subcutaneous route.

Do not inject into a blood vessel, or intramuscularly. Do not rub the site of injection.

Maintenance therapy: Maintenance therapy is recommended to maintain clinical improvement. The first maintenance injection should be given one month after the final injection of the initial course. Subsequent maintenance injections should be given monthly, with review at appropriate intervals, at the discretion of the physician.

Contra-indications, warnings, etc

Contra-indications: Patients suffering from febrile conditions or an acute attack of asthma should not be given an injection until 24 hours after the condition has subsided. It is advisable to avoid use during pregnancy, especially in the first trimester.

Precautions: Patients should be warned not to eat a heavy meal immediately before an injection is due to be given.

In very sensitive patients, it is advantageous to give an antihistamine tablet about one hour before each injection.

Injections should be given slowly by the subcutaneous route. Do not inject into a blood vessel or intramuscularly. Do not rub the site of injection.

Adrenaline Injection BP (Adrenaline 1 in 1,000) should always be kept at hand when giving any desensitising vaccine.

All patients should be instructed to remain under observation in the surgery for at least 20 minutes after each injection and advised to contact the doctor immediately in the unlikely event of a delayed reaction.

The patient should not take any strenuous physical exercise for several hours following the injection.

Reactions: Local reactions, such as slight swelling or irritation, can sometimes occur and may require symptomatic treatment if they persist.

Mild systemic reactions such as rhinitis or urticaria may be treated with antihistamines orally, or by injection if necessary. In mild bronchospasm, a sympathomimetic bronchodilator such as salbutamol and possibly an anti-inflammatory steroid should be given. If required, 0.5 ml Adrenaline Injection BP (1 in 1,000) may be given subcutaneously.

Severe systemic reactions may occasionally arise in the form of typical allergic symptoms; anaphylaxis is rare.

Treatment of anaphylaxis: Anaphylactic shock: characterised by bronchospasm, laryngeal oedema, urticaria and shock. Immediate attention should be given as follows:

1. The patient should be laid down and treated immediately.

† All dosages should be reduced as required for children.

2. 0.5 ml† Adrenaline Injection BP (Adrenaline 1 in 1,000) should be given intramuscularly close to the vaccine injection site. This should be repeated to a total of 2 ml† over 15 minutes if necessary. In extreme cases, 0.5 ml† Adrenaline (1 in 10,000) can be given by slow intravenous injection.

3. If bronchospasm persists, 10–20 ml† of Aminophylline Injection BP (250 mg per 10 ml) should be given by slow intravenous injection at a rate of 2 ml† per minute.

4. In addition, 200–400 mg† of Hydrocortisone Injection BP should be given intravenously. This is to combat persistent bronchospasm which can occur 6–8 hours after the initial collapse.

5. Full supportive measures should be available and employed if necessary and patients should be closely monitored for at least 24 hours after recovery.

† All dosages should be reduced as required for children.

Note: A severe local reaction, or severe systemic reaction such as urticaria or asthma, indicates that the standard vaccine is unsuitable for the treatment of the particular patient, who should be referred to a consultant for advice or transferred to a suitably dilute specific desensitising vaccine (Alavac-S or SDV) containing house dust mite obtainable from Bencard.

(For full prescribing information please refer to the relevant data sheets).

Legal category POM.

Pharmaceutical precautions Migen must be stored in a refrigerator (5°C). It must not be frozen and must be removed 2–3 hours before use.

Package quantities Initial and Maintenance courses each consist of a set of 6 unit-dose syringes prefilled with vaccine, and with needles attached. An instruction leaflet is included with each set.

Further information Migen is a standard vaccine prepared from extract of *Dermatophagoides pteronyssinus*, the predominant species of house dust mite occurring in British homes. The house dust mite is the most commonly implicated allergen in allergic asthma and perennial rhinitis.

Desensitisation with Migen offers a fundamental approach to the management of the mite allergic patient. It should be prescribed when the mite has been implicated as the principal allergen by case history, and preferably confirmed by skin-testing. An appropriate testing solution is available from Bencard.

Patients who benefit from an Initial course of treatment are likely to maintain their clinical improvement with Maintenance therapy.

Migen may be prescribed on NHS form FP10. Both Initial and Maintenance courses are available for immediate supply from stock.

The Bencard Medical Department will advise on any aspect of treatment.

Product licence number 0038/0112.

NACTON® NACTON FORTE®

Presentation *Nacton* (2 mg): White-coloured, scored tablets engraved 'NACTON 2'.

Nacton forte (4 mg): Orange-coloured, scored tablets engraved 'NACTON 4'.

Active ingredients: *Nacton* Poldine Methylsulphate I
Nacton forte: Each tabl Methylsulphate BP.

Uses *Principal action:* proven anticholinergic c doses acts mainly on the stomach, causing gastric by over 50%.

Uses: Peptic ulcer – sus ulcer. Recurrent dyspepsi Whenever hyperacidity c

Nacton and *Nacton f* management of spastic gastrectomy and colostom

Nacton has also provi nocturnal enuresis.

Dosage and administ

Dosage Scheme will give relief without side-effec Alternatively, as demonst results can be achieved b requirements using the T

Standard dosage: 1 tabl times a day (the last at b

Tailored dosage: Initially times a day (the last at *Nacton* Tablet (1 mg) p Continue until the first si then reduce each dose t This level should be the help the patient, *Nacton* available on request.

If treatment is suspens later resumed, the therap up gradually. If the previo than 4 mg taken four time treatment, building up fr times a day.

Children: *Nacton* may nocturnal enuresis in chil is a suitable dose.

Contra-indications, w

Contra-indications and whom tachycardia, difficu ocular tension might g *Nacton* and *Nacton* for close supervision.

Warnings: Like all medic should be kept out of the

Side-effects. There are doses.

Overdosage: *Mild overd* are, in order of frequen hesitancy of micturition c disappear if one or tv resuming treatment at a l

Gross overdosage: Gastr be performed immediat such as thiopentone sodi the stage of excitement.

Pharmaceutical preca

Legal category POM.

1 (2 mg): 50 and 250

ts.

1 and Nacton forte pro-
ealing by halving gastric
ed even at night as each
e is effective for eight to
ous therapy with Nacton
bone marrow, liver or
levelop tolerance to the
on forte permit patients
r normal working life.

psules, overprinted with
ns 50 mg danthron and

ron is a mild peristaltic
wel to encourage normal
sing irritation. Docusate
high prevents excessive
ing of stools.

pation. Constipation in
r immobilised patients.
n must be free of strain,
r thrombosis, episiotomy
r for surgical or radio-
an empty colon – for
; also of great value in
n following diagnostic
idectomy.

For oral administration

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ile at bedtime.

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undiagnosed abdominal

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s to affect the nursing

ound with other types of
blem with Normax, and
een reported. Occasion-
may be observed, due to

s Store in a cool dry

is available in packs of

ently effective twofold
rly helpful in restoring
elderly and infirm. A
llows bedtime dosage,

enabling the patient to produce soft, formed stools on
rising.

Product licence number 0038/0092.

NORVAL*

Presentation *Norval tablets:* Orange film coated
tablets engraved 'Norval' on one side and '30' on the
other. Each tablet contains 30 mg mianserin
hydrochloride.

Also available, orange film coated tablets containing
10 mg and 20 mg mianserin hydrochloride. Each tablet
is engraved 'Norval' on one side and '10' or '20'
respectively on the reverse.

Uses Symptoms of depressive illness.

Dosage and administration *For oral administration:*
The tablets should be swallowed whole without chewing.

Adults: Treatment should normally be initiated, for the
first few days, at 30–40 mg a day as a single bedtime
dose, or in divided doses. The effective maintenance
dosage will normally lie between 30 mg and 90 mg a day
as indicated in the table, though higher levels may be
required in some patients.

<i>Degree of depression</i>	<i>Usual daily dosage</i>
Mild to moderate	30–60 mg nocte or in divided doses
Moderate to severe	60–90 mg nocte or in divided doses. If higher levels are re- quired these should be given in divided doses.

Divided daily dosages up to 200 mg are well tolerated.

It is often advantageous to maintain antidepressant
treatment for several months after initial clinical improve-
ment has occurred.

Elderly: Not more than 30 mg a day initially. This starting
dose should be increased with caution under close
supervision. A lower maintenance dosage than is usual
may be sufficient to produce a satisfactory clinical
response.

Children: Not recommended.

Contra-indications, warnings, etc

Contra-indications: Use is contra-indicated in mania,
severe liver disease and during breast feeding. (Breast
feeding should be discontinued if antidepressant therapy
is considered essential.)

Use in pregnancy: Do not use during pregnancy unless
there are compelling reasons. There is no evidence of
safety in human pregnancy. Animal studies have not
shown hazard.

Precautions: Care should always be taken in patients
with recent myocardial infarction or heart block. How-
ever, serious cardiotoxic effects appear to be rare at
therapeutic dosage, even in patients with pre-existing
cardiac disease, recent myocardial infarction or cardiac
insufficiency.

The elderly are less liable to experience adverse
reactions such as agitation, confusion and postural
hypotension with Norval, than with tricyclics or bridged

tricyclics, but all antidepressant therapy should be used with caution in this group of patients.

Patients posing a high suicide risk always require close initial supervision.

Avoid, if possible, in patients with epilepsy. When treating patients with diabetes, hepatic or renal insufficiency, normal precautions should be exercised and the dosages of any concurrent therapy kept under review. Patients with narrow angle glaucoma or symptoms suggestive of prostatic hypertrophy, should also be monitored even though anticholinergic side-effects are not anticipated with Norval therapy.

There are indications that Norval, like other antidepressants, may precipitate hypomania in susceptible subjects with bipolar affective illness.

Norval may potentiate the central nervous depressant action of alcohol.

If surgery is necessary during Norval therapy, the anaesthetist should be informed of the treatment being given.

Drug interactions: Norval should not be given concurrently with, or within two weeks of cessation of therapy with, monoamine oxidase inhibitors.

Clinical experience has shown that Norval does not interact with the antihypertensives bethanidine, clonidine, hydralazine, guanethidine and propranolol. Nevertheless, the monitoring of blood pressure is recommended for those patients receiving concurrent antihypertensive therapy.

Phenytoin plasma levels should be monitored in patients treated concurrently with Norval.

Concurrent anticoagulant therapy of the coumarin-type (e.g. warfarin) is also permissible, but close additional monitoring should be undertaken.

Interactions have not been reported between Norval and sympathomimetic agents and are unlikely.

Warnings and adverse effects: As improvement may not occur during the first 2–4 weeks of treatment, patients should be closely monitored during this period. It may be advisable to maintain treatment for several months after initial clinical improvement has occurred.

The most commonly occurring side-effect is drowsiness, particularly during the first few days of therapy. Patients should be warned of the possible hazard in driving or operating machinery. Any drowsiness may be potentiated by alcohol.

Serious adverse effects are uncommon. A small number of cases of bone marrow depression, usually presenting as a neutropenia, generally reversible on stopping treatment, have been reported. If a patient develops symptoms of infection, e.g. fever, sore throat or stomatitis, during treatment with Norval, treatment must be stopped and a full blood count obtained.

Jaundice, usually mild, hypomania and convulsions have also been reported at therapeutic dosage and under such circumstances treatment should be withdrawn.

Additional adverse effects that may occur include breast disorders (gynaecomastia, nipple tenderness and non-puerperal lactation), dizziness, postural hypotension, polyarthropathy, skin rash, sweating and tremor.

Psychotic manifestations including mania and paranoid delusions may be exacerbated during antidepressant therapy.

The following adverse effects although not reported with Norval can occur with tricyclics and bridged tricyclics: interference with sexual function; withdrawal symptoms in adults; withdrawal symptoms (e.g. neuromuscular irritability) in neonates whose mothers received

tricyclic or bridged tricyclic pregnancy.

Overdosage: There is no spe by gastric lavage with appr Symptoms of overdosage prolonged sedation. Cardiac tension, convulsions and unlikely to occur.

Pharmaceutical precauti light.

Legal category POM.

Package quantities Norva in foil packs of 30. Each pack of 10 tablets. Also available in tablets. Norval 10 mg tablet of 90 (three blister strips of 3 and 500 tablets. The 20 containers of 100.

Further information Nor a distinctive tetracyclic struc ant benefits over the tricyclic also been shown to possess parable with diazepam.

Antidepressant activity is amitriptyline and imipramine, for its absence of troubles effects; this may be of spec depressed patients who may conditions such as glauco prostatic hypertrophy. There that anticholinergic effects s psychosomatic feature of deJ toms have been shown to therapy. Clinical experience is significantly less toxic tl imipramine and that cardiac p appears to be particularly ef mistic thought' and 'suicid relatively high safety margir tance in view of the high nu to tricyclic overdosage.

Product licence numbers

Norval 10 mg: 0038/0230R

Norval 20 mg: 0038/0247R

Norval 30 mg: 0038/0248R

NULACIN*

Presentation Off-white c with the product name 'NUL/

Whole milk combined with c Magnesium trisilicate

Heavy magnesium oxide

Calcium carbonate

Heavy magnesium carbonate

Peppermint oil q.s.

Calorific content per tablet:

Uses *Principal action:* The antacids and milk protein i continuous neutralisation of the gastric acidity is maintai

The milk fat in Nulacin help excess gastric juice.

Uses: Dyspepsia. Reflux o Peptic ulcer. Whenever gastr

Dosage and administration One or more tablets as required.

For continuous therapeutic effect the tablet should be allowed to dissolve slowly in the mouth, placed between cheek and gum. For quicker relief the tablet should be chewed and swallowed.

Contra-indications, warnings, etc

Contra-indication: As Nulacin contains gluten, it is contra-indicated in coeliac disease.

Warnings and precautions: Nil.

Side-effects: No significant side-effects have been encountered with Nulacin.

Overdosage: Overdosage has not been reported. However, as with all antacids, there is a theoretical danger of alkalosis.

Pharmaceutical precautions Store in a cool dry place. Replace cap of securitainer after use.

Legal category GSL.

Package quantities 100 tablets.

Further information Nulacin contains effective doses of antacids to give rapid relief from gastric pain. Nulacin dissolves slowly in the mouth to give continuous relief which is independent of the rate of stomach emptying. Nulacin is presented in convenient tablets which have a very acceptable malt and mint flavour.

Product licence number 0038/5079.

OROVITE[®] TABLETS
OROVITE[®] ELIXIR

Presentation *Orovite Tablets:* Maroon, sugar-coated tablets overprinted in white with the product name 'OROVITE'.

Orovite Elixir: Orange-flavoured elixir.

Active ingredients

	Tablet (mg)	5 ml elixir (mg)
Thiamine hydrochloride (vitamin B ₁)	50	20
Riboflavin (vitamin B ₂)	5	2
Pyridoxine hydrochloride (vitamin B ₆)	5	2
Nicotinamide	200	80
Ascorbic acid (vitamin C)	100	40

Uses *Principal action:* Orovite contains high concentrations of the water-soluble vitamins B and C to correct disturbed carbohydrate metabolism.

Uses: Deficiency of the B complex and C vitamins, in particular when encountered: (a) in association with alcoholism, as maintenance therapy; (b) as debility after febrile illnesses such as influenza, measles; acute bronchitis, tonsillitis, enteritis, viral pneumonia; (c) in constitutional states in old age or following illness; (d) as debility following operation.

Orovite is also useful as oral maintenance therapy following a course of Parentrovite. (See Parentrovite data sheet.)

Dosage and administration For oral administration only.

Adults: One tablet or two 5 ml spoonfuls elixir three times a day.

Children: One 5 ml spoonful elixir three times a day. (Syrup BP is a suitable diluent.)

If parenteral therapy is required, treatment should be commenced with Parentrovite.

Contra-indications, warnings, etc

Contra-indications: Nil.

Precautions: Care should be exercised when Orovite is co-prescribed with levodopa therapy in Parkinson's Disease since pyridoxine may antagonise the therapy.

Side-effects: Rarely, flushing of the face may occur.

Overdosage: Nil.

Pharmaceutical precautions Store in a cool place. The elixir should be protected from strong light and be well shaken before dispensing into amber glass containers.

Syrup BP is a suitable diluent.

Legal category GSL.

Package quantities *Tablets:* 25, 100, 500.

Elixir, 200 ml, 1 litre.

Further information Vitamins of the B complex play an integral part as co-enzymes in many stages of the intracellular metabolism of carbohydrates. The efficient functioning of this metabolism is essential for normal health. Similarly, ascorbic acid plays an important part in the biochemical reactions of cells and tissues and is normally present in the highest concentrations in those parts of the brain which are the most active metabolically.

Lack of water soluble vitamins results in impairment of normal intracellular metabolism and may lead to certain disorders (see uses). The high concentrations of the water soluble vitamins contained in Orovite rapidly replenish depleted cellular stores and speed the return of normal intracellular metabolism.

Product licence number

Tablets 0038/5092
Elixir 0038/5091

OROVITE '7'

Presentation Orange coloured granules in unit dose sachets.

Active ingredients: Each sachet contains:

Vitamin A (Palmitate)	2,500 units
Vitamin D ₂	100 units
Vitamin B ₁ (Thiamine Mononitrate)	1.4 mg
Vitamin B ₂ (as Riboflavin)	
Sodium Phosphate)	1.7 mg
Vitamin B ₆ (Pyridoxine Hydrochloride)	2.0 mg
Nicotinamide	18 mg
Vitamin C	60 mg

Uses Orovite '7' provides a course of balanced multivitamin therapy for the management of potential vitamin deficiencies.

Dosage and administration For oral administration only.

Adults and children over 5 years of age: The contents of one sachet per day, dissolved in approximately one third of a tumbler of water.

Contra-indications, warnings, etc

Contra-indications: None at the recommended dosage.

Precautions: Care should be exercised when Orovite '7' is co-prescribed with levodopa therapy in Parkinson's Disease since pyridoxine (Vitamin B₆) may antagonise the therapy.

Side-effects: None reported.

Overdosage: Prolonged ingestion of massive doses of vitamins A and D can lead to hypervitaminosis states. Symptoms include dry rough skin, painful joint swellings, anorexia and vomiting; these disappear when treatment is discontinued.

Pharmaceutical precautions Store in a cool dry place.

Legal category GSL.

Package quantities Thirty sachets.

Further information Orovite '7' provides adequate intake of essential vitamins for patients whose daily nutritional requirements may not be met, such as the elderly on restricted diets, patients on imposed dietary regimes, or in cases where impaired absorption is suspected.

Orovite '7' has a convenient and palatable once-daily sachet presentation which improves patient compliance and is especially suitable for patients who may have difficulty in swallowing tablets or measuring doses from bottles.

Product licence number 0079/0164.

PARENTROVITE* IVHP

PARENTROVITE* IMHP

PARENTROVITE* IMM

Presentation Paired amber glass ampoules for injectable administration in three different presentations. Intravenous High Potency (IVHP), Intramuscular High Potency (IMHP) and Intramuscular Maintenance (IMM).

Active ingredients: See table on next page.

Uses *Principal action:* Parentrovite IVHP, IMHP and IMM contain exceptionally high concentrations of the water-soluble vitamins B and C to correct disturbed carbohydrate metabolism.

Uses: Deficiency of the B complex and C vitamins, in particular that encountered: (a) in association with alcoholism; (b) in peripheral neuritis, associated with malabsorption syndromes, alcoholism or diabetic neuropathy; (c) after acute febrile illness, e.g. influenza, pneumonia; (d) in confusional states following severe illness or operation, especially in the elderly; (e) in states of acute malnutrition.

Dosage and administration

Indication	Dosage
(a) In association with alcoholism – acute alcoholic psychosis – delirium tremens – coma or delirium – post-operative confusional states.	2 to 4 pairs Intravenous High Potency ampoules, repeated 4 to 8 hourly for up to 2 days as indicated clinically, followed by 1 pair Intravenous High Potency or Intramuscular High Potency ampoules daily for 5 to 7 days.

Indication	Dosage
(b) Peripheral neuritis associated with malabsorption states, alcoholism or diabetic neuropathy.	1 pair Intravenous High Potency or Intramuscular High Potency ampoules, once or twice daily for 3 to 7 days.
(c) After acute febrile illness	1 to 2 pairs Intramuscular Maintenance ampoules daily.
(d) In confusional states following severe illness especially in the elderly.	"
(e) In states of acute malnutrition.	"
Maintenance therapy for longer term treatment of the above conditions.	1 to 2 pairs Intramuscular Maintenance ampoules daily, until full health is restored, or until continuation therapy by oral route is possible (e.g. with Orovite tablets).

Children: Parenteral therapy is rarely necessary as children usually respond well to oral administration of the vitamin B complex in high dosage: e.g. with Orovite elixir. (See Orovite data sheet.) However, when parenteral administration of vitamins is required, the following dosage guidelines are recommended;

6–10 years: $\frac{1}{2}$ adult dose,

10–14 years: $\frac{2}{3}$ to $\frac{1}{2}$ adult dose.

14 years and over: adult dose.

These dosages may have to be modified in individual cases.

Administration: For parenteral administration only.

The contents of each pair of ampoules (i.e. No. 1 and No. 2) should be mixed together in a single syringe immediately prior to administration.

The intramuscular presentations must not be given intravenously. The intravenous presentation must not be given intramuscularly. When given by infusion with other drugs, Parentrovite should be injected into the drip tubing immediately after mixing.

Intravenous Parentrovite – Contents of each pair of ampoules to be mixed in the syringe before injecting slowly into a vein. Dilution with normal saline may be made for drip infusion.

Intramuscular Parentrovite – Contents of each pair of ampoules to be mixed in the syringe before injecting slowly into the lateral muscles of the thigh or into the gluteal region.

Contra-indications, warnings, etc

Contra-indications: Sensitivity to any of the vitamin: present.

Warnings and Precautions: On very rare occasions: repeated injections of preparations containing high concentrations of thiamine may give rise to anaphylactic shock. Should this occur, appropriate measures, such as the injection of adrenaline and soluble gluco-corticoid: (e.g. hydrocortisone) or anti-histamine preparation: must be taken immediately. Care should be exercised when Parentrovite is co-prescribed with levodopa: therapy in Parkinson's Disease, since pyridoxine may antagonise the therapy.

Active ingredients of Parentrovite	Intravenous		Intramuscular			
	High potency (IVHP)		High potency (IMHP)		Maintenance (IMM)	
	No. 1 (mg)	No. 2 (mg)	No. 1 (mg)	No. 2 (mg)	No. 1 (mg)	No. 2 (mg)
Thiamine hydrochloride (vitamin B ₁)	250		250		100	
Riboflavin (vitamin B ₂)	4		4		4	
Pyridoxine Hydrochloride (vitamin B ₆)	50		50		50	
Nicotinamide		160		160		160
Ascorbic acid (vitamin C)		500		500		500
Anhydrous dextrose		1,000				
Benzyl alcohol			140		80	
† contains 0.2% Chlorocresol				†		†
Volume per ampoule	5 ml	5 ml	5 ml	2 ml	2 ml	2 ml

Side-effects: Flushing of the face has been reported occasionally.

Overdosage: Effects of overdosage are rare. It has been reported, however, that following administration of very large doses (for example over 10 pairs IVHP daily for three or more days) a state of excitement can result which is characterised by rapid, though rational, mental activity. This subsides within 24 hours of stopping treatment, and there is often amnesia for the episode.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities

IV High Potency: 3 pairs, 12 pairs.

IM High Potency: 3 pairs, 12 pairs.

IM Maintenance: 3 pairs, 24 pairs.

Further Information Vitamins of the B complex play an integral part as co-enzymes in many stages of the intracellular metabolism of carbohydrates. The efficient functioning of this metabolism is essential for normal health. Similarly, ascorbic acid plays an important part in the biochemical reactions of cells and tissues and is normally present in the highest concentrations in those parts of the brain which are the most active metabolically.

Lack of the water soluble vitamins results in impairment of normal intracellular metabolism and may lead to certain disorders (see uses). In some cases, such as an alcoholic who develops Wernicke's encephalopathy, lack of immediate treatment can result in permanent brain damage or even death.

The very high concentrations of the water-soluble vitamins contained in Parentrovite, rapidly replenish depleted cellular stores and speed the return of normal metabolism.

Product licence numbers

IV High Potency: 0038/5095

IM High Potency: 0038/5097

IM Maintenance: 0038/5099

POLLINEX*

Presentation Pollinex contains glutaraldehyde-modified extracts of pollen from twelve varieties of common grasses (Bent, Brome, Cocksfoot, Crested Dogtail, False Oat, Fescue, Meadow Foxtail, Meadow-grass, Rye-grass, Timothy, Vernal and Yorkshire Fog) adsorbed on to tyrosine.

Each course of treatment is presented in three unit-dose syringes each prefilled with 0.5 ml of vaccine in graded concentrations as follows:

Syringe no.	Dose: Noon Units
1	300
2	800
3	2,000

The tyrosine content is 4.0% w/v, with Phenol BP as a preservative. The grass pollen extract is modified by glutaraldehyde and adsorbed onto tyrosine, a naturally occurring amino acid, to ensure slow release of the active material, giving a prolonged and efficient desensitising effect.

Uses Indicated for the treatment of classical hayfever and pollen asthma, to give long-term protection whenever grass pollens are considered to be the sole or predominant cause.

Pollinex is formulated from the pollens of twelve common grasses which are responsible for the majority of classical hayfever and pollen asthma cases, and provides a convenient and effective preventive treatment.

Dosage and administration Please note that the section on 'Contra-indications, warnings, etc.' must be studied before Pollinex is administered.

Adrenaline Injection BP (Adrenaline 1 in 1,000) should always be kept at hand when giving any desensitising vaccine.

The administration procedures shown in the leaflet included with each course of Pollinex should be carefully followed.

The course should normally be started by mid-April (in the U.K.) in order to ensure completion before the onset of the grass pollen season. Do not use during the grass pollen season.

Pollinex may be given to adults and children of six years and over. Injections should be given at intervals of 7–14 days. Pollinex must be removed from the refrigerator 2–3 hours before use. The syringe should be shaken thoroughly immediately prior to giving the injection. Injections should be given slowly by the subcutaneous route. Do not inject into a blood vessel or intramuscularly. Do not rub the site of injection.

The three graduated doses of Pollinex constitute a complete course for one year. The administration of an initial course of treatment should produce a significant improvement during the ensuing pollen season. For

continued clinical improvement, it is recommended that a course should be given in each of three successive years.

Contra-indications, warnings, etc

Contra-indications: Patients suffering from febrile conditions or an acute attack of asthma should not be given an injection until 24 hours after the condition has subsided.

It is advisable to avoid use during pregnancy, especially in the first trimester.

Precautions: Patients should be warned not to eat a heavy meal immediately before an injection is due to be given.

In very sensitive patients, it is advantageous to give an antihistamine tablet about one hour before each injection.

Injections should be given slowly by the subcutaneous route. Do not inject into a blood vessel or intramuscularly. Do not rub the site of injection.

Adrenaline Injection BP (Adrenaline 1 in 1,000) should always be kept at hand when giving any desensitising vaccine.

All patients should be instructed to remain under observation in the surgery for at least 20 minutes after each injection and advised to contact the doctor immediately in the unlikely event of a delayed reaction.

The patient should not take any strenuous physical exercise for several hours following the injection.

Reactions:

Local reactions, such as slight swelling or irritation, can sometimes occur and may require symptomatic treatment if they persist.

Mild systemic reactions such as rhinitis or urticaria may be treated with antihistamines orally, or by injection if necessary. In mild bronchospasm, a sympathomimetic bronchodilator such as salbutamol and possibly an anti-inflammatory steroid should be given. If required, 0.5 ml Adrenaline Injection BP (1 in 1,000) may be given subcutaneously.

Severe systemic reactions may occasionally arise in the form of typical allergic symptoms; anaphylaxis is rare.

Treatment of anaphylaxis:

Anaphylactic shock: characterised by bronchospasm, laryngeal oedema, urticaria and shock. Immediate attention should be given as follows:

1. The patient should be laid down and treated immediately.
2. 0.5 ml† Adrenaline Injection BP (Adrenaline 1 in 1,000) should be given intramuscularly close to the vaccine injection site. This should be repeated to a total of 2 ml† over 15 minutes if necessary. In extreme cases, 0.5 ml† Adrenaline (1 in 10,000) can be given by slow intravenous injection.
3. If bronchospasm persists, 10–20 ml† of Aminophylline Injection BP (250 mg per 10 ml) should be given by slow intravenous injection at a rate of 2 ml† per minute.
4. In addition, 200–400 mg† of Hydrocortisone Injection BP should be given intravenously. This is to combat persistent bronchospasm which can occur 6–8 hours after the initial collapse.
5. Full supportive measures should be available and employed if necessary and patients should be closely monitored for at least 24 hours after recovery.

Note: A severe local reaction, or severe systemic reaction such as urticaria or asthma, indicates that the standard

vaccine is unsuitable for the treatment of the particular patient, who should be referred to a consultant for advice or transferred to a suitably dilute specific desensitising vaccine (Alavac-S or SDV) obtainable from Bencard. (For full prescribing information please refer to the relevant data sheets.)

Pharmaceutical precautions Pollinex must be stored in a refrigerator (5°C). It must not be frozen and must be removed 2–3 hours before use.

Legal category POM.

Package quantities Each course of treatment consists of a set of 3 unit-dose syringes prefilled with vaccine, and with needles attached. An instruction leaflet is included with each set.

Further information Pollinex is a short-course 3-injection vaccine which offers a practical and more permanent alternative to temporary palliatives.

Pollinex may be prescribed on the basis of case history and clinical symptoms alone, providing these reveal marked seasonality corresponding with the grass pollen season. Pollinex is prescribable on NHS form FP10 and is available for immediate supply from stock.

The Bencard Medical Department will be pleased to advise on any aspect of treatment.

Product licence number 0038/0111.

PREGNAVITE FORTE* F

Presentation Lilac, sugar-coated tablets, overprinted (FP) in white.

Active ingredients

	Each tablet contains	Hence daily dose (1 tab. three times a day) provides
Vitamin A	1,333 units	4,000 units
Vitamin D ₂	133 units	400 units
Thiamine hydrochloride (vitamin B ₁)	0.5 mg	1.5 mg
Riboflavin (vitamin B ₂)	0.5 mg	1.5 mg
Pyridoxine hydrochloride (vitamin B ₆)	0.33 mg	1.0 mg
Nicotinamide	5.0 mg	15 mg
Ascorbic acid (vitamin C)	13.3 mg	40 mg
Dried ferrous sulphate (equiv. to 25.2 mg Fe)	84 mg	252 mg (equiv. to 75.6 mg Fe)
Calcium phosphate	160 mg	480 mg
Folic acid	0.12 mg	0.36 mg

Uses *Principal action:* Pregnavite Forte F is a balanced dietary supplement containing vitamins including folic acid, with iron and calcium.

Uses: Provision of vitamin and mineral support in pregnancy. Prevention of iron and folic acid deficiency anaemia in pregnancy.

Dosage and administration For oral administration only.

Adults: 1 tablet three times daily, during or after meals.

Children: Pregnavite Forte F is not suitable for children.

Contra-indications, warnings, etc

Contra-indications: Pernicious anaemia.

Side-effects: These are rare with Pregnavite Forte F but

† All dosages should be reduced as required for children.

and mild gastro-intestinal

in children.

On overdosage, the patient should be given desferrioxamine to reduce plasma iron to the desferrioxamine

recommended doses of vitamins A and B₁₂. Symptoms include joint swellings, anorexia and weight loss on discontinuation of

Store in a cool dry

10.

Protonix Forte F provides in addition folic acid, iron in an easily absorbed form, for the effective treatment of iron deficiency in pregnancy. It should be written in full on the prescription but without a signature.

8/5106.

White tablet embossed with 'IN'.

Contains:

100 mg

100 mg

Protonix is a fast acting buffer which acts in the mouth to release the active ingredient. It has a long sustained action and is simple and convenient to use.

Protonix is rapidly hydrolysed to aluminium hydroxide gel, maintaining the gastric

buffering capacity, and is not affected by dried aluminium hydroxide at high acid levels. It is fully effective at all times and is not diminished by

It sometimes causes constipation but is incorporated in Protonix

and dyspepsia; nausea and reflux oesophagitis.

For hyperacidity, dyspepsia, heartburn. One or two

tablets every hour.

Take one hour as required. Effect 1 tablet at a time

should be allowed to dissolve in the sulcus between the lower jaw and the cheek.

For extra rapid relief tablets may be chewed and swallowed.

Contra-indications, warnings, etc

Contra-indications: Nil.

Warnings and precautions: Nil.

Side-effects: No significant side-effects have been encountered with Protonix.

Overdosage: Overdosage has not been reported.

Pharmaceutical precautions Nil.

Legal category GSL.

Package quantities 30 tablets. 240 tablets.

Further information Protonix is a fast-acting buffer antacid which gives relief within minutes of placing a tablet on the tongue.

Protonix tablets are conveniently small and have a pleasant peppermint taste.

Product licence number 0038/5082.

SDV

(Specific Desensitising Vaccine)

Presentation SDV is an aqueous desensitising vaccine consisting of an individually formulated set of multidose vials of allergen extracts in graded concentrations. The No. 1 and No. 2 vials are 1/64th and 1/8th dilutions respectively of the No. 3 vial.

SDV courses are available in various strengths (full, half, quarter, eighth) to meet each particular patient's requirements. If required, special reduced strength courses can also be provided. (See 'Dosage and Administration'). When a vaccine is ordered for any patient with severe symptoms of allergy or any history of asthma a Special Dilution Vial (No. 0, Black label, 1/16th dilution of the No. 1 vial) will be provided automatically (except in cases where a special reduced strength course is supplied) and should be used to initiate therapy. Special Dilution Vials are also available on request for other patients.

The allergen extracts are incorporated in a base of physiological saline with Phenol BP 0.5% w/v as preservative.

Each course of SDV is specially prepared for an individual patient in accordance with the information on causative allergens revealed by case history and skin testing and recorded on Skin Test Reaction Charts or with orders.

For the best clinical results with SDV, no more than 6 allergens should normally be included (with a maximum of 8) in any one course.

If the patient is sensitive to more than eight allergens, those which can be avoided without undue inconvenience should be omitted, and the patient given advice on avoidance; otherwise two separate vaccines will be prepared.

Over 200 standard allergen extracts, including House Dust Mite, are available for inclusion and are listed in the Bencard Skin Testing Solutions Data Sheet.

Uses To provide fundamental treatment for a wide variety of common allergic conditions such as asthma, perennial rhinitis, hayfever and some skin conditions.

Dosage and administration Please note that the section on 'Contra-Indications, Warnings, Etc.' must be studied before SDV is administered.

Adrenaline Injection BP (Adrenaline 1 in 1,000) should always be kept at hand when giving any desensitising vaccine.

The administration procedures shown in the leaflet included with each course of SDV should be carefully followed.

In the dosage schemes which follow, all injections should be given at intervals of 3–7 days, unless otherwise stated.

These schemes should be followed for all SDV patients, irrespective of the course strength selected.

The vial should be shaken thoroughly immediately prior to withdrawing a dose.

Sterile syringes should always be used for the withdrawal of doses. Since each vial is used more than once, aseptic precautions must be sufficient to avoid the risk of microbial contamination.

Injections should be given slowly by the subcutaneous route. Do not inject into a blood vessel or intramuscularly. Do not rub the site of injection.

If a reaction occurs, the dosage should be adjusted accordingly (see Contra-indications, warnings etc).

SDV: Selection of course strength.

The strength of course should be selected according to the patient's previous history of asthma and severity of allergic symptoms as outlined below. When in doubt, the lowest strength course should be selected, or consultant advice sought.

Adults (aged 15 years or over):

<i>Clinical condition</i>	<i>Course strength</i>
Severe symptoms of allergy (e.g. eczema) or any history of asthma	Quarter
Moderate symptoms of allergy with no history of asthma	Half
Mild symptoms of allergy with no history of asthma	Full

Children:

Alavac-S (specific vaccine-alum adsorbed allergens) is normally preferred to SDV for the treatment of children. Please refer to the product data sheet for prescribing information. SDV may be considered when a vaccine containing allergens which are not included in the Alavac-S range is required. In such cases the following dosage schemes are recommended.

8–14 years:

<i>Clinical condition</i>	<i>Age</i>	<i>Course strength</i>
Severe symptoms of allergy (e.g. eczema) or any history of asthma	8–14	Consultant advice should be sought. If treatment is required a course of one-eighth strength or lower (special reduced strength) can be provided
Moderate symptoms of allergy with no history of asthma	8–11	Eighth
	12–14	Quarter
Mild symptoms of allergy with no history of asthma	8–11	Quarter
	12–14	Half

Under 8 years:

The use of SDV for children is not recommended by B. Consult consultant advice, treat specially reduced strength provided, with a dosage individual patient's requirements.

SDV: Dosage recommendations not contain pollen allergen:

Treatment should be given. Should be timed to end the patient's seasonal sensitivity. May for grass pollen sensitivity. For tree pollen sensitivity, treatment it is recommended each of three successive

Recommended dosage, not contain pollen allergen.

Not to be used during treatment

Commence with the first course and proceed to the No. 2 (B label) vial as indicated

If a reaction occurs, the dosage should be reduced: see 'Adjustment of dosage'

<i>Vial Number*</i>	<i>Injections</i>
1. Green label	1 2 3 4 5 6
2. Buff label	7 8 9 10 11 12
3. Red label	13 14 15 16 17 18

*When a Special Dilution is initiated, treatment, dosage provided in an accompanying leaflet.

Surplus vaccine may be used in the next season.

Extended treatment: onset of the pollen season it may be beneficial to fortnightly intervals, 4 weeks before the pollen season.

SDV: Dosage recommendations not contain pollen allergen:

Courses may be given in the following order:

Commence with the first course and proceed to the No. 2 (B label) vial as indicated

If a reaction occurs, the dosage should be reduced: see 'Adjustment of dosage'

Injection Number	Dosage
	0.1 ml 0.2 ml 0.3 ml 0.5 ml 0.7 ml 1.0 ml
	0.1 ml 0.2 ml 0.3 ml 0.5 ml 0.7 ml 1.0 ml
	0.1 ml 0.2 ml 0.3 ml 0.5 ml 0.7 ml 1.0 ml

/ial (No. 0, Black label) is supplied to instructions relating to its use are on leaflet.

ment following the initial course is

for use only with vaccines which

which consists of a series of recommended particularly for

patients with perennial symptoms provided that the initial treatment course has been well tolerated.

Maintenance therapy should commence between 1 and 2 weeks after completion of the initial course and should follow the dosage scheme below. Treatment may be continued at the discretion of the physician, with review at appropriate intervals.

Maintenance Dosage Schemes. (See tables.)

N.B. Care must be taken when administering the first injection from a new No. 3 vial as in a small number of cases, a local or general reaction may occur. If a reaction occurs during treatment, dosage should be reduced: see 'Adjustment of Dosage'.

Contra-indications, warnings, etc

Contra-indications: Patients suffering from a febrile condition or an acute attack of asthma should not be given an injection until 24 hours after the condition has subsided.

It is advisable to avoid use during pregnancy, especially in the first trimester.

Precautions: Patients should be warned not to eat a heavy meal immediately before an injection is due to be given.

In very sensitive patients it is advantageous to give an antihistamine tablet about one hour before each injection.

Injections should be given slowly by the subcutaneous route. Do not inject into a blood vessel or intramuscularly. Do not rub the site of injection.

Adrenaline Injection BP (Adrenaline 1 in 1,000) should always be kept at hand when giving any desensitising vaccine.

Maintenance Therapy: (using No. 3 vial supplied with Initial Course).

Interval Since Previous Injection*	Dosage (ml) (From No. 3 Vial)	Duration
1-2 weeks after completion of Initial Course	1.0 ml (or maximum tolerated dose if lower)	Continue until contents of No. 3 vial are exhausted.
1 week	1.0 ml (or maximum tolerated dose if lower)	Then introduce new No. 3 vial as described below.

Maintenance Therapy: Dosage scheme to be followed when introducing a new No. 3 vial.

Interval Since Previous Injection*	Dosage (ml) (From No. 3 Vial)	Duration
1 week	0.1 ml	Maintenance therapy may be continued at the discretion of the physician, with review at appropriate intervals.
1 week	0.2 ml	
1 week	0.4 ml	
1 week	0.8 ml	
1 week	1.0 ml	
2 weeks	1.0 ml	
4 weeks	1.0 ml	

be suitable for resumption of maintenance therapy following an interruption of treatment – see

required if more than 4 weeks elapse:

aintenance therapy following completion of the initial course;

se injections.

ist be modified as follows:

has elapsed treatment may be resumed with caution, using the dosage scheme specified above for the vial.

e elapsed since the previous injection, it is advisable not to attempt maintenance therapy but to re-start with commencing with the lowest strength (No. 1, green label) vial.

se for use with pollen-containing vaccines.

All patients should be instructed to remain under observation in the surgery for at least 20 minutes after each injection and advised to contact the doctor immediately in the unlikely event of a delayed reaction.

The patient should not take any strenuous physical exercise for several hours following the injection.

Reactions: (see also 'Adjustment of Dosage'):

Local reactions, such as slight swelling or irritation, can sometimes occur and may require symptomatic treatment if they persist.

Mild systemic reactions such as rhinitis or urticaria may be treated with antihistamines orally, or by injection if necessary. In mild bronchospasm, a sympathomimetic bronchodilator such as salbutamol and possibly an anti-inflammatory steroid should be given. If required, 0.5 ml Adrenaline Injection BP (Adrenaline 1 in 1,000) may be given subcutaneously.

Severe systemic reactions may occasionally arise in the form of typical allergic symptoms; anaphylaxis is rare.

Treatment of anaphylaxis:

Anaphylactic shock: characterised by bronchospasm, laryngeal oedema, urticaria and shock. Immediate attention should be given as follows:

1. The patient should be laid down and treated immediately.
2. 0.5 ml Adrenaline Injection BP (Adrenaline 1 in 1,000) should be given intramuscularly close to the vaccine injection site. This should be repeated to a total of 2 ml over 15 minutes if necessary. In extreme cases, 0.5 ml Adrenaline (1 in 10,000) can be given by slow intravenous injection.
3. If bronchospasm persists, 10–20 ml of Aminophylline Injection BP (250 mg per 10 ml) should be given by slow intravenous injection at a rate of 2 ml per minute.
4. In addition, 200–400 mg of Hydrocortisone Injection BP should be given intravenously. This is to combat persistent bronchospasm which can occur 6–8 hours after the initial collapse.
5. Full supportive measures should be available and employed if necessary and patients should be closely monitored for at least 24 hours after recovery.

Adjustment of Dosage (in the event of the occurrence of a reaction):

Reaction to the first injection:

If the patient has a significant reaction to the first dose from the No. 1 vial, the complete course should be returned direct to Bencard. A Special Dilution vial (No. 0-Black label; 1/8th dilution of the No. 1 vial) will be prepared free of charge and returned with a complete new course.

Treatment should recommence from the dilute vial according to the dosage scheme issued with it, but no attempts should be made to exceed the maximum tolerated dose.

Reactions to subsequent injections:

Local

Mild reaction: Reduce the dose by one step.

Severe reaction: Reduce the dose by two steps.

Systemic

Mild reaction: Reduce the dose by two steps.

Severe reaction: Treatment should be discontinued.

Except in cases where a severe systemic reaction has occurred, the course may be continued with caution up to the top dose quoted, or to the highest dose tolerated without significant reaction.

† All dosages should be reduced as required for children.

Pharmaceutical precautions SDV must be stored in a refrigerator (2–8°C). It must not be frozen. Vaccine left over from SDV courses containing pollen allergens must not be used the following year.

Vaccine left over from the No. 3 vial of courses which do not contain pollen allergens may be used for maintenance therapy (see Maintenance therapy for vaccines which do not contain pollen allergens).

Legal category POM.

Package quantities Each course of treatment consists of a set of three multidose vials of vaccine in grade concentrations. An instruction leaflet is supplied with each set.

The No. 3 vial is also available for physicians practising maintenance therapy with SDV courses which do not contain pollen allergens (see Dosage and Administration).

Normal delivery time for a complete course or a single vial is about two weeks to allow for individual formulation and sterility testing.

Further information Ordering Procedure: FP10 form (or other prescriptions) should be taken to a chemist who will arrange the supply of the vaccine.

The prescription should be accompanied by the following information:

When available a Skin Test Reaction Chart or a list of the allergens to be included in the vaccine with a note of the patient's sensitivity to each one, or the reference number of a previous course.

Patient's name

Patient's date of birth and/or age

The Bencard Medical Department will be pleased to advise on any aspect of treatment.

Product licence number 0038/5000.

VITAVEL* SYRUP

Presentation *Appearance:* Orange coloured syrup.

Active ingredients: One 5 ml spoonful contains:

Vitamin A	4000 units
Vitamin D ₂	300 units
Vitamin B ₁ (Thiamine hydrochloride)	0.8 mg
Vitamin C	16 mg
Glucose	25% w/v

in an orange flavoured sucrose base.

Uses *Principal action:* Vitavel is a multivitamin dietary supplement.

Uses: As a course of vitamin supplementation therapy in premature babies and in infancy, during periods of rapid growth in childhood and adolescence, during illness and convalescence. For adults, during pregnancy and lactation or when tablets cannot be tolerated.

Dosage and administration For oral administration only.

Children and adults: One or two 5 ml spoonfuls daily.

Infants: 2.5 ml to 5 ml in a little water daily. (Syrup B is a suitable diluent.)

Contra-indications, warnings, etc

Contra-indications: Nil.

Side-effects: None reported.

Overdosage: Prolonged ingestion of massive doses of vitamins A and D can lead to hypervitaminosis state.

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ough skin, painful joint swellings, but these disappear on discontin-

Precautions Store in a cool place. Protected from strong light and be dispensing into amber glass container suitable diluent.

Further information Vitavel provides the essential vitamins to ensure health in children of all ages. Vitavel is well tolerated and extremely palatable and can be mixed with many foods and preparations. There is no oiliness or fishiness in the taste, in contrast to many comparable medications.

Product licence number 0038/5083.

Syrup 200 ml, 1 litre.

**Trade Mark*

Bengué & Company Limited

St Ives Road

Maidenhead

Berkshire SL6 1RD

BENGUÉ'S BALSAM*

Presentation Creamy yellow, soft, greasy ointment: odour of menthol and methyl salicylate. Menthol 20%, methyl salicylate 20% in lanolin base.

Uses Topically as a rubefacient and counter-irritant for the alleviation of rheumatic and nerve pains; as a decongestant by application to the chest or inhalation from hot water in head colds, coughs and laryngo-bronchitis.

Dosage and administration Apply with gentle massage to the affected area.

Contra-indications, warnings, etc Not to be used as an inhalant in children under the age of six years.

Pharmaceutical precautions Store in a cool place. Incompatible with aqueous liquids or emulsions.

Legal category GSL.

Package quantities Tubes of 25 g.

Further information Nil.

Product licence number 0102/5005.

BENGUÉ'S BALSAM SG*

Presentation White, non-greasy cream: odour of menthol and methyl salicylate. Menthol 10%, methyl salicylate 15% in vanishing cream base.

Uses Topically as a rubefacient and counter-irritant for the alleviation of rheumatic and nerve pains; as a decongestant by application to the chest or inhalation from hot water in head colds, coughs and laryngo-bronchitis.

Dosage and administration Apply with gentle massage to the affected area.

Contra-indications, warnings, etc Not to be used as an inhalant in children under the age of six years.

Pharmaceutical precautions Store in a cool place.

Legal category GSL.

Package quantities Tubes of 25 g.

Further information Nil.

Product licence number 0102/5006.

CORTENEMA*

Presentation Off-white, slightly viscous suspension. Each 60 ml unit contains hydrocortisone 100 mg in aqueous isotonic saline.

Uses An adjunct in the treatment of idiopathic specific ulcerative colitis. It is most useful in involving the rectum, sigmoid and descending colon. Rectal steroid therapy brings about prompt and proctological remissions in a significant number of patients, but it does not alter the progressive nature of ulcerative colitis. This form of treatment is not recommended for patients during periods of remission.

Dosage and administration The usual dose is 100 ml of Cortenema Retention Enema daily for the first 7 days, and every second day thereafter. The enema should be given intra-rectally in the evening before bedtime. The patient should be made to retain the medication for at least 1 hour, preferably all night. This may be facilitated by sedation and/or antidiarrhoeal medication. If proctological improvement fails to occur after three weeks, this form of treatment should be discontinued.

Instruct the patient to lie on his left side for instillation. The bottle must be shaken well to ensure homogeneity. Expose the lubricated tip of the protective sheath, grasping the neck where it is most rigid. Carefully insert the tip into the rectum in the distal sacrum. Slowly express the contents by compressing the container. After instillation, the patient should lie on his left side for at least thirty minutes to allow distribution of the hydrocortisone throughout the descending colon and rectum. In order to reach the more distant segments of the colon, Cortenema may be given with isotonic saline, from 100 ml to 300 ml, administered by intra-rectal drip.

Contra-indications, warnings, etc Cortenema is not suitable in cases where several complications are present, including obstruction, abscesses, fistulae and sinus tracts, are present. Patients with ulcerative disease are unsuitable because of perforation of the bowel wall.

Pharmaceutical precautions Store in a cool place. Protect the enemas from light.

Legal category POM.

Package quantities Cartons of 7 x 60 ml units.

Further information The flexible disposable container with lubricated applicator nozzle is designed for ease of self-administration for out-patient use. To obtain optimum distribution of the enema it is important that patients should follow the illustrated directions enclosed in each pack.

Product licence number 0102/5010.

DERBAC* LIQUID WITH MALATHION

Presentation A white, creamy liquid containing malathion 0.5% w/w.

Uses Eradication of head lice and pubic lice and their eggs. Treatment of scabies.

Dosage and administration *Adults and children:*

1. Treatment of head lice.
 - a) Apply Derbac Liquid to the roots of the hair and scalp, paying special attention to the partings, back of the neck, fringes and around ears.
 - b) Leave the hair to dry naturally and wash in ordinary shampoo the next day.
 - c) After shampoo wash, remove dead eggs (nits) with the Derbac metal comb *while the hair is wet*.
2. Treatment of pubic lice.
 - a) Apply freely to all parts of the hair in the affected areas, paying special attention to the roots.
 - c) Leave for at least one hour and then remove by washing with a bland shampoo or soap. If more convenient, Derbac Liquid can be left on overnight.
3. Treatment of scabies.
 - a) Take a fairly prolonged soap and water bath, rubbing the principal areas of involvement with a brush or wash-cloth.
 - c) Apply Derbac Liquid to the entire skin surface, excepting the head. This is best done by someone other than the patient to avoid missing some areas.
 - c) Do not bathe for 24 hours. Put on fresh clothing. No special sterilisation of clothing is necessary; ordinary laundering or dry cleaning and hot iron pressing are sufficient.
 - d) The itching may not subside immediately; calamine lotion may be applied if necessary.

Not to be used in children under the age of six months except under medical supervision.

Contra-indications, warnings, etc There are no known contra-indications to the use of Derbac Liquid. As with all medicated products, keep out of the eyes, as some irritation may occur.

It is advisable that clinic workers in regular contact with this product should wear rubber gloves when carrying out treatment.

Derbac Liquid is for external use only and should be kept out of the reach of children. If Derbac Liquid is inadvertently swallowed, a doctor or casualty department should be contacted at once.

Continued prolonged treatment with Derbac Liquid should be avoided. It should not be used more than once a week for three weeks at a time.

Treatment of overdosage: It is most unlikely that a toxic dose of malathion will be ingested. Treatment consists of gastric lavage, assisted respiration and, if necessary, administration of atropine.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities Bottles of 50 ml and 155 ml.

Further information For less severe infestations use Derbac Shampoo or Derbac Soap.

Product licence number 0102/0005.

DERBAC* SHAMPOO WITH CARBARYL

Presentation A yellow opalescent liquid containing carbaryl 0.5% w/w in a shampoo base.

Uses Treatment of head lice (pediculosis).

Dosage and administration *Adults and children:* For less severe infestations wash the hair thoroughly with Derbac Shampoo, rinse with clean water, apply a further quantity of shampoo and work into a rich lather. Allow to remain on the head for five minutes. Rinse with clean water and remove nits with the Derbac Comb.

Not to be used in children under the age of six months except under medical supervision.

Contra-indications, warnings, etc There are no known contra-indications to the use of Derbac Shampoo. As with all medicated shampoo products, keep out of the eyes, as some irritation may occur.

It is advisable that clinic workers in regular contact with this product should wear rubber gloves when carrying out treatment.

Derbac Shampoo is for external use only and should be kept out of the reach of children. If Derbac Shampoo is inadvertently swallowed, a doctor or casualty department should be contacted at once.

Continued prolonged treatment with Derbac Shampoo should be avoided. It should not be used more than once a week for three weeks at a time.

Treatment of overdosage: It is most unlikely that a toxic dose of carbaryl will be ingested. Treatment consists of gastric lavage, assisted respiration and, if necessary, administration of atropine.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities Bottles of 50 ml.

Further information For severe cases of infestation, Derbac Liquid with Malathion should be used.

Product licence number 0102/0006.

DERBAC* SOAP

Presentation An ivory-white soap tablet containing γ -benzene hexachloride 1% w/w and cresol 0.779% w/w.

Uses As an adjunct to therapy with Derbac Liquid and Derbac Shampoo and for scalp hygiene.

Dosage and administration *Adults and children:*

1. For severe cases of infestation with head lice use Derbac Liquid. Apply freely to all parts of the hair, paying special attention to the roots and the scalp. Leave to dry naturally, then remove by washing with a bland shampoo or Derbac Soap. Remove nits using the Derbac Comb.
2. For less severe infestations wash the hair thoroughly with Derbac Soap, rinse with clean water, apply a further quantity of cleanser and work into a rich lather. Allow to remain on the head for 15 minutes, rinse with clean water and remove nits with the Derbac Comb.

Contra-indications, warnings, etc There are no known contra-indications to the use of Derbac Soap. As with all medicated products, keep out of the eyes, as some irritation may occur.

It is advisable that clinic workers in regular contact with this product should wear rubber gloves when carrying out treatment.

Derbac Soap is intended for external use only and should be kept out of the reach of children.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities Tablets of 74 g (2½ oz).

Further information Nil.

Product licence number 0102/5900.

NESTOSYL* OINTMENT

Presentation Buff-coloured, greasy ointment; odourless. Benzocaine 2%, butyl aminobenzoate 2%, resorcin 2%, zinc oxide 10%, hexachlorophane 0.1%.

Uses Topically for the relief of local pain and irritation in lacerated skin conditions; also in haemorrhoids and anal pruritus.

Dosage and administration Apply and cover if necessary with a light dressing.

Contra-indications, warnings, etc Idiosyncrasy to aminobenzoates. Not to be used for babies.

Pharmaceutical precautions Store in a cool place. Replace cap after use. Incompatible with aqueous liquids and emulsions.

Legal category P.

Package quantities Tubes of 30 g supplied with rectal nozzles.

Further information Nil.

Product licence number 0102/5015.

OPOBYL*

Presentation Spherical pills approx. 7.5 mm diameter, coated deep blue with name of product printed in black. Desiccated liver 50 mg, sodium tauroglycocholate 50 mg, aqueous extract of boldo 10 mg, podophyllin 2 mg, alcoholic extract of euonymus 2 mg, aloes 20 mg per pill.

Uses Hepatic insufficiency. Biliary stasis. Habitual constipation caused by intestinal sluggishness.

Dosage and administration *Adults:* One or two pills before or after meals.

Not recommended for children.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Tubes of 50 pills.

Further information Nil.

Product licence number 0102/5017.

PYOREX* MEDICATED TOOTHPASTE

Presentation Homogeneous pink paste, odour a taste of aniseed and peppermint. Acetarsol lithic equivalent to acetarsol 0.45%, aminacrine hydrochlor 0.006%, sodium ricinoleate 0.76%.

Uses Topically, for cleansing the teeth and prevention and treatment of pyorrhoea, stomatitis & gingivitis.

Dosage and administration Apply to gums tw daily.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Tubes of 50 g.

Further information Nil.

Product licence number 0102/5021.

RHINAMID*

Presentation Clear, colourless aqueous liquid; od of rosemary; bitter taste. Sulphanilamide 0.4%, ephedrine hydrochloride 1.0%, butacaine sulphate 0.026%.

Uses As an antiseptic and nasal decongestant, inflammatory and congestive affections of rhinopharynx.

Dosage and administration Two to three drops i each nostril two to five times daily.

Contra-indications, warnings, etc Sulphanilamide sensitivities. The prolonged use of vasoconstrictor: not recommended in chronic rhinitis.

Pharmaceutical precautions To avoid crystallisation do not store in a very cold place.

Legal category POM.

Package quantities Dropper bottles of 30 ml.

Further information Nil.

Product licence number 0102/5022.

*Trade Mark

Berk Pharmaceuticals Limited
St. Leonards House
St. Leonards Road
Eastbourne East Sussex BN21 3UU



ARVIN*

Presentation A sterile, clear, colourless aqueous solution of anicrod for intravenous and subcutaneous injection. Each 1 ml contains 70 International units put up in isotonic saline. pH is 6.8, phosphate content approximately 0.0025 M, chlorbutol approximately 0.005% w/v.

The International unit is defined as the specific biological activity contained in 0.307 mg of the International Standard for anicrod.

Uses For the prevention of deep venous thrombosis after surgical repair of fractured neck of femur, and of re-thrombosis after thrombolytic therapy or vascular surgery.

For the treatment of established deep vein thrombosis, central retinal and branch vein thrombosis, priapism, pulmonary hypertension of embolic origin, embolism after insertion of prosthetic cardiac valves.

Arvin acts enzymatically on the fibrinogen molecule to form friable, unstable non cross-linked particles 1–2 μ m long, easily digested by plasmin and removed by reticulo-endothelial phagocytosis and/or fibrinolysis. Other clotting factors are not affected and unlike thrombin Arvin does not directly activate Factor XIII or plasminogen, does not degrade pre-formed fully cross-linked thrombin fibrin or produce platelet aggregation. It does not cause the release of ADP, ATP, potassium or serotonin from platelets. Platelet survival and counts are normal.

When the fate of Arvin labelled with 125 I is followed, half the radioactivity disappears from the plasma in three to five hours, and at about four days 10% remains.

The blood viscosity in patients receiving Arvin is progressively reduced by 30–40% of the pre-treatment levels.

Dosage and administration *Induction Dose i.v.*

Route: The first dose of Arvin must be given slowly so that the physiological methods of dealing with the particulate fibrin are not overloaded.

2–3 units/kg body weight in 50–500 ml Sodium Chloride Injection BP by intravenous drip during a period of 4 to 12 hours, usually six to eight hours, according to the situation. Dextran must not be used.

There is no information concerning the safety of reducing the induction dose duration to less than four hours in man.

Maintenance Doses i.v. Route: 2 units/kg body weight in 10–50 ml Sodium Chloride Injection BP by intravenous injections at 12 hour intervals, given slowly, taking about five minutes over each injection. Alternatively, the maintenance dose can be given by slow drip or pump infusion.

It is considered that the ideal period of treatment in patients with conditions such as deep vein thrombosis, central retinal vein thrombosis, etc. is of the order of seven days. Some patients have been successfully treated with Arvin for periods of up to 28 days.

Subcutaneous dosage for the prophylaxis of DVT in patients undergoing surgery for fractured neck of femur: Four ampoules as a single s.c. injection immediately after surgery then one ampoule daily for the next four post-operative days.

Control methods and recommended aims: There are three usual methods of estimating the effect of Arvin on the plasma fibrinogen. The reference and aims are given below and copies of the methods are available on application to the Company.

The general aim is to ensure that fibrinogen levels are maintained at or below 50 mg/100 ml and the clot quality observation test is adequate for this purpose.

1. **Method:** Clot quality observation test, Reid, H. A., Chan, K. E., and Thean, P. C. (1963): *Lancet*, i, 621.

Aim: Grade 4 ('Mini-clot'). Diameter of clot = 2 to 3 mm.

2. **Method:** Gravimetric method modification by Pitney, W. R., of Ratnoff, O. D., and Menzie, C. (1951): *J. Lab. Clin. Med.*, 37, 316.

Aim: Plasma fibrinogen $\leq$ 50 mg %.

3. **Method:** Titre in saline and protamine sulphate. Modification by Royal Postgraduate Medical School, London, of Sharp, A. A., Warren, B. A., Paxton, A. M., and Allington, M. J. (1968): *Lancet*, i, 493.

Aim: Saline	Protamine
0 to $\frac{1}{2}$	$\frac{1}{2}$ to $\frac{1}{4}$

Contra-indications, warnings, etc

Contra-indications: Severe infections and diffuse intravascular coagulation – there is some evidence that the Arvin effect may be dangerous in septicæmic states with or without evidence of diffuse intravascular coagulation.

Plasma expanders – Artificial plasma expanders (e.g. Dextran) may cause severe bleeding in defibrinated patients and should not be administered during or within 10 days of Arvin therapy.

Pregnancy – Arvin was not found to be teratogenic in animal studies, but some foetal deaths occurred as a result of placental haemorrhages in animals given high doses. Arvin should not, therefore, be used during pregnancy. The defibrination mechanism of Arvin might be expected on theoretical grounds to interfere with the normal implantation of the fertilised egg.

Gastro-intestinal pathology – the presence of lesions liable to bleed, such as peptic ulcer, ulcerative colitis, etc.

Ulcero-genic drugs – similarly, patients on drug regimes known to cause gastro-intestinal bleeding should not be given Arvin.

Haematological defects – underlying defects interfering with haemostasis, such as a platelet count $< 100,000/\text{cu mm}$. are also contra-indications.

Reticulo-endothelial and lytic systems – drugs that block the reticulo-endothelial system (e.g. dextrans), or the physiological lytic system (e.g. EACA), should not be used concurrently with Arvin.

Side-effects: Haemorrhage – if necessary, the effects of Arvin may be rapidly reversed by the specific antidote described below. In most instances this is unnecessary – stopping Arvin therapy will allow the fibrinogen to return to haemostatic levels within a few hours.

Whole blood, plasma or albumin may be given as needed, but artificial plasma expanders must not be used until plasma fibrinogen levels have returned to normal.

Minor bleeding and oozing – these are simply dealt with by pressure.

Skin rash – reactions are rare and have responded to antihistamine.

Precautions: Induction Dose – the first dose of Arvin must not be given faster than over a period of four hours. Six to eight hours is the ideal duration.

Pretreatment investigations – it is recommended that a blood film, platelet count and fibrinogen estimation should be made before treatment.

Daily control – it is considered necessary to repeat the fibrinogen estimation each day when Arvin is given by the intravenous route.

Arvin should not be given in association with artificial plasma expanders such as Dextran.

Cardiovascular disease – the following cardiovascular conditions may be complicated by defibrination: malignant hypertension, acute pericarditis; sub-acute bacterial endocarditis, retinopathy, grade 3 or worse; diabetic retinopathy; resting diastolic pressure > 120 mm Hg.

Other conditions – similarly, defibrination may cause bleeding in uraemia > 100 mg%; renal colic with calculus; cerebrovascular accidents; history of neurosurgery.

Circulatory insufficiency – If the Induction Dose is given rapidly there may be an initial rise in blood viscosity. Where there is circulatory insufficiency the period of administration should be lengthened to 12 hours.

Coronary thrombosis – in view of some evidence of delay in wound healing in experimental animals, it is considered at the present time that Arvin should not be used in coronary thrombosis, until further data on safety are available.

Migraine – a few patients with a history of migraine have experienced headaches after Arvin injections. Maintenance doses should be given very slowly to such patients.

Minor surgery – it is possible to carry out minor surgery (e.g. opening an abscess) while the patient is on Arvin, but each case must be carefully judged for risk of bleeding.

Major surgery – usually intravenous Arvin is not recommended before, during or within 48 hours of major surgery. An exception is to prevent rethrombosis after vascular surgery when the risk of bleeding does exist. Arvin should be given immediately post-operatively.

Intramuscular route – this is not recommended as an alternative to intravenous administration owing to the risk of inducing antibody formation. Subcutaneous Arvin has shown good control of fibrinogen levels and continues to be studied.

ESR – during treatment with Arvin, the erythrocyte sedimentation rate falls to about 1 mm/hour and cannot be used as an index of pathological activity.

Treatment of overdosage: A specific antidote to Arvin has been prepared.

It is filled in 1 ml ampoules and each 1 ml is sufficient to neutralise 70 International units of Arvin *in vivo*.

The need for the antidote has been very rare, but it is recommended that it is always available when Arvin is

used. Antidote should be used in the event of severe haemorrhage, or if major surgery becomes necessary. The following procedure is recommended for the use of the antidote:

1. 1 in 1,000 adrenaline should be available on the giving tray.

2. Give 0.2 ml antidote subcutaneously and observe for an erythematous reaction for half hour.

3. If satisfactory, give 0.8 ml antidote intramuscularly and observe for a nodular reaction for a further half hour.

4. If satisfactory, give 1 ml intravenously.

5. Give 5 g human fibrinogen intravenously (available from the Regional Blood Transfusion Centre). If this is not available, give 1 litre fresh plasma or whole blood.

The whole procedure takes about one hour and the plasma fibrinogen is normal at the end of it.

In emergencies the intramuscular dose may be omitted. It is recommended that the subcutaneous test dose is never omitted. In the case of a reaction after the subcutaneous dose, do not give any more antidote but give fresh plasma or whole blood. If a nodular reaction after the intramuscular dose is observed, it is expected that any serum sickness to follow will be very mild owing to the highly purified state of the globulin.

The above steps are those usually taken when it is considered adequate to return the plasma fibrinogen to normal levels in about one hour. *In the case of life-threatening bleeding, however, when immediate neutralisation of the Arvin effect is essential, the highly purified nature of the antidote allows intravenous injection without the usual trial doses, with a normal supportive corticosteroid/antihistamine regime ready if anaphylactic shock develops. Fibrinogen should also be administered as in paragraph 5 above.*

Pharmaceutical precautions Store under refrigeration (4–10°C). Do not freeze.

Legal category POM.

Package quantities Ampoules 1 ml containing 70 International units per ml. Pack of 4.

Further information *Clinical effects:* The properties of Arvin provide *controlled therapeutic defibrination* to prevent the formation and extension of thrombi and the dissemination of emboli. Despite marked hypocoagulability, spontaneous haemorrhage is rarely observed, although serosanguineous oozing or frank haemorrhage may be seen in incompletely healed operation wounds. Consistent clinical features include the absence of thromboembolic events during treatment, normal menstruation, absence of fibrinogen rebound and a very low incidence of rethrombosis after treatment is stopped. The plasma fibrinogen returns to haemostatic levels within 12 hours and to normal levels usually around the 10th post treatment day, but in a few patients this may be delayed for a further 10 days. Apart from apparently avoiding rebound hypercoagulation, this slow return of fibrinogen allows a smooth change over to oral anticoagulants when necessary. While Arvin does not lyse established thrombi, rapid resolution of secondary oedema has been noted frequently and is believed to result from improved flow in the microcirculation.

Product licence number 0152/0099.

ASILONE®

Presentation *Tablets:* White, square tablets marked 'ASILONE'. Each tablet contains activated dimethicone

270 mg and the equivalent Dried Aluminium Hydroxide BP 500 mg.

Orange Tablets: Orange, square tablets marked 'ASILONE'. Each orange flavoured tablet contains activated dimethicone 270 mg and the equivalent of Dried Aluminium Hydroxide BP 500 mg.

Suspension: White suspension containing in each 5 ml activated dimethicone 135 mg and the equivalent of Dried Aluminium Hydroxide BP 420 mg and Light Magnesium Oxide BP 70 mg.

Gel: Thick white suspension containing in each 5 ml, activated dimethicone 135 mg and the equivalent of Dried Aluminium Hydroxide BP 420 mg and Light Magnesium Oxide BP 70 mg.

Asilone for Infants: White, blackcurrant-flavoured suspension containing in each 5 ml, activated dimethicone 27 mg and the equivalent of Dried Aluminium Hydroxide BP 84 mg and Light Magnesium Oxide BP 14 mg.

Uses Mucosal protective, antifatulent and antacid; dyspepsia, flatulence and abdominal distension; heartburn in pregnancy; heartburn in hiatus hernia; drug-induced gastritis, dietary induced gastritis; symptomatic relief in peptic ulceration.

Asilone for Infants: The treatment of wind pains, 'gripes' and regurgitation in infants over one month of age.

Dosage and administration *Tablets and orange tablets:* 1–2 tablets chewed or sucked before meals and at bedtime. For heartburn they should be sucked slowly.

Suspension & gel: One or two 5 ml spoonfuls before meals and at bedtime.

Asilone for infants: Infants 1–3 months: 2.5 ml 3 to 4 times daily before or during a feed.

3 months and over: one 5 ml spoonful three to four times daily before or during a feed.

In windy colic it may be necessary to continue dosage for 24 hours before relief is achieved. Asilone for Infants may be given at the recommended dosage for several weeks, if that is necessary, but should not be continued for more than 48 hours without medical advice, as symptoms may not be due to intestinal gas. It should not be used in infants under one month of age.

Contra-indications, warnings, etc There are no known contra-indications to Asilone, but it is probably wise to avoid taking preparations containing antacids in the first trimester of pregnancy.

Very rarely, minor disturbances of bowel function have been reported.

Asilone Tablets and Asilone Orange Tablets each contain 1 g sucrose per tablet and are therefore less suitable for diabetic patients than the Suspension and Gel which contain no sugars.

Pharmaceutical precautions No special precautions.

Diluent for Asilone for Infants, Asilone Suspension and Gel: Purified Water BP.

Legal category

Tablets: GSL.

Suspension: GSL.

Gel: P.

Asilone for infants: P.

Orange tablets: P.

Package quantities *Tablets:* Packs of 12 and 100.

Suspension: Bottles of 100 ml, 300 ml and 500 ml.

Gel: Bottles of 300 ml and 500 ml.

Asilone for infants: Bottles of 100 ml.

Orange tablets: packs of 100.

Further information The sodium content of the adult Asilone range is low. Asilone is, therefore, particularly suited to the management of gastro-oesophageal conditions where there is co-existing hypertension, congestive heart failure, hepatic failure and/or renal failure.

Asilone suspension: typical sodium content 0.032 to 0.097 mmol per 10 ml.

Asilone gel: typical sodium content 0.040 to 0.090 mmol per 10 ml.

Product licence numbers

Tablets 0152/5025

Suspension 0152/5026

Gel 0152/0082

Asilone for Infants 0152/0087.

Orange Tablets 0152/0139

ATENSINE*

Presentation White Diazepam Tablets BP 2 mg, marked 'BERK 2', with single break line.

Yellow Diazepam Tablets BP 5 mg, marked 'BERK 5', with single break line.

Blue Diazepam Tablets BP 10 mg, marked 'BERK 10', with single break line.

Uses Acute and chronic anxiety, tension states and muscle spasm.

Dosage and administration *Acute and chronic anxiety states:* Mild anxiety in ambulant patients 2 mg t.i.d.

Severe anxiety states, 15–30 mg daily in divided doses.

Children: 1–5 mg daily in divided doses.

Insomnia associated with anxiety: 5–30 mg before retiring.

Conditions associated with muscle spasm: Spastic children with minimal brain damage: 2–40 mg daily in divided doses.

Cerebral palsy of adults, particularly associated with athetoid movements: 2–60 mg daily in divided doses.

Upper motor neuron spasticity: 5–60 mg daily in divided doses.

Muscle spasm of varied aetiology, fibrositis, cervical spondylosis: 2–15 mg daily in divided doses.

Premedication for dental operations: One 5 mg tablet the night before the appointment, 5 mg on waking and 5 mg two hours before the appointment.

Atensine should be given to elderly and debilitated patients in doses half those recommended for ordinary adults.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to benzodiazepines.

Acute pulmonary insufficiency.

Acute narrow angle glaucoma.

Use in pregnancy: Not to be taken during pregnancy, especially in the first trimester, unless there are compelling reasons.

Precautions: Chronic pulmonary insufficiency.

In chronic renal or hepatic disease.

In labour. High single doses or repeated low doses have been reported to produce hypotonia, poor sucking and hypothermia in the neonate and irregularities in the foetal heart.

Avoid if possible in lactation.

The concurrent use of other CNS depressant drugs should be avoided.

Warnings and adverse effects: Common adverse effects include drowsiness, sedation, unsteadiness and ataxia.

Performance and alertness may be impaired during the first week of administration. Patients should be warned of the possible hazard when driving or operating machinery. These effects may be potentiated by alcohol.

The elderly and the debilitated are particularly liable to experience these symptoms, together with confusion, especially if organic brain symptoms are present.

Rebound insomnia has been reported following abrupt cessation of treatment.

Abnormal psychological reaction to benzodiazepines have been reported. Rare behavioural adverse effects include paradoxical aggressive outbursts, excitement, confusion, and the uncovering of depression and suicidal tendencies.

Other rare adverse effects including hypotension, gastro-intestinal and visual disturbances, skin rashes, urinary retention, headache, vertigo, changes in libido, blood dyscrasias and jaundice have also been reported.

As with any benzodiazepine, excessive or prolonged use of Atensine may result in the development of psychological dependence with withdrawal symptoms on discontinuation.

Treatment of overdose: Ataxia is usually the most serious symptom. Gastric lavage may be carried out, followed by observation. Very occasionally a respirator may be required but Atensine generally causes few problems in overdose. In children behavioural changes are likely.

Pharmaceutical precautions Store in a cool dry place protected from light.

Legal category POM.

Package quantities *Tablets 2 mg:* Containers of 50, 250, 1,000 and 5,000.

Tablets 5 mg: Containers of 50, 100, 250, 1,000 and 5,000.

Tablets 10 mg: Containers of 500.

Further information Nil.

Product licence numbers

Tablets 2 mg 0152/0058

Tablets 5 mg 0152/0059

Tablets 10 mg 0152/0158.

BERKDOPA*

Presentation *Tablets:* White Levodopa Tablets BP 500 mg, with double break line to permit quartering.

Uses Anti-Parkinsonian agent idiopathic, postencephalitic and arteriosclerotic Parkinsonism.

Dosage and administration It is essential that 'Berkdopa' be administered in quite small doses at the beginning of treatment and built up slowly until satisfactory alleviation of symptoms is obtained. 'Berkdopa' should be given in divided doses immediately after food. The following dosage regimen is only a guide to

treatment, and it should be noted that dosage can be initiated at a lower level, if desired, or increased by increments of up to 1 g every three or four days depending on patient response.

Dosage – a guide to treatment

Week 1: 250 mg daily in divided doses.

Week 2: 500 mg daily in divided doses.

Week 3: 250 mg t.i.d.

Week 4: 500 mg t.i.d.

Week 5: 750 mg t.i.d.

Week 6: 1,000 mg t.i.d.

Week 7: 1,250 mg t.i.d.

Week 8: 1,500 mg t.i.d.

Thereafter increments of 500 mg per day may be given every three or four days until the dosage is built up to a maximum of 8 g 'Berkdopa' per day or until a level is reached where satisfactory alleviation of symptoms is obtained.

The optimum alleviation of symptoms may occur at a lower dose, sometimes even 1 g per day is adequate. The decision as to what dosage level to adopt must be that of the physician.

Treatment for up to six months may be necessary before maximal improvement is achieved. Treatment with anticholinergic agents may be continued.

Contra-indications, warnings, etc Berkdopa is contra-indicated in concomitant administration with monoamine oxidase inhibitors. If the patient is being treated with one of these drugs it must be withdrawn before Berkdopa is administered and a period of 14 days should elapse between the withdrawal and the commencement of Berkdopa therapy.

Berkdopa is contra-indicated in cases of severe psychosis or neuro-psychosis and narrow angle glaucoma (but may be used in wide angle glaucoma provided there is adequate control of intra-ocular pressure). Levodopa may be implicated in activation of a malignant melanoma. Berkdopa should not be used in persons with a history of, or who may suffer from, a malignant melanoma.

Special care should be taken when using Berkdopa in endocrine, renal, hepatic, pulmonary or cardiovascular disease, particularly when there is a history of myocardial infarction, and in patients with peptic ulcer. Care should also be taken when patients have to be treated with sympathomimetic drugs, for example in the treatment of bronchial asthma and with antihypertensive drugs, particularly methyl dopa and ganglion blocking agents.

Periodic evaluation of hepatic, haemopoietic, renal and cardiovascular function is advised.

Pyridoxine (vitamin B₆) which is often in multivitamin preparations blocks the effects of levodopa.

Drugs affecting central amine mechanisms such as Rauwolfia alkaloids (reserpine) phenothiazines, thioxanthenes, butyrophenones and amphetamines should be avoided if possible. If their administration is essential care should be exercised and interactions or unusual side effects should be watched for.

When other drugs are given in conjunction with Berkdopa the patients should be carefully observed for any untoward side-effects.

The established medical principle of prescribing medicaments in early pregnancy only when absolutely indicated should be observed for Berkdopa.

Nausea and vomiting may occur, especially if the rate of build-up of dosage is too rapid, or if not taken immediately after food. Anorexia and hypotension may also occur during the initial period of treatment. At higher

doses, involuntary movements, psychiatric disturbances and sometimes cardiac arrhythmia may be seen.

At higher levels of drug dosage, dyskinesias are sometimes induced, such as involuntary facial movements, tongue protrusion and twisting, head nodding and rotation. These may be reduced or abolished by a small reduction of between 0.5–1 g of Berkodopa per day.

Psychiatric disturbances such as mild elation, depression, anxiety, agitation, etc. can be encountered.

Treatment of overdosage: The effects of overdosage are qualitatively similar to the side effects of Berkodopa, but are of greater magnitude. Treatment should include gastric lavage and administration of intravenous fluids. The heart should be monitored for possible dysrhythmias and appropriate treatment instituted if necessary.

Pharmaceutical precautions Store in a cool place, protect from light and moisture.

Legal category POM.

Package quantities *Tablets:* Containers of 100 and 500.

Further information Levodopa is primarily useful in treating the akinesia and rigidity of Parkinsonism. Parkinson tremor is often but not always alleviated. Levodopa will also treat the 'mental akinesia' of Parkinson's disease and will induce a mood elevation and a feeling of well-being. The dysphagia, hypersalivation and dysarthria of Parkinsonism may also be relieved by levodopa.

Product licence numbers

Tablets 500 mg 0152/5036

BERKFURIN*

Presentation Plain yellow Nitrofurantoin Tablets BP 50 mg and 100 mg. Single break line.

Uses Urinary antibacterial agent. Urinary tract infection.

Dosage and administration The average adult dose is 400 mg daily:

Tablets 50 mg: 2 tablets with each meal and 2 at bedtime with milk.

Tablets 100 mg: 1 tablet with each meal and 1 at bedtime with milk.

Treatment should continue for 14 days and courses should be separated by 4 weeks.

Berkfurin is not recommended for children.

Contra-indications, warnings, etc Severe renal impairment – serum creatinine above 2 mg%, creatinine clearance below 40 ml/minute – anuria, oliguria and uraemia. Previous sensitivity to nitrofurantoin.

Polyneuropathy may occur and impaired renal function increases the risk of this complication because of raised blood levels.

Therefore, where renal function is poor, the dose of 'Berkfurin' should be reduced and the drug should be withdrawn at once if paraesthesia is reported. Similar caution is necessary in cases of diabetes mellitus, anaemia, B-avitaminosis and alcoholism. Severe renal damage is an absolute contra-indication to the use of 'Berkfurin'.

Nausea and vomiting sometimes occur and cease on reducing the dose. Allergic reactions, both generalised and cutaneous, occur occasionally and in these cases

the drug should be withdrawn. Anaemia, both megaloblastic and haemolytic, has occurred after nitrofurantoin therapy and there have been reports of liver damage.

Treatment of overdosage: Vomiting may occur but other serious symptoms are unlikely. Gastric lavage might be beneficial in the first hours after ingestion followed by conservative management.

Pharmaceutical precautions Store in a cool place, protect from light.

Legal category POM.

Package quantities *Tablets 50 mg:* Containers of 100.

Tablets 100 mg: Containers of 100.

Further information Nil.

Product licence numbers

Tablets 50 mg 0152/5030

Tablets 100 mg 0152/5031.

BERKMYCEN*

Presentation *Tablets:* Yellow film-coated Oxytetracycline Tablets BP 250 mg engraved BERK 1C5 on one side.

Capsules: Red/yellow Oxytetracycline Capsules BP 250 mg.

Uses Antibiotic.

Infections caused by oxytetracycline-sensitive organisms. These include acute and chronic bronchitis, pneumonia, urinary tract infections, brucellosis, pertussis, rickettsial fevers and psittacosis.

Dosage and administration *Adults:* 250 mg every six hours. In severe infections dosage may be increased to 250 mg every three hours after an initial loading dose of 1 g.

Contra-indications, warnings, etc 'Berkmycen' should only be given to patients with renal dysfunction or failure if its use is considered essential.

Milk, or antacids containing aluminium, magnesium or calcium, interfere with the absorption of oxytetracycline. If gastric irritation occurs the tablets should be taken with food. As with all tetracyclines, 'Berkmycen' should be used with caution in patients with hepatic or renal dysfunction.

Berkmycen should not be used in late pregnancy or given to children during the period of tooth development, unless it is essential to use a tetracycline because of resistance to other antibiotics.

Like all tetracyclines, 'Berkmycen' may produce gastro-intestinal irritations, giving rise to nausea, abdominal discomfort and diarrhoea. Intestinal overgrowth of resistant organisms (*Candida albicans* in particular) may occur. Drug fever and allergic skin rashes may occur rarely.

Treatment of overdosage: Serious symptoms are unlikely. Gastric lavage might be beneficial in the first hours after ingestion followed by conservative management. Milk will reduce absorption.

Pharmaceutical precautions Incompatible with alkalis and chloramphenicol.

Legal category POM.

Package quantities *Tablets*: Containers of 1,000 and 5,000.

Capsules: Containers of 100.

Further information 'Berkmycen' oxytetracycline is an antimicrobial agent active against most pathogenic bacteria, both Gram-positive and Gram-negative, except for the majority of strains of *Proteus vulgaris* and *Pseudomonas aeruginosa*. *Salmonella* species and *Mycobacterium tuberculosis* show resistance, as do the yeasts and fungi, but 'Berkmycen' is effective against *Actinomyces*, *Entamoeba histolytica*, *Trichomonas vaginalis*, treponemata and some rickettsias and viruses.

Product licence numbers

Tablets 0152/0094

Capsules 0152/5040.

BERKOLOL*

Presentation

1. Pink, film-coated, Propranolol Tablets BP 10 mg embossed BERK 121, with breakline on reverse.
2. Pink, film-coated, Propranolol Tablets BP 40 mg embossed BERK 221, with breakline on reverse.
3. Pink, film-coated, Propranolol Tablets BP 80 mg embossed BERK 321, with breakline on reverse.
4. Pink, film-coated, Propranolol Tablets BP 160 mg embossed BERK 421, quadrisected with double breakline on reverse.

Uses Berkolol is a competitive blocker of adrenergic β -receptor sites. It is used in the treatment of hypertension, angina pectoris, cardiac dysrhythmias, tachycardia, anxiety and essential tremor. It may also be used as a prophylactic in migraine, and as adjunctive therapy in thyrotoxicosis.

Dosage and administration Dosage requires individual adjustment. A heart rate of 55/min or less is an indication that dosage should be increased no further.

Adults: Hypertension: Initially, 80 mg twice daily, increased where necessary at weekly intervals. The usual maintenance dosage is 160–320 mg daily. Lower doses may be effective when a diuretic or other antihypertensive drug is given concurrently.

Angina pectoris: Initially, 40 mg twice or thrice daily increased by the same amount at weekly intervals until control is achieved, or the maximum daily dose of 480 mg is reached.

Anxiety, migraine, essential tremor: 40 mg twice or thrice daily, increased at weekly intervals if needed to a daily total of 80–160 mg.

Dysrhythmias, anxiety tachycardia, hypertrophic obstructive cardiomyopathy, thyrotoxicosis: 10–40 mg three or four times daily.

Children: Dysrhythmias, thyrotoxicosis: The minimum effective dosage, based on 0.25–0.5 mg/kg body weight, three or four times daily.

Migraine: Children under the age of 12 may be given 20 mg two or three times daily. Older children may be given adult dosage.

Contra-indications, warnings, etc

Contra-indications: Second or third degree heart block; History of bronchospasm; Prolonged fasting; Metabolic acidosis.

Precautions: Although there is no evidence that pro-

pranolol is teratogenic, Berkolol should not be used in pregnancy unless it is considered essential.

Berkolol should be used with great caution in patients with heart failure, unless that is due to thyrotoxicosis alone. Concomitant therapy with digitalis and diuretics is usually desirable in these cases.

Berkolol should be withdrawn 24 hours before elective surgery, as it may interfere with response to stress. If this cannot be done, 1–2 mg atropine should be given intravenously before anaesthesia commences and anaesthetics such as ether, chloroform, cyclopropane and trichloroethylene, which may cause myocardial depression, should not be used.

Warnings and adverse reactions: Treatment with beta-blocking agents must not be stopped suddenly. If it is necessary to withdraw Berkolol, this should be done gradually, or another beta-blocker should be substituted.

Bradycardia and hypotension are usually a sign of overdosage, but may rarely be due to intolerance of the drug. In the latter case Berkolol should be withdrawn and, if necessary, the patient should be treated as for overdosage. Heart block and congestive heart failure have been reported.

Dry eyes and skin rash have been reported during treatment with β -adrenergic blocking agents. If these symptoms are not attributable to some other cause, Berkolol should be withdrawn.

Berkolol may cause or precipitate Raynaud's phenomenon, intermittent claudication or peripheral arterial insufficiency. Bronchospasm may occur, particularly in patients with a history of asthma or hay fever.

There have been rare reports of blood dyscrasias during treatment with propranolol.

Minor side-effects include cold extremities, nausea, vomiting diarrhoea, fatigue or insomnia. These are usually transient and are less common if the drug is introduced gradually.

Treatment of overdosage: The clinical features can include bradycardia, severe hypotension, bronchospasm, hypoglycaemia, delirium and unconsciousness. Initially isoprenaline should be infused, and if marked bradycardia is present atropine should be given intravenously (0.6–3 mg; 50 mcg/kg in children): if the response is limited, glucagon therapy must be instituted (50–150 mcg/kg intravenously over one minute followed by 1–5 mg/hour infused). Bronchospasm may be treated by nebulized salbutamol or intravenous aminophylline or salbutamol.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities

<i>Tablets 10 mg</i>	containers of 100 and 500
<i>Tablets 40 mg:</i>	containers of 100 and 1,000
<i>Tablets 80 mg:</i>	containers of 100 and 500
<i>Tablets 160 mg:</i>	containers of 100

Further information Nil.

Product licence numbers

<i>Tablets 10 mg</i>	0152/0150
<i>Tablets 40 mg</i>	0152/0151
<i>Tablets 80 mg</i>	0152/0152
<i>Tablets 160 mg</i>	0152/0153.

BERKOZIDE*

Presentation Plain white Bendrofluazide Tablets BP 2.5 mg and 5 mg. The 5 mg tablets have a single break line.

Uses Diuretic. Oedema, cardiac failure, inhibition of lactation, hypertension.

Dosage and administration In cardiac failure, 5–10 mg daily or on alternate days, a usual maintenance dosage being 5–10 mg on three days per week. For premenstrual oedema, 'Berkozide' may be given 5 mg daily for three to four days before menstruation. For inhibition of lactation 5 mg in the morning and 5 mg at noon for five days is usually adequate. In hypertension the dosage should be 2.5–5 mg daily. Bendrofluazide potentiates other antihypertensive agents, the dosage of which should be reduced and then adjusted as necessary.

Berkozide is not recommended for children.

Contra-indications, warnings, etc 'Berkozide' is contra-indicated in severe renal insufficiency and hypercalcaemia and should be used with caution in patients with renal or hepatic disorders. It may precipitate hepatic coma in advanced cirrhosis.

Potassium supplements should be given (preferably on non-diuretic days) when the dosage of 'Berkozide' is high or when diet is inadequate. It may be necessary to reduce the dosage of digitalis if this is given concurrently.

Toxic effects such as nausea, allergy, skin rashes or blood dyscrasias are rare. Hypokalaemia may develop with long use of 'Berkozide', but this risk is reduced by administration on alternate days. Like other thiazides, bendrofluazide may provoke hyperglycaemia and glycosuria in diabetic patients and may precipitate latent diabetes mellitus. It may also precipitate acute attacks of gout. Breast feeding should be avoided since thiazide diuretics are secreted in mother's milk.

Treatment of overdosage: Replace fluids with saline while monitoring plasma sodium and potassium. Potassium replacement may be required.

Pharmaceutical precautions No special precautions.

Legal category POM.

Package quantities *Tablets 2.5 mg:* Containers of 100 and 1,000.

Tablets 5 mg: Containers of 100 and 1,000.

Further information Bendrofluazide is an oral diuretic of the thiazide group which inhibits proximal tubular resorption of sodium chloride.

Product licence numbers

Tablets 2.5 mg 0152/5081

Tablets 5 mg 0152/5084.

CAPLENAL®

Presentation

100 mg tablets: white biconvex tablets containing 100 mg of Allopurinol, engraved BERK 1 K1 on one side with a break-line on the reverse.

300 mg tablets: white biconvex tablets containing 300 mg of Allopurinol, engraved BERK 2 K1 on one side with a break-line on the reverse.

Uses *Gout:* Primary hyperuricaemia.

Secondary hyperuricaemia: Prophylaxis of uric acid and calcium oxalate stones.

Dosage and administration *Adults:* The initial dose is 100–200 mg. The maintenance dose is 200–600 mg/daily. Maximum single dose 300 mg. It has rarely been found necessary to exceed 900 mg per day. The dose should be adjusted by monitoring serum uric

acid and/or urinary uric acid levels at appropriate intervals until the desired effect is attained, which may take one to three weeks.

Children: 10–20 mg/kg body weight/day. Use in children is mainly indicated in malignant conditions, especially leukaemia and certain enzyme disorders, for example Lesch-Nyhan syndrome.

Initiation of therapy: In the early stages of treatment with allopurinol, as with the uricosuric agents, an acute attack of gouty arthritis may be precipitated. Therefore it is advisable to give a prophylactic dose of a suitable anti-inflammatory agent or colchicine (0.5 mg three times a day) for at least one month.

Use with uricosurics: As allopurinol does not interfere with the action of uricosuric agents, they may be given concurrently. When changing from uricosuric therapy to allopurinol 1–3 weeks overlap of treatments is recommended to ensure a continuous hypouricaemic effect.

Use in neoplasia: When giving allopurinol to prevent uric acid nephropathy in neoplastic conditions, it is advisable to start treatment with allopurinol before cytotoxic therapy.

Dose recommendations in impaired renal function: Since allopurinol and its metabolites are excreted via the kidney, impairment of renal function may lead to retention of the drug and its metabolites with consequent prolongation of action. Thus, the amount and frequency of the dosage may require reduction as indicated by monitoring serum uric acid levels. The following schedule is provided for guidance in adults.

If creatinine clearance exceeds 20 ml/minute – give standard dose.

If creatinine clearance is between 10 and 20 ml/minute – give 100–200 mg/day.

If creatinine clearance is between 2 and 10 ml/minute – give 100 mg/day or at longer intervals.

Dose recommendations in renal dialysis: Allopurinol and its metabolites are removed by renal dialysis. If frequent dialysis is required an alternative schedule of 300–400 mg allopurinol after each dialysis with none in the interim should be considered.

Contra-indications, warnings, etc

Contra-indications: Acute gout. Known intolerance of allopurinol.

Precautions: Treatment should not be started during or immediately after an acute attack of gout. When 6-mercaptopurine or azathioprine is given concurrently with allopurinol, only one quarter of the usual dose of those drugs should be given because inhibition of xanthine oxidase will prolong their activity. There is no unequivocal evidence that allopurinol potentiates the activity of other cytotoxic drugs. If allopurinol is given concomitantly with chlorpropamide when renal function is poor, there may be an increased risk of prolonged hypoglycaemia activity.

The dosage of allopurinol should be reduced in patients with renal or hepatic diseases.

There is no evidence that allopurinol taken orally causes foetal abnormalities. However, as with all drugs, due caution should be exercised in pregnancy.

Warnings and adverse effects: Adverse reactions in association with allopurinol are usually rare and mostly of a minor nature. The incidence is higher in the presence of renal and/or hepatic disorders. The possible potentiation of anticoagulant action should be borne in mind when a patient on anticoagulants is given allopurinol.

Skin reactions are the most common reactions and may occur at any time during treatment. They may be pruritic, maculopapular, sometimes scaly or purpuric and rarely exfoliative. Allopurinol should be withdrawn immediately should such reactions occur. After recovery from mild reactions allopurinol may, if desired, be reintroduced at a low dose (e.g. 50 mg/day) which may be gradually increased. If the rash recurs, allopurinol should be permanently withdrawn.

Exfoliative skin reactions associated with other signs of hypersensitivity including fever, lymphadenopathy, arthralgia and eosinophilia occur rarely. If they do occur, it may be at any time during treatment. Allopurinol should then be withdrawn immediately and permanently. Corticosteroids may be beneficial in overcoming such reactions. Patients manifesting generalised hypersensitivity reactions usually have pre-existing renal and/or hepatic disorders.

Nausea and vomiting have been reported. This reaction is not a significant problem and can be avoided by taking allopurinol after meals.

There have been occasional reports of transient reduction in the numbers of circulating formed elements in the blood, usually in association with pre-existing renal and/or hepatic disorders. The clinical significance has yet to be demonstrated.

Exacerbation of acute gouty attacks may occur in the early stages of hypouricaemic therapy. In those conditions where the body's miscible urate pool is greatly increased (e.g. malignant diseases and its treatment: Lesch-Nyhan syndrome), the rise in xanthine concentration resulting from the action of allopurinol may lead to tissue deposition of xanthine. Adequate hydration will reduce the risk of xanthine deposition in the kidney and fluid intake should ensure adequate urinary output. Xanthine crystals have been seen in muscle tissue of patients receiving allopurinol but this appears to have no clinical significance.

The following complaints have been reported occasionally, but do not appear to have a clear cause and effect relationship with allopurinol: fever, general malaise, headache, vertigo, somnolence, taste perversion, hepatic necrosis, granulomatous hepatitis, abnormal liver function tests, hyperlipaemia, visual disorder, cataracts, macular changes, neuropathy, impotence, diabetes mellitus, furunculosis, alopecia, hypertension, haematuria, oedema.

Treatment of overdose: No reports of overdose or acute intoxication with Caplenal are available.

Pharmaceutical precautions Store below 25°C in a dry place.

Legal category POM.

Package quantities

100 mg tablets: containers of 100 and 500 tablets

300 mg tablets: containers of 100 tablets

Further information Nil.

Product licence numbers

Tablets 100 mg 0152/0154

Tablets 300 mg 0152/0176

CEPLAC

Presentation Rose coloured tablets engraved CEPLAC on one face and plain on the reverse face. Each tablet contains 6 mg erythrocine.

Uses As an aid to the efficient teaching of oral hygiene.

Dosage and administration *Adults and children:* The patient should be given a Ceplac Tablet in the surgery. This will at once demonstrate the shortcomings of his current oral hygiene techniques and make it easier to gain his co-operation.

When he has been shown the correct method of brushing his teeth, he should be sent home with a supply of Ceplac Tablets and instructions on how to use them. Ceplac will play a central role in helping him to acquire the habit of regular and correct tooth brushing.

Initially, at least once a day, the patient should crush one Ceplac Tablet between his teeth before cleaning them, and distribute saliva to all tooth and gum surfaces with the aid of the tongue for at least half a minute. He should then spit out into a bowl of running water, and rinse his mouth once or twice with water.

He should then brush his teeth in the way he has been shown until all red stain has been removed.

Once a sound brushing technique has been established the patient can use Ceplac once or twice a week after brushing, as a check on continuing proficiency.

In the same way, patients should be given Ceplac on each successive visit to the surgery, to assess their progress.

Contra-indications, warnings, etc There are no known contra-indications or adverse reactions.

Treatment of overdose: Gastric lavage.

Pharmaceutical precautions No special precautions.

Legal category GSL.

Package quantities Packs of 12 and 1,000 tablets.

Further information Ceplac stains bacterial plaque and food debris a brilliant red. The stain is non-persistent and is easily removed from lips or clothing with soap and water.

Product licence number 0152/5032.

CREMALGIN®

Presentation Pink balm containing methyl nicotinate 1.0% w/w histamine dihydrochloride 0.1% w/w capsin 0.1% w/w glycol salicylate 10.0% w/w.

Uses Rubefacient balm. In the treatment of rheumatism sciatica lumbago, fibrositis and muscular stiffness.

Dosage and administration Two or three times daily or as required. Place a sufficient quantity on the skin over the affected area and massage gently and smooth the cream through the skin.

Contra-indications, warnings, etc Cremalgin is contra-indicated in those patients with salicylate hypersensitivity. Erythematous reactions may occur in sensitive patients.

Pharmaceutical precautions No special precautions.

Legal category GSL.

Package quantities Tubes of 25 g and 50 g.

Further information Nil.

Product licence number 0152/5019.

DOMICAL®

Presentation Round film-coated bi-convex Amitriptyline Tablets BP marked 'D': 10 mg tablets are blue, 25 mg are orange and 50 mg are red-brown.

Uses Amitriptyline is an antidepressant of the tricyclic group.

It is indicated by symptoms of a depressive illness especially when sedation is required.

Dosage and administration *Adults:* Initially 75 mg/day in divided doses or as a single dose at night, increasing to 200 mg/day according to clinical response. Maintenance dose is 50–100 mg at night.

Elderly or adolescent patients: 10–50 mg daily initially (see 'Precautions').

Children: Domical is not recommended for children under 12 years of age.

Contra-indications, warnings, etc

Contra indications: History of myocardial infarction, arrhythmias, particularly heart block of any degree, congestive cardiac failure, coronary artery insufficiency.

Receipt of monoamine oxidase inhibitors within the last two weeks.

Mania. Severe liver disease. Hypersensitivity to any tricyclic antidepressant. Breast feeding.

Precautions: Safety in pregnancy and lactation has not been established. Do not use during pregnancy nor in nursing mothers unless there are compelling reasons.

The elderly or debilitated are particularly liable to experience toxic effects, especially agitation, confusion and postural hypotension. The initial dose should be increased with great caution under close supervision. Half the normal maintenance dose may be sufficient to produce a satisfactory clinical response.

All patients with severe depression should be closely supervised, particularly during the early stages of therapy when partial response may increase the risk of suicide.

Domical should be used with great caution in patients with a history of narrow angle glaucoma, urinary retention, epilepsy or recent convulsions, hepatic insufficiency, hyperthyroidism, cardiovascular disorders or blood dyscrasias, or symptoms suggestive of prostatic hypertrophy.

Tricyclic antidepressants potentiate the central nervous depressant action of alcohol.

Anaesthetics given during tri/tetracyclic antidepressant therapy may increase the risk of arrhythmias and hypotension. If surgery is necessary, the anaesthetist should be informed that a patient is being so treated.

Drug interactions: In patients who have been treated previously with monoamine oxidase inhibitors, at least two weeks should elapse before treatment with Domical is started, with great caution, commencing with low dosage and slow increments.

Amitriptyline may decrease the antihypertensive effect of guanethidine, debrisoquine, bethanidine and possibly lonidine. It is advisable to review all antihypertensive therapy during treatment with tricyclic antidepressants.

Amitriptyline should not be given with sympathomimetic agents such as ephedrine, isoprenaline, norrenaline, phenylephrine and phenylpropanolamine, or with ethchlorvynol.

The antidepressant action of Domical may be decreased by barbiturates and increased by methylenediamine.

The dose of thyroid hormone medication may need to be reduced if amitriptyline is given concurrently.

Warnings and adverse reactions: As improvement may not occur during the first month of therapy, patients should be closely monitored during this period.

Cardiac arrhythmias and severe hypotension are likely to occur with high dosage or in deliberate overdosage. They may also occur in patients with pre-existing heart disease taking normal dosage.

Confusion may occur at high doses or in elderly patients, requiring reduction of dosage.

Drowsiness is not uncommon in the early stages of treatment, and patients should be warned not to drive or operate machinery until it has been established that their alertness is not impaired.

The following adverse effects, although not necessarily all reported with amitriptyline, have occurred with tricyclic antidepressants:

Atropine-like side-effects including dry mouth, disturbances of accommodation, tachycardia, constipation and hesitancy of micturition are common early in treatment, but usually lessen.

Other common adverse effects include nausea, sweating, postural hypotension, dizziness, tremor and rashes. Interference with sexual function may occur.

Serious adverse effects are rare. These include bone marrow depression, agranulocytosis, cholestatic jaundice, hypomania, convulsions and peripheral neuropathy.

Withdrawal symptoms which may occur on abrupt cessation of therapy include insomnia, irritability and excessive perspiration. There have also been reports of withdrawal symptoms in neonates whose mothers received tricyclic antidepressants during the third trimester of pregnancy.

Psychotic manifestations, including mania and paranoid delusions may be exacerbated during treatment with tricyclic antidepressants.

Treatment of overdosage: The major symptoms are likely to be coma and respiratory depression. Primary therapy must be aimed at correction of hypoxia, acidosis and electrolyte imbalance. Gastric lavage should be performed and the ECG monitored. If convulsions occur they may be treated with diazepam. Serious dysrhythmias are rare and DC conversion may be preferable to anticholinesterase agents, which can exacerbate convulsions.

Pharmaceutical precautions No special precautions.

Legal category POM.

Package quantities *Tablets 10 mg:* Containers of 500.

Tablets 25 mg: Containers of 500.

Tablets 50 mg: Containers of 100.

Further information Nil.

Product licence numbers

Tablets 10 mg 0152/0065

Tablets 25 mg 0152/0066

Tablets 50 mg 0152/0114.

DOPAMET®

Presentation Yellow film-coated Methyldopa Tablets BP. 125 mg (marked 'BERK 1C3'). 250 mg (marked 'BERK 2C3'). 500 mg (marked 'BERK 3C3').

Uses Hypertension.

Dosage and administration *Initiating therapy:*

Adults: 250 mg twice a day for two days, increased at intervals of not less than two days by an additional 250–500 mg daily until satisfactory control is achieved. This normally follows within 12–24 hours of reaching the effective dose for the individual patient, which is generally in the range of 500–2,000 mg daily. It is seldom necessary to exceed 3,000 mg daily and, because methyldopa is largely excreted by the kidneys, patients with impaired renal function may respond to comparatively low doses.

The requirement of 'Dopamet' may be reduced by giving a thiazide diuretic concurrently; downward adjustments of dosage should likewise be made at intervals of not less than 48 hours.

In the few cases where tolerance develops, effective control can frequently be restored by increasing the dosage of 'Dopamet' or by adding a diuretic to the regimen.

When patients are on other hypotensive agents and it is desired to change them over to 'Dopamet', drug interactions must be carefully watched for.

Reserpine and other Rauwolfia alkaloids, hydralazine and mebutamate when used alone or in any combination should be discontinued before treatment with 'Dopamet' is started.

Ganglion blocking agents and adrenergic blocking agents used alone or in combination should be withdrawn cautiously and progressively. During the first week of transfer the dosage of blocking agent should be reduced by a half and 'Dopamet' added at a dosage of 250 mg twice a day. The blocking agent is then reduced still further and the dosage of 'Dopamet' adjusted upwards by 250–500 mg stages at two- to seven-day intervals to maintain optimal control of the blood pressure.

Monoamine oxidase inhibitors should be discontinued before treatment with 'Dopamet' commences. It should then be used cautiously in case of delayed excretion of the monoamine oxidase inhibitors.

Contra-indications, warnings, etc Dopamet should not be given in cases of active liver disease, such as acute hepatitis and active cirrhosis, and in patients known to be sensitive to methyldopa. Dopamet is not recommended where phaeochromocytoma is suspected, since methyldopa fluoresces at the same wavelengths as catecholamines in urine samples; spuriously high concentrations of urinary catecholamines may be reported and this will interfere in the diagnosis of phaeochromocytoma. Dopamet should not be used with reserpine, other Rauwolfia alkaloids, hydralazine, mebutamate and monoamine oxidase inhibitors. When methyldopa is used with other antihypertensive agents, potentiation of antihypertensive action may occur. The progress of patients should be carefully followed to detect side reactions or manifestations of drug idiosyncrasy. Patients may require reduced doses of anaesthetics when on methyldopa. If hypotension does occur during anaesthesia, it can usually be controlled by vasopressors. Since experience of methyldopa in pregnancy is still limited, Dopamet is not currently recommended for pregnant women or for nursing mothers, but in serious cases the benefits of the drug might be weighed against any potential risk.

Sedation is the most frequent side-effect and may occur even at the starting dose level. It usually wears off after an effective maintenance dosage has been estab-

lished. Depression may occur and corrective treatment with tricyclic antidepressants may antagonise the therapeutic effect of Dopamet. Other minor side-effects are headache and a feeling of weakness but again these wear off with time. Symptoms of cerebrovascular insufficiency associated with effective lowering of blood pressure may also occur, including dizziness, light-headedness and faintness. If such symptoms occur, dosage should be reduced. Symptoms due to postural hypotension are fewer and less severe with Dopamet than with other hypotensive agents and exercise hypotension rarely occurs. If such symptoms do occur, the dose of Dopamet should be reduced. Occasionally bradycardia, nasal stuffiness, mild dryness of the mouth and gastro-intestinal symptoms – including distension, constipation, flatus and diarrhoea – may occur. These are generally relieved by reducing the dosage. Vomiting has been reported in very few patients and sore or black tongue has been observed rarely. Weight gain and oedema occur infrequently and are usually relieved by administering a thiazide diuretic. If oedema becomes progressive or other signs of heart failure appear after the addition of a thiazide diuretic, Dopamet should be discontinued. On rare occasions breast enlargement, lactation, impotence, skin rash, mild arthralgia, myalgia, paraesthesias, Parkinsonism, psychic disturbances – including nightmares and reversible mild psychosis – have been reported. A rise in blood urea has been found in some cases. Rarely, urine from patients receiving Dopamet may darken on exposure to air simply because of the chemical breakdown of methyldopa or its metabolites. Cases of acquired haemolytic anaemia have occurred in association with methyldopa. Should clinical symptoms suggest the possibility of anaemia, appropriate tests should be undertaken. If haemolysis is found to be present Dopamet should be discontinued. In addition some patients on continued therapy with methyldopa develop a positive direct Coombs test, but this rarely develops in the first six months of therapy and if it has not developed within 12 months it is not likely to do so. Prior knowledge of a positive Coombs reaction will aid in evaluation of cross-matching for transfusion. If a patient with a positive Coombs reaction shows an incompatible minor cross-match, an indirect Coombs test should be performed. If this is negative, transfusion with blood otherwise compatible in the major cross-match may be carried out. If positive, the advisability of transfusion should be determined by a haematologist.

A reversible thrombocytopenia has occurred on rare occasions and reversible reduction of the white blood cell count has been seen with a primary effect on the granulocytes. The granulocyte count, however, returns promptly to normal when the drug is discontinued. Rare cases of clinical agranulocytosis have been reported. Or rare occasions fever occurs, usually within the first three weeks of administering methyldopa, in some cases accompanied by eosinophilia or abnormalities in one or more liver function measurements. Jaundice with or without fever may also occur, usually within the first two to three months of therapy. In some patients the findings are consistent with cholestasis. Rare cases of fatal hepatic necrosis have been reported. It is advisable to take a total and differential white blood cell count and to perform liver function tests at intervals during the first 6–12 weeks of treatment, or if the patient develops an unexplained fever. Should fever, abnormality in the liver function or jaundice occur, therapy should be withdrawn. Dialysis may remove methyldopa. Hypertension may therefore, recur after this procedure.

Rarely involuntary choreoathetotic movements have been observed during therapy with methyldopa in patients with severe bilateral cerebrovascular disease. Should these movements occur, therapy should be discontinued.

When a thiazide diuretic is added to the dosage regimen, an excessive drop in blood pressure may occur so that the dosage of Dopamet may be reduced by half when a thiazide is used additionally. Careful observation of changes in blood pressure must be made. If Dopamet is added to the regimen of a patient taking a thiazide diuretic then the initial dosage should be limited to 375 mg per day for the first two days and the dosage increased gradually at intervals of not less than two days until adequate control of the blood pressure is obtained.

Treatment of overdose: Gastric lavage may be helpful if carried out within a reasonable time after ingestion and can be assisted by dialysis if the overdose has been substantial. Other treatment should be symptomatic, with general support provided to maintain cardiac output, blood volume, electrolyte balance and urinary output.

Pharmaceutical precautions Store in a cool dry place and protect from light.

Legal category POM.

Package quantities *Tablets 125 mg:* Containers of 250.

Tablets 250 mg: Containers of 250, 1,000 and 2,500.

Tablets 500 mg: Containers of 250 and 500.

Further information 'Dopamet' is an effective hypotensive agent which possesses significant advantages over the ganglion blocking and postganglion blocking agents, controlling high blood pressure throughout the day and night after a basic regimen particular to the patient has been established. It usually reduces supine as well as standing blood pressure and produces little or no postural or exertional hypotension. Normal or elevated plasma renin activity may decrease in course of methyldopa therapy.

Product licence numbers

Tablets 125 mg 0152/0093

Tablets 250 mg 0152/5021

Tablets 500 mg 0152/0080.

DRYPTAL* TABLETS 40 mg

Presentation White Frusemide Tablets BP 40 mg marked 'BERK 2B2' single break line.

Uses Diuretic. Oedema of cardiac, hepatic or renal origin. Pulmonary oedema. Toxaemia of pregnancy. Mild or moderate hypertension.

Dosage and administration The usual initial dosage is 1 tablet daily, thereafter adjusted to the minimum effective dose which may range from $\frac{1}{2}$ tablet (20 mg) on alternate days to 3 tablets (120 mg) daily.

Children: From 1 to 3 mg/kg body weight.

Contra-indications, warnings, etc Dryptal is contra-indicated in the presence of electrolyte deficiency, hepatic cirrhosis or digitalis intoxication and should be used with great caution in advanced renal failure. Patients with prostatic hypertrophy or impairment of micturition have an increased risk of developing acute retention. Cephaloridine nephrotoxicity may be in-

creased by concomitant administration of potent diuretics such as frusemide.

During prolonged use and at high dosage a close check should be kept upon plasma electrolytes.

Dryptal may potentiate the action of cardiac glycosides and of hypotensive agents, the dosage of which may need to be reduced. Dryptal may also precipitate diabetes, or necessitate increased dosage of insulin.

Serum uric acid levels tend to rise during treatment with Dryptal and an acute attack of gout may occasionally be precipitated.

Other reported side-effects include nausea, gastric upset and malaise. The incidence of allergic reactions such as skin rashes is very low but when these occur treatment should be withdrawn. Bone marrow depression has been reported as a rare complication and necessitates withdrawal of treatment.

Only when it is essential should Dryptal be given in the first trimester of pregnancy or to nursing mothers.

Treatment of overdose: Correct dehydration and electrolyte depletion. Reversible deafness may occur.

Pharmaceutical precautions Store in a cool dry place protected from light.

Legal category POM.

Package quantities Containers of 50, 250 and 1,000.

Further information Nil.

Product licence number 0152/0083.

DRYPTAL* TABLETS 500 mg

Presentation Yellow, flat, bevel-edged Frusemide Tablets BP 500 mg engraved Berk 3B2 on one side and with a double breakline on the other.

Uses Diuretic for the management of oliguria due to acute or chronic renal insufficiency with a GFR below 20 ml/minute.

Dosage and administration In patients with chronic renal insufficiency an initial daily dose of 250 mg ($\frac{1}{2}$ tablet) is employed. If a satisfactory diuresis is not produced then the dose may be increased in steps of 250 mg at four to six hourly intervals up to a maximum dose of 2,000 mg (4 tablets) as a single dose.

In cases of acute renal failure which have been initially controlled using Dryptal injection oral therapy may be substituted for parenteral therapy regarding one 500 mg tablet as approximately equal to 250 mg of injection. Appropriate dosage adjustments may then be made according to the observed clinical response.

Contra-indications, warnings, etc During treatment with high-dosage forms of Dryptal, fluid balance should be carefully controlled. In the case of patients with shock, steps should be taken to normalise blood pressure and circulating blood volume before commencing therapy. Regular checks of plasma electrolytes, particularly sodium, potassium, chloride and bicarbonate should be carried out, and electrolyte replacement therapy instituted if necessary.

Contra-indications: Dryptal tablets 500 mg are contra-indicated in renal failure as a result of poisoning by nephrotoxic or hepatotoxic agents and in renal failure associated with hepatic coma.

Warnings: The dosage of concurrently administered

cardiac glycosides or antihypertensive agents may require adjustment.

Cephaloridine nephrotoxicity may be increased by concomitant administration of potent diuretics such as frusemide.

Latent diabetes may become manifest or the insulin requirements of diabetic patients may increase.

Precautions: The safety of high dosage frusemide in pregnancy has not been established and Dryptal tablets 500 mg should be used with caution, weighing potential benefit to the patient against possible hazard to the foetus.

Treatment of overdose: Correct dehydration and electrolyte depletion. Reversible deafness may occur.

Side-effects: Dryptal tablets 500 mg are generally well tolerated. Side-effects of a minor nature such as nausea, malaise or gastric upset may occur but are not usually severe enough to cause withdrawal of treatment. The incidence of allergic reactions such as skin rashes is very low but when these occur treatment should be withdrawn. In common with other sulphonamide-based diuretics hyperuricaemia may occur and, in rare cases, clinical gout may be precipitated. Bone marrow depression has been reported as a rare complication and necessitates withdrawal of treatment.

Pharmaceutical precautions Store in a cool dry place protected from light.

Legal category POM.

Package quantities Containers of 100.

Further information Nil.

Product licence number 0152/0145.

DRYPTAL* INJECTION 20 mg/2 ml

Presentation Dryptal Injection 20 mg contains 20 mg Frusemide BP in 2 ml.

Uses Dryptal is a diuretic recommended for use in all indications when a prompt and effective diuresis is required. Indications include cardiac oedema, renal oedema, peripheral oedema due to mechanical obstruction or changes in the walls of the veins, ascites, toxæmia of pregnancy, hypertension and miscellaneous conditions such as acute barbiturate poisoning, after prostatectomy and in cases where other diuretics have failed to produce the desired effect.

Dosage and administration Dryptal has an exceptionally wide therapeutic range the effect being proportional to the dosage. Dryptal is best given as a single dose either daily, on alternate days, or on three successive days of the week.

Parenteral administration: Intravenous injections of Dryptal must be given slowly. In cases of emergency or when oral therapy is precluded an initial dose of 20–40 mg (1–2 ampoules) i.m. or i.v. is recommended. Further adjustment may then be necessary according to the observed clinical response.

Parenteral doses for children range from 0.5–1.5 mg/kg body weight.

Contra-indications, warnings, etc

Contra-indications: Dryptal is contra-indicated in electrolyte deficiency and precomatose states associated with liver cirrhosis.

Warnings: Patients with prostatic hypertrophy or impairment of micturition have an increased risk of developing acute retention.

The dosage of concurrently administered cardiac glycosides or antihypertensive agents may require adjustment.

Cephaloridine nephrotoxicity may be increased by concomitant administration of potent diuretics such as frusemide.

Latent diabetes may become manifest or the insulin requirements of diabetic patients may increase.

Infusion rates in excess of 4 mg/min are associated with an increased risk of ototoxicity, usually reversible hearing loss.

Precautions: Caution should be observed in patients liable to electrolyte deficiency.

The use of Dryptal during the first trimester of pregnancy should be subject to the normal precautions which apply to any drug at this time. As Dryptal may inhibit lactation it should be used with caution in nursing mothers.

Treatment of overdose: Correct dehydration and electrolyte depletion. Reversible deafness may occur.

Side-effects: Dryptal is generally well tolerated. Side-effects of a minor nature such as nausea, malaise or gastric upset may occur but are not usually severe enough to cause withdrawal of treatment.

The incidence of allergic reactions such as skin rashes is very low but when these occur treatment should be withdrawn.

In common with other sulphonamide-based diuretics hyperuricaemia may occur and, in rare cases, clinical gout may be precipitated.

Bone marrow depression has been reported as a rare complication and necessitates withdrawal of treatment.

Pharmaceutical precautions Dryptal should be stored in a cool dry place protected from light in the original containers.

Injections of Dryptal should not be mixed with any other preparation. Opened ampoules should be used immediately and any remainder discarded.

Legal category POM.

Package quantities Dryptal ampoules are available in packs of 10 × 2 ml.

Further information Dryptal produces a prompt and effective diuresis which lasts for approximately two hours following parenteral administration. Therefore the time of administration can be adjusted to suit the patient's requirements.

Product licence number 0152/0149.

DRYPTAL* INJECTION 50 mg/5 ml

Presentation Dryptal injection 50 mg contains 50 mg Frusemide BP in 5 ml.

Uses Dryptal is a diuretic recommended for use when a prompt and effective diuresis is required. The intravenous formulation is appropriate for use in emergencies. Indications include cardiac oedema, pulmonary oedema, hepatic oedema, renal oedema and cases in which other therapy has failed to produce the desired response.

Dosage and administration Dryptal injection must always be given slowly. The diuretic effect of Dryptal is

proportional to the dosage. Up to 50 mg may be given initially, if larger doses are required, they should be given by slow infusion and titrated according to the response. In such cases the use of Dryptal 250 mg ampoules should be considered.

Contra-indications, warnings, etc Intravenous injections of Dryptal, **must** always be given slowly.

Contra-indications: Dryptal is contra-indicated in electrolyte deficiency and pre-comatose states associated with liver cirrhosis.

Warnings: Patients with prostatic hypertrophy or impairment of micturition have an increased risk of developing acute retention.

The dosage of concurrently administered cardiac glycosides or antihypertensive agents may require adjustment.

Cephaloridine nephrotoxicity may be increased by concomitant administration of potent diuretics such as frusemide.

Latent diabetes may become manifest or the insulin requirements of diabetic patients may increase.

Infusion rates in excess of 4 mg/min are associated with an increased risk of ototoxicity, usually reversible hearing loss.

Precautions: Caution should be observed in patients liable to electrolyte deficiency. The use of Dryptal during the first trimester of pregnancy should be subject to the normal precautions which apply to any drug at this time.

As Dryptal may inhibit lactation it should be used with caution in nursing mothers.

Treatment of overdose: Correct dehydration and electrolyte depletion. Reversible deafness may occur.

Side-effects: Dryptal is generally well tolerated. Side-effects of a minor nature such as nausea, malaise or gastric upset may occur but are not usually severe enough to cause withdrawal of treatment.

The incidence of allergic reactions such as skin rashes is very low but when these occur treatment should be withdrawn.

In common with other sulphonamide-based diuretics hyperuricaemia may occur and in rare cases, clinical gout may be precipitated.

Bone marrow depression has been reported as a rare complication and necessitates withdrawal of treatment.

Pharmaceutical precautions Dryptal 50 mg should be stored in a cool dry place protected from light in the original containers. Injections of Dryptal should not be mixed with any other preparations. Opened ampoules should be used immediately and any remainder discarded.

Legal category POM.

Package quantities Dryptal ampoules 50 mg are available in packs of 10 × 5 ml.

Further information Nil.

Product licence number 0152/0149.

DRYPTAL* INJECTION 250 mg/25 ml

Presentation Dryptal 250 mg ampoules contain 250 mg Frusemide BP in 25 ml.

Uses Dryptal 250 mg is a diuretic preparation for the management of oliguria due to acute or chronic renal insufficiency with a GFR below 20 ml/minute.

Dosage and administration Dryptal 250 mg should be administered by intravenous injection at a rate not exceeding 4 mg/min.

The recommended initial dose is one 25 ml ampoule (250 mg) diluted in approximately 225 ml Sodium Chloride Injection BP or Ringer's Solution for Injection administered over one hour. This gives an approximate drip rate of 80 drops/minute, ensuring that the infusion is at the level of 4 mg/minute.

If a satisfactory increase in urine output, such as 40–50 ml/hour, is not attained within the next hour a second infusion of two 25 ml ampoules (500 mg) in an appropriate infusion fluid should be given, the total volume of the infusion being governed by the patient's state of hydration. If a satisfactory output is still not achieved within one hour of the end of the second infusion, a third infusion consisting of four 25 ml ampoules (1,000 mg) can be given. The rate of infusion should not exceed 4 mg/min.

If the third infusion using the maximum intravenous dose of 1,000 mg over four hours is not effective, then dialysis will probably be required.

In oliguric or anuric patients with significant fluid overload, it may not be practicable to administer high-dose Dryptal injection by the method suggested above. Under these circumstances, the use of a constant-rate infusion pump (e.g. Sage pump) with micrometer screw-gauge adjustment may be considered for direct administration of the injection in to the vein. The rate of administration should not exceed 4 mg/min.

If the Dryptal infusion produces a satisfactory response of 40–50 ml/hour, then the effective dose (up to 1,000 mg) can be repeated every 24 hours. Alternatively, maintenance therapy can be continued with oral Dryptal 500 mg tablets when one 500 mg tablet may be regarded as being approximately equal to one 250 mg ampoule. Appropriate dosage adjustments may then be made according to the observed clinical response.

Contra-indications, warnings, etc During treatment with high-dosage forms of Dryptal, fluid balance should be carefully controlled. In the particular case of patients with shock, steps should be taken to correct the blood pressure and circulating blood volume before commencing therapy. Regular checks of plasma electrolytes, particularly sodium, potassium, chloride and bicarbonate, should be carried out, and electrolyte replacement therapy instituted accordingly.

Intravenous injections of Dryptal **must** be given slowly.

Infusion rates in excess of 4 mg/min are associated with an increased risk of ototoxicity, usually reversible hearing loss.

Contra-indications: Dryptal injection 250 mg is contra-indicated in renal failure as a result of poisoning by nephrotoxic or hepatotoxic agents and in renal failure associated with hepatic coma.

Warnings: The dosage of concurrently administered cardiac glycosides or antihypertensive agents may require adjustment.

Cephaloridine nephrotoxicity may be increased by concomitant administration of potent diuretics such as frusemide.

Latent diabetes may become manifest or the insulin requirements of diabetic patients may increase.

Precautions: The safety of high dosage frusemide in pregnancy has not been established and Dryptal injection 250 mg should be used with caution depending on the

severity of the condition. As Dryptal may inhibit lactation it should be used with caution in nursing mothers.

Treatment of overdosage: Correct dehydration and electrolyte depletion. Reversible deafness may occur.

Side-effects: Dryptal injection 250 mg is generally well tolerated. Side-effects of a minor nature such as nausea, malaise or gastric upset may occur but are not usually severe enough to cause withdrawal of treatment.

The incidence of allergic reactions such as skin rashes is very low but when these occur treatment should be withdrawn.

In common with other sulphonamide-based diuretics hyperuricaemia may occur and, in rare cases, clinical gout may be precipitated.

Bone marrow depression has been reported as a rare complication and necessitates withdrawal of treatment.

Pharmaceutical precautions Dryptal ampoules 250 mg should be stored in a cool place protected from light. Frusemide may precipitate in solutions of low pH and therefore dextrose solutions are not suitable infusion fluids for Dryptal injections 250 mg. The injection solution should not be mixed with other drugs in the infusion bottle.

Opened ampoules should be used immediately and any remainder of either the ampoule content or the prepared infusion solution should be discarded.

Legal category POM.

Package quantities Dryptal ampoules 250 mg are available in packs of 10 × 25 ml.

Further information Diuresis should commence within a few minutes and last for approximately two hours. A diuretic effect is seen during the infusion and its duration is related to the infusion time.

Product licence number 0152/0149.

ERYCEN[®]

Presentation Plain orange film-coated Erythromycin Tablets BP 250 mg (Erythromycin base).

Uses Infections caused by erythromycin-sensitive organisms especially Gram-positive pyogenic cocci and some Gram-negative bacteria, notably *Haemophilus* and *Neisseria* groups.

Dosage and administration *Adults:* 1 tablet every four to six hours increased to 4 g or more per day in unusually severe infections.

Contra-indications, warnings, etc Known sensitivity to erythromycin. Use in conjunction with other anti-infectives, except when specifically warranted.

Precautions: Caution should be exercised in administering erythromycin to patients with impaired hepatic function, since the antibiotic is excreted principally by the liver.

Side-effects are rare and usually mild. Nausea, vomiting, diarrhoea and pruritus have occurred. Allergic reactions are rare and mild, although anaphylaxis has occurred. Treatment should not usually be continued for longer than ten days. The rare possibility of superinfection caused by overgrowth of non-susceptible bacteria or fungi should be borne in mind during prolonged or repeated therapy, especially when other antibacterial agents are simultaneously employed.

Treatment of overdosage: It is unlikely that serious symptoms will occur; observation and conservative management are indicated.

Pharmaceutical precautions Store in a cool dry place.

Package quantities Containers of 100 and 500 tablets.

Legal category POM.

Further information Erythromycin is bacteriostatic and bactericidal, depending on the concentration. Its antimicrobial spectrum is similar to that of penicillin G but it shows increased activity against some Gram-negative bacteria.

Product licence number 0152/0132.

IMBRILON[®]

Presentation Opaque yellow Indomethacin Capsules BP 25 mg (marked 'BERK 1J3 25') and 50 mg (marked 'BERK 2J3 50').

Cream-coloured Indomethacin Suppositories BP 100 mg. The base is polyethylene glycol.

Uses Non steroidal analgesic and anti-inflammatory agent. Indicated in active rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and acute gout. Also may be indicated in severe acute periarticular disorders such as bursitis, tendinitis, synovitis, tenosynovitis and capsulitis.

Dosage and administration Indomethacin Capsules should always be given with food, milk or an antacid to lessen the chance of gastro-intestinal disturbance.

Imbrilcon Suppositories should be given singly, one night and morning.

Adults: 50–100 mg daily.

Children: Paediatric dosage not established.

Contra-indications, warnings, etc

Contra-indications: It is not known if indomethacin is safe to use in children or in pregnancy or during lactation and it should not be given to such patients.

Active peptic ulcer, a history of recurrent gastro-intestinal lesions, sensitivity to indomethacin or to aspirin are also contra-indications.

Precautions and drug interactions: Indomethacin should be used with caution in patients with hepatic or renal dysfunction. Hepatitis and jaundice have been reported rarely. Patients should be warned not to drive or operate machinery, if they become dizzy.

In common with other anti-inflammatory analgesic antipyretic agents, indomethacin may mask the signs and symptoms of infectious disease and this should be borne in mind in order to avoid delay in starting treatment for infection.

Indomethacin should be used with caution in patients with an existing, albeit controlled, infection.

Particular care should be taken with older patients who are more susceptible to side-effects from indomethacin.

Treatment of overdosage: Gastric lavage should be given if indomethacin is considered still to be part of the stomach contents.

Otherwise supportive therapy is required and a watch should be kept for gastro-intestinal bleeding for several days.

Warnings and adverse effects: It must be expected that about 20% of patients will complain of side-effects, but starting treatment at a low dosage and increasing it gradually until symptomatic relief is obtained will minimise their incidence.

The most common side-effects are headache, dizziness and dyspepsia. If headache persists, even after dosage reduction, indomethacin should be withdrawn.

Other CNS side-effects which may occur include mental confusion, depression, convulsions, coma, de-personalisation and tinnitus. These are often transient and disappear with time or on reduction of dosage.

Indomethacin may aggravate psychiatric disorders, epilepsy and Parkinsonism.

Gastro-intestinal disorders which occur most frequently are nausea, anorexia, vomiting, epigastric distress, abdominal pain and diarrhoea. Giving indomethacin with food, milk or antacids lowers the incidence of these side-effects. Ulceration of the oesophagus, stomach or duodenum may also occur, accompanied by haemorrhage and perforation (a few fatalities have been reported). Gastro-intestinal bleeding without obvious ulceration may also occur. If this happens indomethacin treatment should be discontinued.

Blood dyscrasias, particularly thrombocytopenia, have been reported.

Blurred vision and orbital and peri-orbital pain are seen infrequently. Corneal deposits and retinal disturbances have been reported in some patients with rheumatoid arthritis on prolonged therapy with indomethacin, and ophthalmic examinations are desirable in patients given prolonged treatment.

Oedema and increased blood pressure also sometimes occur, as does haematuria.

Hypersensitivity reactions include pruritus, urticaria, angitis, erythema nodosum. Skin rash and hair loss may also occur.

Acute respiratory distress including sudden dyspnoea and asthma, have been reported on rare occasions. Bronchospasm may be precipitated in patients suffering from, or with a previous history of bronchial asthma or allergic disease.

Pharmaceutical precautions Containers should be kept closed, in a cool place and protected from light.

Legal category POM.

Package quantities *Capsules 25 mg:* Containers of 500.

Capsules 50 mg: Containers of 100.

Suppositories 100 mg: Containers of 30.

Further information Nil.

Product licence numbers

Capsules 25 mg 0152/0072

Capsules 50 mg 0152/0074

Suppositories 100 mg 0152/0127.

MELITASE*

Presentation White Chlorpropamide Tablets BP, scored on reverse. 100 mg marked 'BERK 3D4' and '50 mg marked 'BERK 4D4'.

Uses As an oral hypoglycaemic agent in uncomplicated table, mild and moderately severe, nonketotic, maturity-onset type diabetes mellitus, where dietary treatment alone has failed. Chlorpropamide can often be used in

patients of this type in place of insulin. Its hypoglycaemic effect, however, occurs only when the β cells of the islet tissue in the pancreas retain some functional capacity. It has no effect on glucose tolerance.

Chlorpropamide is valueless in the treatment of severe diabetes.

Chlorpropamide should not be used to replace dietetic therapy where this is indicated.

Dosage and administration In uncomplicated maturity onset diabetes, the initial and maximum dose, taken as two 250 mg tablets, is 500 mg, which should be reduced to a maintenance level as soon as possible. Since three days are necessary for blood levels of chlorpropamide to become stable at a particular dosage changes should not be made at shorter intervals and should be in steps of 50–100 mg. Most patients are stabilised on a dosage of 100–375 mg daily.

Several weeks may be required to achieve a correct dosage level and the patient's blood sugar should be monitored throughout where possible and the urine tested for glycosuria at least four times daily in all cases.

Elderly patients should be started on half the usual dosage since they are often very sensitive to the sulphonylureas and may develop hypoglycaemia if given full dosage.

Contra-indications, warnings, etc 'Melitase' is contra-indicated in diabetic ketosis diabetes complicated by fever trauma or gangrene and in patients with impaired renal hepatic or thyroid function.

Patients taking 'Melitase' may become intolerant of alcohol, a reaction not unlike the disulfiram alcohol reaction being produced. Patients should be warned of this possibility.

The hypoglycaemic effect of 'Melitase' may be increased by coumarin derivatives, MAO inhibitors, salicylates and propranolol.

Because of the possibility of blood dyscrasia a white cell count should be performed and should be repeated in five days should an infection or symptoms of infection appear.

'Melitase' should not be used as a substitute for dietary treatment.

Gastric and intestinal disturbance, jaundice, headache, tinnitus, weakness, paraesthesia and skin rashes have been observed. Blood dyscrasias have been reported and include agranulocytosis, leucopenia and thrombocytopenia. A prolonged hypoglycaemia may very occasionally be produced by chlorpropamide.

Treatment of overdose: Hypoglycaemic coma can occur up to five days after an overdose. Repeated infusions of intravenous glucose may be required. The patient should be carefully monitored as sudden relapses are likely. Gastric lavage and haemodialysis will help to remove the excess Melitase.

Pharmaceutical precautions No special precautions.

Legal category POM.

Package quantities

Tablets 100 mg: Containers of 500.

Tablets 250 mg: Containers of 500.

Further information Nil.

Product licence numbers

Tablets 100 mg 0152/0101

Tablets 250 mg 0152/0102.

MUCODYNE*

Presentation *Mucodyne Syrup*: Clear amber syrup containing carbocisteine 250 mg in each 5 ml.

Mucodyne paediatric syrup: Clear red syrup containing carbocisteine 125 mg in each 5 ml.

Mucodyne Capsules: Opaque yellow capsules marked 'MUCODYNE 375', each containing carbocisteine 375 mg.

Uses Mucolytic agent for the adjunctive therapy of respiratory tract disorders characterised by excessive or viscous mucus including Glue Ear in children.

Mucodyne reduces the viscosity of bronchial secretions and facilitates expectoration. There is also evidence that during treatment with Mucodyne the physical and chemical characteristics of the mucin components of sputum return to a more normal pattern, with reduction of fucose and sulphate content and an increase in the proportions of sialomucins.

Dosage and administration *Mucodyne Syrup*: *Adults*: 15 ml three times a day initially, reduced to 10 ml three times a day when a satisfactory response has been obtained.

Mucodyne paediatric syrup: 2–5 years: 2.5–5 ml four times a day.

5–12 years: 10 ml three times a day.

Mucodyne capsules: *Adults*: Two capsules three times a day, reduced to one capsule four times a day when a satisfactory response has been obtained.

Contra-indications, warnings, etc Although tests in mammalian species have revealed no teratogenic effects, Mucodyne is not recommended during the first trimester of pregnancy.

There have been very rare reports of skin rashes or gastro-intestinal bleeding occurring during treatment with Mucodyne.

Treatment for overdose: Gastric lavage may be beneficial, followed by observation. Gastrointestinal disturbance is the most likely symptom of Mucodyne overdose.

Pharmaceutical precautions Mixture with linctus of pholcodeine causes precipitation of carbocisteine from solution. Dilution of Mucodyne Syrup may be effected with unpreserved Syrup BP but diluted preparations should not be kept for more than 14 days.

Legal category POM.

Package quantities *Mucodyne Syrup*: Bottles of 200 ml. Bottles of 300 ml with dosage cap.

Mucodyne paediatric syrup: Bottles of 300 ml with dosage cap.

Mucodyne Capsules: Containers of 100.

Further information Nil.

Product licence numbers

Syrup 0152/0042

Paediatric syrup 0152/0166

Capsules 0152/0098.

NITRADOS*

Presentation White, round, flat, bevel-edged Nitrazepam Tablets BP, marked BERK 1N4, with single break line on reverse, each containing 5 mg Nitrazepam BP.

Uses Hypnotic of the benzodiazepine group, indicated for the relief of insomnia due to anxiety or stress. It may also be used as adjunctive therapy in the treatment of sleep disturbances due to organic causes.

At therapeutic doses nitrazepam induces sleep lasting some six to eight hours, from which the sleeper may be readily aroused if necessary. There is less confusion upon awakening than is observed with the barbiturates, especially in the elderly.

Dosage and administration *Adults*: Usually 5 mg before retiring. This may be increased to 10 mg when necessary or to 20 mg in hospitalised patients.

Smaller doses, 2.5–5 mg are more suitable for elderly patients.

Children: Nitrados is not recommended for the routine treatment of children but 2.5 mg may be given when necessary to children aged one to six years and 5 mg to children aged seven years or older.

Contra-indications, warnings, etc Nitrados should only be used with great caution in patients with impairment of renal or hepatic function, or who are elderly or debilitated. Particular consideration should be given to respiratory function.

Concomitant administration with CNS depressants (including alcohol), general anaesthetics, narcotic analgesics, monoamine oxidase inhibitors and anti-depressants may result in an accentuation of their effects.

Patients should be warned of the possibility of drowsiness occurring, particularly in the first few days of therapy and advised to moderate their use of alcohol. They should also be warned not to drive or operate machinery if Nitrados affects their alertness.

Although animal experiments have revealed no teratogenic effects, nitrazepam is not recommended during the first trimester of pregnancy.

Side-effects are few at the recommended dosage although fatigue, drowsiness or light-headedness are occasionally noted and confusion may occur in the elderly.

Excessive or prolonged use of nitrazepam may result in the development of psychological dependence with withdrawal symptoms on discontinuance.

Treatment of overdose: Drowsiness and ataxia will be the predominant initial symptoms and the patient may be unconscious for up to 36 hours. Gastric lavage may be useful but Nitrados causes few serious problems in overdose. In children behavioural changes are likely.

Pharmaceutical precautions Protect from light, heat and moisture.

Legal category POM.

Package quantities Containers of 50 and 500 tablets

Further information Nil.

Product licence number 0152/0130.

NODILON*

Presentation White tablets each containing 80 mg Trimethoprim BP and 400 mg Sulphamethoxazole BP.

Uses Antibacterial agent. Nodilon is effective in-vitro against a wide range of Gram-positive and Gram-negative organisms. It is not active against *Mycobacterium tuberculosis* or *Treponema pallidum*.

Pseudomonas aeruginosa is usually insensitive.

Nodilon is of value in the treatment of the following.

Respiratory tract infections:

Acute and chronic bronchitis, bronchiectasis, empyema, lung abscess, lobar- and broncho-pneumonia, Pneumocystis carinii pneumonitis, otitis media and sinusitis.

Genito-urinary tract infections:

Urethritis, cystitis, pyelitis, pyelonephritis and prostatitis. Gonorrhoea.

Gastro-intestinal tract infections:

Typhoid and paratyphoid fevers, chronic carrier states with Salmonella typhi and paratyphi, cholera, shigellosis.

Skin infections:

Pyoderma, abscesses and wound infections.

Other bacterial infections:

Acute and chronic osteomyelitis, acute brucellosis, septicaemias and other infections caused by sensitive organisms.

Dosage and administration *Adults:* Standard dosage: 2 tablets twice daily. Maximum dosage (for particularly severe infections): 3 tablets twice daily.

Minimum dosage and dosage for long-term treatment (more than 14 days): 1 tablet twice daily.

Children over 12 years: As for adults.

6-12 years: 1 tablet twice daily.

In acute infections, Nodilon should be given for at least five days or until the patient has been symptom-free for two days.

In prostatitis and brucellosis, treatment should last for a period of at least 4 weeks.

Dosage in gonorrhoea: In uncomplicated gonorrhoea 4 tablets every 12 hours for two days or 5 tablets followed eight hours later by a further dose of 5 tablets is recommended.

In the treatment of Pneumocystis carinii pneumonitis the dosage is 20 mg Trimethoprim/100 mg Sulphamethoxazole/kg/day in 2 divided doses for 2 weeks.

Dosage recommendations in renal impairment: If Nodilon is given to patients with renal impairment then the following dosage scheme, based on creatinine clearance, is suggested (no information is available for children with renal failure).

Creatinine clearance:

Above 25 ml/min	Standard dosage.
15-25 ml/min	Standard dosage for a maximum of three days followed by half the standard dosage every 24 hours.
Below 15 ml/min	Not to be administered unless haemodialysis facilities are available. Under this condition half the standard dosage may be given every 24 hours.

Measurements of plasma concentrations of sulphamethoxazole at intervals of two to three days are recommended in samples obtained 12 hours after administration of Nodilon. If the concentration of total Sulphamethoxazole exceeds 150 mcg/ml, then treatment should be interrupted until the value falls below 120 mcg/ml.

Contra-indications, warnings, etc Contra-indicated in severe renal insufficiency where repeated measurements of the plasma concentration cannot be performed. In cases with renal impairment a modified dosage schedule as described above is indicated. In such patients, measurement of the plasma concentration of

the drug is advisable, and an adequate urinary output should be maintained.

Contra-indicated in patients showing marked liver parenchymal damage or blood dyscrasias.

Nodilon should not be given to patients with a history of trimethoprim, sulphonamide or co-trimoxazole sensitivity.

Nodilon should not be given to premature babies nor to full-term infants during the first six weeks of life. The drug should not be given during pregnancy. The usual caution in prescribing any drug for women of child-bearing age should also be exercised with Nodilon.

If Nodilon treatment is prolonged, especially in patients with suspected impairment of folate metabolism, it is suggested that complete blood counts including thrombocytes should be performed fortnightly for the first month, and then monthly.

Nausea, vomiting, glossitis and skin rashes can occur. Isolated cases of severe skin sensitivity reactions such as erythema multiforme (Stevens-Johnson syndrome), and epidermal necrolysis (Lyell syndrome) have occurred.

As Nodilon contains a sulphonamide, the possibility of blood dyscrasias, like those associated with sulphonamides, should be borne in mind.

The changes reported with Co-trimoxazole consist mainly of thrombocytopenia, purpura, leucopenia, neutropenia and very rarely agranulocytosis. They have usually proved to be reversible on withdrawal of the drug. Elderly patients are more susceptible to these blood changes.

During long-term therapy, isolated cases of megaloblastic changes in the bone marrow have been reported; these are reversible with calcium folinate therapy.

Due to the relatively high degree of protein binding of sulphamethoxazole, patients receiving oral anticoagulants of the coumarin group should be monitored to ensure appropriate anticoagulant control.

Patients receiving pyrimethamine in doses in excess of 25 mg weekly who are also receiving Nodilon should have their blood pictures monitored because of the occasional report of megaloblastic anaemia apparently occurring in these circumstances.

Care should be taken when giving Nodilon to diabetic patients on sulphonylureas as it may increase the hypoglycaemic action of these drugs.

Treatment of overdosage: Gastric lavage may be useful. Forced diuresis is advised, and alkalisation of the urine will increase the elimination of the sulphamethoxazole. Calcium folinate 3-6 mg given intramuscularly for five to seven days should counteract the bone-marrow depressant effects of trimethoprim. General supportive measures should be taken.

Pharmaceutical precautions Store in a cool dry place. Protect from light.

Legal category POM.

Package quantities Securitainers of 50 and 1,000 tablets.

Further information Absorption by the oral route is rapid; significant plasma levels are obtained within an hour. Peak levels are reached between two and four hours and are maintained over a period of 12 hours.

In the treatment of tonsillo-pharyngitis due to Group A beta-haemolytic streptococci, eradication of these organisms from the oro-pharynx is less rapid than with some other antibiotics.

Both sulphamethoxazole and trimethoprim may be

found in breast milk but this does not contraindicate the use of Nodilon in lactating mothers.

Product licence number 0152/0163

PACITRON®

Presentation Film-coated, oblong orange-yellow tablets marked 'PCT 500', each containing L-tryptophan 500 mg.

Uses L-tryptophan is a metabolic precursor of 5-hydroxytryptamine (serotonin) which acts as a neurotransmitter in the central nervous system. It is indicated in endogenous and reactive depression and in depressive phases of manic-depressive psychosis.

Dosage and administration *Adults:* 3-6 g daily in divided doses. In the case of outpatients, it is generally found that a dosage of 2 tablets three times a day is sufficient. In more severely depressed patients, especially those in hospital, dosage of 12 tablets daily may be required. The last dose should be taken before bed.

Children: There is insufficient evidence to establish paediatric dosage and use is not recommended in children.

L-tryptophan may also be given to patients responding inadequately to monoamine oxidase inhibitors (MAOI), but when the two are given together the side-effects of both may be increased. Pacitron should therefore be introduced more slowly, beginning at 1 tablet daily for the first week and 2 tablets daily for the second. Normal dosage may be given from the third week onwards, but Pacitron should be discontinued at once if headache or blurring of vision occurs.

Contra-indications, warnings, etc The use of Pacitron should not replace standard management in patients with severe depression and/or a risk of suicide.

There is no absolute contra-indication to the use of this dosage of L-tryptophan, which is a normal and essential constituent of the diet. When given along with MAOI it may sometimes provoke a reaction resembling alcoholic intoxication, and when taken alone it may occasionally cause drowsiness particularly in the early stages of treatment. Patients should be warned to avoid driving or handling machinery until their reaction is known.

In patients taking Pacitron along with or following treatment with phenothiazines or benzodiazepines, there have been rare reports of sexual disinhibition and of reversible Parkinsonian-like rigidity and dyskinesias. Since these other drugs may reduce plasma binding of tryptophan, it is recommended that initial dosage of Pacitron should not exceed 1 tablet thrice daily if the patient is taking or has just finished treatment with a major tranquilliser.

Nausea occurs in a few patients early in treatment, and may be of central origin, but can usually be relieved by taking Pacitron after food.

There is as yet no information on the effects of prolonged administration of Pacitron. It is therefore advised that after six months' therapy at full dosage, the patient's condition should be re-assessed with a view to lowering or discontinuing medication unless clear evidence of benefit from the use of the product is present.

Pacitron is not advised, except for relatively short periods, in patients with active bladder disease or known bladder lesions.

The safety of large doses of L-tryptophan during pregnancy has not been established and use in pregnant women and nursing mothers is not advised.

Treatment of overdosage: No serious consequences are known to result from overdosage. Gastric lavage might be helpful followed by observation and general supportive measures.

Pharmaceutical precautions No special precautions.

Legal category POM.

Package quantities Containers of 100 tablets.

Further information As with other antidepressant therapy, the full effect of Pacitron may not develop for two or three weeks and patients should be told this.

Product licence number 0152/0117.

PONOXYLAN®

Presentation White gel containing 10% w/w polynoxylin.

Uses Topical broad spectrum antibacterial and healing agent.

Ponoxylan Gel is indicated in all infective skin conditions including furunculosis and pustular acne. It is of great value in burns wounds and cutaneous infected conditions including staphylococcal nasal infections. It reduces inflammation in intertrigo and many eczematoid eruptions.

It is of considerable value in dermatology as an alternative to broad spectrum antibiotic therapy with or without corticosteroids.

Dosage and administration Ponoxylan Gel should be gently applied to the affected areas.

Contra-indications, warnings, etc There are no known contra-indications. There are no special precautions to be taken with Ponoxylan Gel.

Ponoxylan is virtually insoluble and is therefore not absorbed into the blood stream. Systemic toxicity is thus nil. There have been no reports of sensitivity to polynoxylin. A very occasional patient may experience stinging or pain following application.

Pharmaceutical precautions No known incompatibilities.

Legal category P.

Package quantities Tubes of 25 g.

Further information Nil.

Product licence number 0152/5042.

PRAMIDEX®

Presentation White Tolbutamide Tablets BP 500 mg marked 'BERK 5E5', single break line.

Uses As an oral hypoglycaemic agent in the treatment of mild and moderately severe uncomplicated diabetes mellitus, particularly of the maturity-onset type, where control cannot be achieved by diet alone.

The hypoglycaemic effect of tolbutamide only occurs when the β cells of the islet tissue in the pancreas are intact and when they retain some functional capacity. It is therefore presumed that tolbutamide stimulates the

pancreas to a greater insulin output. It has no effect on glucose tolerance.

It follows that Pramidex has no place in the treatment of the severe diabetic, but finds its chief use in the treatment of maturity-onset diabetes, responding inadequately to dietary treatment alone. In some of these patients it can replace low doses of insulin or reduce the requirement for high doses.

Dosage and administration Pramidex should be given with or just before meals for optimum control of blood sugar.

1st day: 4–8 tablets.

2nd day: 3–6 tablets.

3rd day: 2–4 tablets.

Maintenance: 1–3 tablets daily, the exact dose being that sufficient to correct glycosuria and hyperglycaemia without producing hypoglycaemia. The full effect of therapy may take up to a week to develop.

Where a patient is already taking insulin, the change to tolbutamide may be effected directly where the dose of insulin is 15 units or less per day. Where insulin is being given in greater amounts, the number of units should be decreased over several days and a watch should be kept for glycosuria.

Contra-indications, warnings, etc Diabetes complicated by fever, trauma or gangrene and diabetic retinosis. Impaired renal, hepatic or thyroid function. Pramidex is contra-indicated during pregnancy. Sulphafurazole is thought to potentiate the action of tolbutamide and the concurrent administration of these two drugs is contra-indicated.

Gastric irritation may occur and may be reduced by giving in divided doses. Skin sensitisation weakness, paraesthesias, tinnitus, headache, intolerance to alcohol and jaundice have all been observed. Reversible blood dyscrasias have also occurred. A very small proportion of patients are thought to have difficulty in metabolising tolbutamide and in consequence develop hypoglycaemia even on low dose.

If fever or a sore throat occurs, a white cell count should be performed and should be repeated after five days as blood abnormalities may develop slowly.

Severe hypoglycaemia has occurred with the concomitant administration of coumarins.

The possibility of thrombocytopenia should be borne in mind and a platelet count performed if indicated.

Cases which respond initially to tolbutamide may elapse at a later date and this should be considered as possibility should glycosuria or hyperglycaemia appear.

Pramidex should not be used as a substitute for dietary treatment in obese diabetics.

Treatment of overdosage: Gastric lavage. Hypoglycaemia may be counteracted with dextrose and, if necessary, glucagon.

Pharmaceutical precautions No special precautions.

Legal category POM.

Package quantities Containers of 500 tablets.

Further information Nil.

Product licence number 0152/0061.

'RIMPERAN'

Presentation *Tablets:* White tablet marked 'PRIM-

PERAN' with single break line on reverse. Each tablet contains 10 mg metoclopramide monohydrochloride.

Lime-coloured syrup: Each 5 ml contains 5 mg metoclopramide monohydrochloride.

Clear ampoules: 10 mg metoclopramide monohydrochloride in 2 ml.

Uses For the relief of upper gastro-intestinal symptoms including heartburn, nausea and vomiting in flatulent dyspepsia gastritis and duodenitis.

As an anti-emetic agent for the treatment of nausea and vomiting accompanying the following conditions.

Intolerance to essential drugs such as digitalis, antibiotics and antibacterials, tuberculostatic agents, cytostatic and cytotoxic drugs.

Gastro-intestinal disorders, including peptic ulcers, gastritis and sequelae of gastrectomy.

Malignant disease.

Uraemic conditions.

Deep X-ray or cobalt therapy.

Post-anaesthetic vomiting.

Barium-meal examinations.

Post-operative gastric hypotonia.

Post vagotomy syndrome.

To facilitate barium-meal examinations:

(a) where barium-meal studies are held up by spasm of the duodenal cap making examination for the presence of the ulcer difficult;

(b) to facilitate examination of the hypotonic stomach with delayed emptying, gastric stasis and pyloric channel syndrome.

To facilitate duodenal intubation procedures.

Dosage and administration The daily dose level of Primperan is based upon 0.5 mg/kg body weight, in divided doses, which in normal circumstances should not be exceeded. It is particularly desirable to adhere to this level in children and young adults.

General therapeutic dosage:

Tablets: Adults: 1 tablet (10 mg) three times daily.

Young adults: (15–20 years): $\frac{1}{2}$ –1 tablet two to three times daily.

Syrup: Adults: Two 5 ml spoonfuls (10 mg) three times daily.

Young adults (15–20 years): One to two 5 ml spoonfuls two to three times daily.

Children (5–14 years): Half to one 5 ml spoonful three times daily.

Ampoules: Adults: 1 ampoule (10 mg) i.m. or i.v. one to three times daily according to the severity of the condition.

Young adults (15–20 years): $\frac{1}{2}$ –1 ampoule i.m. or i.v. one to three times daily.

Children (5–14 years): Up to $\frac{1}{2}$ ampoule i.m. or i.v. one to three times daily.

To facilitate barium meal examinations and small bowel intubations:

Ampoules: Adults: One (10 mg) to two (20 mg) ampoules i.m. or i.v. 5–10 minutes before the examination.

Children (5–14 years): Up to $\frac{1}{2}$ an ampoule, according to age, i.m. or i.v. 5–10 minutes before the examination.

Oral: Adults: Four 5 ml spoonfuls or 2 tablets (20 mg) 10–15 minutes before the examination.

Young adults (15–20 years): Two 5 ml spoonfuls or 1 tablet (10 mg) 10–15 minutes before the examination.

Children (5–14 years): Half to one 5 ml spoonful 10–15 minutes before the examination.

Contra-indications, warnings, etc Since atropine effectively blocks the action of 'Primperan', the concomitant administration of this and other anticholinergic drugs should be avoided.

As both Primperan and phenothiazines may cause benign transient dystonia, care should be exercised in the event of both drugs being prescribed concurrently.

The recommended dosage should not be exceeded, particularly in children, young adults and other patients of low body weight, who may be more liable to dystonic reactions.

Primperan is not recommended during pregnancy, although animal tests in several mammalian species have revealed no teratogenic effect.

'Primperan' has given rise to a remarkably low incidence of side-effects, with absence of serious toxicity and excellent tolerance by oral and parenteral routes. Although rare, drowsiness and dystonic reactions have been reported, these are reversible usually disappearing within 24 hours of stopping treatment.

The rarely occurring symptoms include spasm of facial extra-ocular or cervical muscles which may be constant or rhythmic. There may also be a generalised increase in muscle tone. Anti-Parkinsonian drugs of the anticholinergic type may be used to counteract these reactions.

Treatment of overdosage: Gastric lavage and intensive supportive therapy should be initiated. Dystonic symptoms are likely and may be treated in severe cases with atropine, benztropine or other anticholinergic agents. Generalised convulsions may appear in infants.

Pharmaceutical precautions No known incompatibilities.

Diluent for Syrup: Syrup BP.

Diluent for ampoules: Water for injection BP.

Protect from direct light.

Legal category POM.

Package quantities *Tablets:* Containers of 100 and 500.

Syrup: Bottles of 100 ml.

Ampoules: Boxes of 10 × 2 ml.

Further information Primperan has the unique action of normalising the hypomotile stomach and small intestine and also possesses a powerful antiemetic effect.

Product licence numbers

Tablets 0152/5001

Syrup 0152/5002

Ampoules 0152/5003.

SILBE* INHALANT

Presentation Clear liquid for aerosolisation containing Papaverine Hydrochloride BP 0.95% w/v, Adrenaline Acid Tartrate BP 1% w/v, Atropine Methonitrate BP 0.125% w/v, Chlorbutol BP 1% w/v, Hyoscine Hydrobromide BP 0.050% w/v.

Uses For the treatment of Bronchospasm occurring in asthma.

Dosage and administration Adults should inhale for one to two minutes and children for half to one minute.

Treatment should be started as soon as an attack is imminent and may be repeated two or three times a day.

Contra-indications, warnings, etc 'Silbe' Inhalant is contra-indicated in hyperthyroidism, hypertension, coronary disease.

Side-effects: Palpitations, cardiac dysrhythmias may develop in adrenaline-sensitive patients.

Treatment of overdosage: Gastric lavage if taken by mouth. Observation and intensive supportive therapy.

Pharmaceutical precautions Keep bottles tightly closed.

Legal category POM.

Package quantities Bottles of 25 ml.

Further information Nil.

Product licence number 0152/5066.

SILBEPHYLLINE*

Presentation *Tablets:* White tablets marked 'BERK' with single break line on reverse. Each tablet contains 200 mg Diprophylline PhEur.

Clear ampoules: Each ampoule contains 500 mg Diprophylline PhEur in 2 ml.

White suppositories: Each contain 400 mg Diprophylline PhEur.

Red syrup: Each 5 ml contains 100 mg Diprophylline PhEur.

Uses Bronchodilator. Chronic bronchitis, bronchial asthma and congestive heart failure.

'Silbephylline' is a soluble, neutral, stable theophylline derivative. It dilates bronchiolar vessels and relaxes bronchial musculature. When injected there is direct myocardial stimulation and dilation of coronary and other circulatory vessels. 'Silbephylline' also has a mild diuretic action.

Dosage and administration *Adults: Tablets: Acute conditions:* 2 tablets every six hours.

Maintenance therapy: 1–2 tablets three times daily.

Suppositories: 2 inserted within 24 hours or one at night.

Injection: Intramuscularly: 1 ampoule two or three times daily.

Intravenously: 1 ampoule by slow administration over one to two minutes.

Syrup: Adults: Two to four 5 ml spoonfuls every six hours.

Children: Under 1 year: 0.5–1.5 ml every six hours.

1–2 years: 2 ml every six hours.

3–5 years: 3 ml every six hours.

6–12 years: 5 ml every six hours.

Dilution of syrup may be effected with Syrup Simplex.

Contra-indications, warnings, etc No known contra-indications.

Intravenous injections must be given slowly, otherwise headache, palpitation, dizziness, nausea and fall in blood pressure may occur.

Reported side-effects are few and mild. Overdosage may produce symptoms of xanthine poisoning – e.g. nausea, headache, vomiting, thirst, restlessness and shock.

Treatment of overdosage: Gastric lavage and intensive symptomatic therapy. Convulsions, acidosis, hypokalaemia and possibly cardiac dysrhythmia may require correction.

Pharmaceutical precautions No special precautions.

Diluent for ampoules: Water for Injection BP.

Diluent for syrup: Syrup BP.

Legal category

Tablets	P.
Ampoules	POM.
Suppositories	P.
Syrup	P.

Package quantities *Tablets:* Packs of 100 and 500.

Ampoules: Boxes of 10 × 2 ml.

Suppositories: Boxes of 10.

Syrup: Bottles of 100 ml.

Further information Nil.

Product licence numbers

Tablets	0152/5008
Ampoules	0152/5009
Suppositories	0152/5011
Syrup	0152/5010

ETRACHEL*

Presentation *Tablets:* Orange film-coated Tetracycline Tablets BP 250 mg engraved BERK 3C7.

Capsules: Orange Tetracycline Capsules BP 250 mg.

Syrup: Red Syrup (Tetracycline Syrup BPC) containing tetracycline equivalent to tetracycline hydrochloride 25 mg per 5 ml.

Uses Infections caused by organisms sensitive to tetracycline. These include pneumonia, acute and chronic bronchitis, whooping cough, psittacosis, urinary tract infections, amoebic dysentery, brucellosis and chlamydial fevers.

Dosage and administration *Adults:* 1 tablet or capsule or 2 teaspoonfuls syrup every six hours.

Children: $\frac{1}{2}$ –1 teaspoonful syrup every six hours according to age.

Contra-indications, warnings, etc Tetrachel is contra-indicated in patients with advanced renal insufficiency and in those hypersensitive to tetracyclines.

Administration of Tetrachel with milk, antacids, calcium or iron preparations may affect absorption.

Tetracyclines should only be administered with great caution to patients with hepatic insufficiency. Careful monitoring of dosage by serum levels is necessary.

Prolonged use of an anti-infective agent may result in the development of superinfection due to micro-organisms resistant to the anti-infective.

Tetracyclines are absorbed to some extent by developing bones and teeth and may produce staining and enamel hypoplasia. For this reason, during the second half of pregnancy, during breast feeding and in children up to the age of eight years, tetracycline should only be administered if considered essential by the physician, and for as short a treatment period as feasible. Repeated courses should be avoided. The effect appears to be

related to total dosage given and not only to duration of treatment.

Tetracyclines should only be administered with great caution to patients with renal insufficiency and dosage may need to be reduced.

Tetracyclines may prolong the action of coumarin anticoagulants, and may themselves delay coagulation.

Tetracyclines should only be used with great caution in conjunction with other potentially hepatotoxic drugs.

Cross-resistance between tetracyclines may develop in micro-organisms, and cross-sensitisation in patients.

Tetrachel should not be used in conjunction with penicillins.

Side-effects may include nausea, vomiting or diarrhoea, and glossitis, stomatitis, vaginitis or pruritus and due to candidal overgrowth. Resistant staphylococci may occasionally give rise to enterocolitis. Skin rashes and allergic reaction are rare.

Treatment of overdosage: Serious symptoms are unlikely. Gastric lavage might be beneficial in the first hours after ingestion followed by conservative management. Milk will reduce absorption.

Pharmaceutical precautions Incompatible with alkalis and chloramphenicol.

Diluent for syrup: Syrup BP.

Legal category POM.

Package quantities *Tablets:* Packs of 100 and 1,000.

Capsules: Containers of 100 and 500.

Syrup: Containers of 500 ml.

Further information Nil.

Product licence numbers

Tablets	0152/0095
Capsules	0152/5005
Syrup	0152/5006

TRIMOPAN*

Presentation

Trimopan 200 mg tablet: White, circular, biconvex tablets, marked 'Berk 3H7' on one side with a single breakline on the reverse. Each tablet contains 200 mg Trimethoprim BP.

Trimopan 100 mg tablets: White, circular, biconvex tablets marked 'Berk 2H7' on one side with a single break-line on the reverse. Each tablet contains 100 mg Trimethoprim BP.

Trimopan suspension: White suspension containing 50 mg Trimethoprim BP in each 5 ml.

Uses Trimopan has potent antimicrobial activity due to its selective inhibition of bacterial dihydrofolate reductase. It is effective *in-vitro* against most Gram-positive and Gram-negative aerobic organisms, including *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, *E. coli*, *Enterobacter*, *Proteus* and *Streptococcus faecalis*.

Exceptions include anaerobic bacteria. *Mycobacterium tuberculosis*, *Neisseria gonorrhoeae*, *Pseudomonas aeruginosa* and *Treponema pallidum*.

Indications: Treatment of susceptible infections caused by trimethoprim-sensitive organisms including urinary tract and respiratory tract infections.

Prophylaxis of recurrent urinary tract infections.

Dosage and administration

Adults and children over 12 years of age: Treatment of urinary tract infections and all other susceptible infections: 200 mg twice daily.

Long-term prophylaxis of recurrent urinary tract infections: 100 mg at night.

Children 4 months to 12 years of age: Treatment of urinary tract infections and all other susceptible infections is based on a dosage of 6 mg/kg body weight daily subdivided into two equal doses. Suggested regimens are:

4 months–2 years	25 mg twice daily
2–6 years	50 mg twice daily
6–12 years	100 mg twice daily

Long-term prophylaxis of recurrent urinary tract infections is based on 2.5 mg/kg body weight daily given as a single dose at night. Suggested regimens are:

4 months–2 years	25 mg at night
2–8 years	50 mg at night
8–12 years	100 mg at night

Contra-indications, warnings, etc *Contra-indications:* Severe hepatic insufficiency. Severe renal insufficiency, unless blood trimethoprim concentrations can be monitored regularly.

Megaloblastic anaemia and other blood dyscrasias.

Trimethoprim should not be administered to pregnant women, premature infants or children under 4 months of age.

Precautions: In patients with marked impairment of renal function, care should be taken to avoid accumulation and resulting adverse haematological effects. Regular haematological tests should be undertaken in patients receiving long-term treatment and those predisposed to folate deficiency. Particular care should be exercised in the haematological monitoring of children on long-term therapy. The usual caution in prescribing any drug for women of childbearing age should be exercised with trimethoprim. Trimethoprim is excreted in breast milk but is not contra-indicated for short term use in lactating mothers.

Side-effects: Nausea, vomiting, gastrointestinal disturbance, headache, skin rashes and pruritus have been reported but are rare.

Isolated cases of megaloblastic anaemia during prolonged therapy with trimethoprim in doses higher than those recommended have been reported but these are reversible with discontinuation of therapy and administration of calcium folinate.

Treatment of overdosage: Symptomatic treatment, gastric lavage and forced diuresis can be used. Depression of haematopoiesis by trimethoprim can be counteracted by intramuscular administration of calcium folinate.

Pharmaceutical precautions No special precautions.

Legal category POM.

Package quantities

200 mg tablets: Containers of 100 tablets
Cartons of 70 tablets consisting of 5 calendar foils of 14 tablets each

100 mg tablets: Containers of 100 tablets.

10 mg/ml suspension: Bottles of 100 ml.

Further information Nil.

Product licence numbers

200 mg tablets	0152/0162
100 mg tablets	0152/0156
10 mg/ml suspension	0152/0160.

UBRETID*

Presentation *Tablets:* White tablets marked 'UBRETID' with single break line on reverse. Each tablet contains 5 mg distigmine bromide.

Ampoules: Clear ampoules each containing 0.5 mg distigmine bromide in 1 ml.

Uses Anticholinesterase. Post-operative urinary retention. Post operative ileus and intestinal atony. To assist emptying of the neurogenic bladder. As an adjuvant in the treatment of myasthenia gravis.

'Ubretid' distigmine bromide is an anticholinesterase with a much longer duration of action than neostigmine or pyridostigmine. In man, maximum inhibition of plasma cholinesterase occurs nine hours after a single intramuscular dose of 0.5 mg 'Ubretid', and persists for approximately 24 hours returning to normal after 48 hours.

Dosage and administration *In prevention of urinary retention, ileus or intestinal atony following surgery:* 1 'Ubretid' Ampoule by intramuscular injection given 12 hours after surgery is usually adequate prophylaxis and this may be repeated at 24-hourly intervals until normal function is restored. Caution should be exercised in the timing of this initial dose, where doubt exists as to the integrity of any bowel anastomosis. When injections are not convenient, 1 'Ubretid' Tablet may be given daily half-an-hour before breakfast.

In neurogenic bladder: 1 'Ubretid' Tablet daily or on alternate days, half-an-hour before breakfast, on an empty stomach. Intramuscular injections may be given in place of tablets for the first few days of therapy.

In myasthenia gravis – tablets only should be used.

Adults: Dosage to be individualised for each patient, dependent upon the severity of the condition, the degree and duration of response and the side-effects encountered. The tablets should always be taken on an empty stomach half an hour before breakfast. Dosage should commence at 1 tablet daily and may be adjusted at intervals of three to four days to a total not exceeding 4 tablets daily.

Children: Up to 2 tablets daily, according to age.

Contra-indications, warnings, etc 'Ubretid' is contra-indicated in cases of severe post-operative shock serious circulatory insufficiency and serious spastic and mechanical ileus.

'Ubretid' should not be administered to pregnant women.

'Ubretid' should be used with caution in conditions where the potentiation of acetylcholine effects is undesirable, e.g. vagotonia, bronchial asthma, cardiac disease peptic ulcer, epilepsy and Parkinsonism.

In myasthenia gravis, where short-acting cholinergic drugs are taken concurrently, their dosage should be reduced to the minimum required to control symptoms.

The patient should be supervised in the early stages of dosage regulation to guard against the possibility of myasthenic crisis or cholinergic crisis.

Overdosage with 'Ubretid' would be expected to give rise to the signs of anticholinesterase poisoning. Atropine (up to 2 mg i.m.) should be given at once and repeated at intervals indicated by the clinical progress until signs:

of mild atropinisation appear (dry mouth, mydriasis). The patient is best kept fully atropinised for 24 hours.

Muscarinic side-effects of 'Ubretid' are usually few and mild, and can be controlled with atropine, giving 2 mg intramuscularly and maintaining atropinisation for at least 24 hours.

Treatment of overdosage: Oral absorption is poor unless Ubretid is taken on a completely empty stomach. Observation may be sufficient. Generalised parasympathomimetic symptoms should be antagonised by atropine.

Pharmaceutical precautions No special precautions.

Diluent for ampoules: Water for Injection BP.

Legal category POM.

Package quantities *Tablets:* Containers of 20 and 100 tablets.

Ampoules: Boxes of 10.

Further information Nil.

Product licence numbers

Tablets 0152/5034

Ampoules 0152/5035.

VIDOPEN*

Presentation Red and pink Ampicillin Capsules BP 250 mg marked VIDOPEN 250 and 500 mg marked VIDOPEN 500.

Pink powder for Syrup 125 mg/5 ml (Ampicillin Mixture BPC), or Syrup Forte 250 mg/5 ml (strong Ampicillin Mixture BPC), wild cherry flavoured and containing ampicillin trihydrate equivalent to the stated quantities of ampicillin.

Uses Ampicillin is a broad-spectrum antibiotic active against *Shigella*, *Escherichia coli*, *Proteus mirabilis*, *Haemophilus influenzae*, *Bordetella pertussis* and other Gram-negative bacteria. *Actinomyces muris ratti* and other Actinomycetes, as well as penicillin-sensitive Gram-positive pathogens. Vidopen is therefore indicated in a wide range of infections, particularly those of the respiratory, urinary and digestive tracts where there may be multiple pathogens.

Vidopen is not effective against organisms resistant to penicillin, since it is inactivated by penicillinase.

Dosage and administration Vidopen should be taken half an hour before meals.

Adults: ENT infections: 250 mg four times daily.

Bronchitis: 250 mg four times daily, or up to 1 g four times daily in acute exacerbations.

Pneumonia: 500 mg four times daily.

Urinary tract infections: 500 mg three times daily.

Gastro-intestinal infections: 500–750 mg three or four times daily.

Children: Over 20 kg bodyweight: Adult dosage.

Under 20 kg bodyweight:

Moderately severe infections: 100 mg/kg/day in divided doses every six or eight hours.

Severe infections: 200 mg/kg/day in divided doses every six hours.

Contra-indications, warnings, etc Known sensitivity to penicillin or the cephalosporins is a contra-indication. Patients should be questioned on this before Vidopen is prescribed.

Safety in pregnancy has not been established.

A rash may occur, particularly in patients with infectious mononucleosis. If it does, Vidopen should be discontinued.

Gastro-intestinal symptoms may occur but usually resolve rapidly when treatment is stopped. If they persist they may indicate overgrowth of resistant organisms, requiring specific treatment.

Ampicillin is inactivated by penicillinase and should therefore not be used to treat infections which have survived treatment with penicillin.

Treatment of overdosage: Serious symptoms are unlikely. Observation.

Pharmaceutical precautions Store in a cool dry place.

The suspension, when made up, should be stored in a cool place and used within seven days. It may be diluted with Syrup BP.

Legal category POM.

Package quantities *Capsules 250 mg:* Containers of 250 and 1,000.

Capsules 500 mg: Containers of 100 and 500.

Syrup: Bottles of 100 mg.

Syrup Forte: Bottles of 100 ml.

Further information Nil.

Product licence numbers

Capsules 250 mg 0152/0118

Capsules 500 mg 0152/0119

Syrup 125 mg/5 ml 0152/0120

Syrup 250 mg/5 ml 0152/0121.

*Trade Mark

Bioglan Laboratories Limited
Spirella Building
Bridge Road
Letchworth, Herts SG6 4ET



VITA-E* (BIOGLAN*) GELUCAPS*
VITA-E* (BIOGLAN*) GELS
VITA-E* SUCCINATE (BIOGLAN)
VITA-E* (BIOGLAN*) OINTMENT

Presentation *Vita-E Gelucaps 75 i.u.*: Yellow oval coated tablets, 14.5 mm diameter, each containing d- α -tocopheryl acetate equivalent to 75 i.u. vitamin E.

Vita-E Gels 75 i.u.: Yellow oval soft gelatin capsules 11 mm diameter, each containing d- α -tocopheryl acetate equivalent to 75 i.u. vitamin E.

200 i.u.: Yellow oblong soft gelatin capsules, 16.5 mm diameter, marked 'BLE 200', each containing d- α -tocopheryl acetate equivalent to 200 i.u. vitamin E.

400 i.u.: Red oblong soft gelatin capsules, 19 mm diameter, marked 'BLE 400', each containing d- α -tocopheryl acetate equivalent to 400 i.u. vitamin E.

Vita-E Ointment 30 i.u./g: Yellow soft paraffin BP each gram containing d- α -tocopheryl acetate equivalent to 30 i.u. vitamin E.

Vita-E Succinate tablets 200 i.u.: Yellow circular scored tablets. Engraved 'BIOGLAN' on one side and '200 I.U.E.' on other, each containing d- α -tocopheryl acid succinate equivalent to 200 i.u. of vitamin E.

Uses *Indications*: Intermittent claudication, and as a prophylactic against cardiovascular degeneration.

Vita-E preparations provide a powerful anti-oxidant for a variety of diseases, all of which have one thing in common – a local decrease in oxygen supply.

The ointment is indicated for burns, pressure sores, external ulcers and wounds.

Dosage and administration *Vita-E Gelucaps*: Oral – chewed and eaten during meals.

Vita-E Gels: swallowed intact and taken with meals.

Vita-E Succinate tablets: Oral – taken with meals.

Vita-E Ointment: Application to affected area.

Intermittent claudication: 600–1,600 i.u. daily.

Cardiovascular degeneration: 75–400 i.u. daily.

The doses recommended are larger than nutritional studies would demand, but smaller dosage is generally

insufficient for successful therapy. The maintenance dose equals the therapeutic dose.

Vitamin E is not recommended for self-medication since as a therapeutic agent and when used with other medications, d'alpha tocopherol may enhance/lessen the effect of those medications. A physician should be consulted.

Contra-indications, warnings, etc Fish-liver oils should not be given at the same time, as they appear to have a detrimental effect on the vitamin. If iron is indicated, separate the doses by about nine hours.

The digitalis requirement is often reduced with vitamin E therapy, and full digitilisation is often achieved by what is ordinarily a maintenance digitalis dose. Insulin dosages in diabetic cardiacs must be watched closely for the insulin requirement may be considerably reduced very suddenly.

Hyperthyroidism is usually contra-indicated.

Pharmaceutical precautions Store in a cool place.

Legal category GSL.

Package quantities *Vita-E Gelucaps (75 i.u.)* are available in containers of 100.

Vita-E Gels (75 i.u., 200 i.u. and 400 i.u.) are available in containers of 100 and 500 Gels.

Vita-E Succinate tablets (200 i.u.) are available in containers of 100 and 500.

Vita-E Ointment 30 i.u./g available in 50 g double-wall ointment jars.

Further information Wounds and burns heal more rapidly with an absolute minimum of scar formation when Vita-E Ointment (30 i.u./g) is used in conjunction with Vita-E by mouth.

Product licence numbers

Vita-E Gelucaps 75 i.u.	0041/5000
Vita-E Gels 75 i.u.	0041/5006
Vita-E Gels 200 i.u.	0041/5012
Vita-E Gels 400 i.u.	0041/5013
Vita-E Succinate tablets 200 i.u.	0041/5005
Vita-E Ointment 30 i.u./g	0041/5019

***Trade Mark**

Boehringer Ingelheim Limited

Southern Industrial Estate

Bracknell

Berkshire RG12 4YS



ALUPENT®

Presentation *Alupent Tablets*: White/off white compressed tablets, scored and impressed with the letters 'At' on one side and with the Company symbol on the reverse. Each tablet contains orciprenaline sulphate 20 mg.

Alupent Syrup: Clear, colourless syrup with vanilla-like flavour. Each 5 ml contains orciprenaline sulphate 10 mg.

Alupent Metered Aerosol: 15 ml vial (300 metered doses) available as complete unit with mouthpiece or as refill vial only. Each metered dose contains orciprenaline sulphate 0.75 mg (0.67 mg available to the patient).

Alupent Inhalant Solution: Clear, colourless stabilised solution of orciprenaline sulphate 5%.

Alupent Ampoules: Ampoules for injection. Each ampoule contains orciprenaline sulphate 0.5 mg in 1 ml.

Uses *Action*: Alupent is a sympathomimetic amine with bronchodilator properties.

Indications: Alupent is indicated for the relief of bronchospasm, as in asthma, bronchitis and emphysema.

Alupent Tablets and Syrup are suggested for maintenance therapy.

Alupent Metered Aerosol and Inhalant Solution are indicated for the relief of acute attacks. Alupent ampoules are for maintenance therapy in patients unable to take other dosage forms. On occasions the ampoules have been used for treatment of acute attacks.

Dosage and administration *Orally*

	<i>Tablets 20 mg</i>	<i>Syrup 10 mg in 5 ml</i>
<i>Adults</i>	1 four times daily	2 × 5 ml four times daily
<i>Children 3-12 years</i>	½ four times daily to 1 three times daily	1 × 5 ml four times daily to 2 × 5 ml three times daily
<i>Children 1-3 years</i>	Syrup recommended	½ × 5 ml four times daily to 1 × 5 ml four times daily
<i>Children 0-1 year</i>	Syrup recommended	½ × 5 ml three times daily to 1 × 5 ml three times daily

By inhalation: Individual response may vary, and the appropriate dose for any patient is best decided by the attending doctor. The recommendations below provide general guidelines.

Metered Aerosol 0.75 mg per puff (0.67 mg available to the patient):

Adults: 1 or 2 puffs. Not to be repeated within 30 minutes. No more than 12 puffs in 24 hours.

Children 6-12 years: 1 or 2 puffs. Not to be repeated within 30 minutes. No more than 4 doses in 24 hours.

Children under 6 years: 1 puff. Not to be repeated within 30 minutes. No more than 4 puffs in 24 hours.

Inhalant Solution 5%: The dose recommended for use in a gas driven nebulizer (eg Bennett, Bird) is:

Adults: 0.2 ml of Alupent 5% Solution (equivalent to 10 mg orciprenaline sulphate) diluted with sterile sodium chloride 0.9% solution or sterile distilled water to 2 ml, and inhaled completely.

Children (under 8 years): 0.1 ml of Alupent 5% solution (equivalent to 5 mg orciprenaline sulphate) diluted with sterile sodium chloride 0.9% solution or sterile distilled water to 2 ml and inhaled completely.

For other nebuliser systems, the dilution may be adjusted for the recommended volumes.

The inhalant solution should not be allowed to come into prolonged contact with metallic components. Thus, when a nebuliser is not in use the reservoir should be emptied and a fresh solution used at each session.

By intra-muscular injection:

	<i>Adults</i>	<i>Children 6-12 years</i>	<i>Children under 6 years</i>
<i>Ampoules 0.5 mg in 1 ml</i>	1 ampoule repeated after 30 minutes if necessary	1 ampoule	½ ampoule

Diluents: Alupent Syrup may be diluted with either Syrup BP or Sorbitol Solution BPC. Alupent inhalant solution may be freshly diluted with either sterile sodium chloride 0.9% solution or sterile distilled water.

Contra-indications, warnings, etc

Contra-indications: Thyrotoxicosis.

Precautions: Caution should be observed should it be necessary to administer Alupent to patients with myocardial insufficiency, angina, cardiac dysrhythmias, hypertension or hypertrophic subvalvular aortic stenosis. In view of the possible interaction between sympathomimetic amines and monoamine oxidase inhibitors, care should be exercised if it is proposed to administer an MAO inhibitor concurrently with Alupent. Caution should be observed with the use of Alupent if a patient is already receiving other sympathomimetic agents as cardiovascular effects may be additive.

Patients must be instructed in the correct use of a metered aerosol, and warned not to exceed the prescribed dose. Patients should also be warned to seek medical advice if a reduced response becomes apparent.

Although Alupent has been in wide general use for many years, there is no definite evidence of ill-consequence during human pregnancy. Only in doses much higher than the equivalent maximum therapeutic dose in man were effects on foetal development seen in animals. Alupent treatment may result in the prolongation of pregnancy and inhibition of labour. Medicines should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

Beta-adrenergic blocking agents may antagonise Alupent and reduce its bronchodilator effect if administered concurrently.

Side-effects: Transitory sympathomimetic side-effects, such as tremor, palpitation, tachycardia and headache, have occasionally been reported, as have nausea and abdominal discomfort.

Overdosage: A fatal dose has not been reported but the following single doses should be considered toxic – 1.5 mg by IV injection, 3.0 mg by IM or SC injection, 0.15 mg/min by IV infusion, 200 mg orally.

Overdosage may be manifest by tachycardia, palpitation, increase in systolic blood pressure, decrease in diastolic blood pressure, tremor and anxiety. It is suggested that the patient should be treated symptomatically, but care should be taken if beta-adrenergic blocking drugs are used in patients liable to bronchospasm.

Pharmaceutical precautions Alupent preparations should be protected from heat, light and air. Aerosol vials should not be incinerated or opened.

Legal category POM.

Package quantities *Tablets:* Packs of 50, 250 and 1,000

Syrup: Packs of 250 ml and 2 litres.

Metered Aerosol: 15 ml vial (300 metered doses) complete with mouthpiece. 15 ml refill vial.

Inhalant Solution: 10 ml.

Ampoules: Packs of 6.

Further information Nil.

Product licence numbers

Alupent Tablets	0015/0046
Alupent Syrup	0015/0001
Alupent Metered Aerosol	0015/5002
Alupent Inhalant Solution	0015/5001
Alupent Ampoules	0015/5000

ALUPENT* EXPECTORANT

Presentation *Alupent Expectorant Tablets:* White/off white compressed tablets, scored and impressed with the letters $\frac{AtB}{\overline{817}}$ on one side, and with the Company symbol on the reverse. Each tablet contains orciprenaline sulphate 20 mg and bromhexine hydrochloride 8 mg.

Alupent Expectorant Mixture: Colourless, clear liquid. Each 5 ml contains orciprenaline sulphate 10 mg and bromhexine hydrochloride 4 mg.

Uses *Action:* Alupent Expectorant provides the dual action of the bronchodilator Alupent (orciprenaline sulphate) and the mucolytic agent Bisolvon (bromhexine hydrochloride).

Alupent is a sympathomimetic amine with bronchodilator properties. Bisolvon stimulates the mucous glands to produce a secretion which is less viscous and has a reduced content of acid glycoprotein fibres.

Indications: Alupent Expectorant is indicated for conditions in which both bronchospasm and sputum are present, e.g. in asthma or bronchitis. During infective episodes a suitable antibiotic should also be given.

Dosage and administration

Orally

	Adults	Children 5–10 years	Children under 5 years
<i>Tablets</i>	1 four times daily	$\frac{1}{2}$ three or four times daily	Mixture recommended
<i>Mixture</i>	2 × 5 ml four times daily	1 × 5 ml three or four times daily	1 × 5 ml twice daily

Diluent: Alupent Expectorant Mixture may be diluted with Syrup BP or with Sorbitol Solution BPC.

Contra-indications, warnings, etc

Contra-indications: Thyrotoxicosis.

Precautions: Caution should be observed should it be necessary to administer Alupent Expectorant to patients with myocardial insufficiency, angina, cardiac dysrhythmias, hypertension or hypertrophic subvalvular aortic stenosis. In view of the possible interaction between sympathomimetic amines and monoamine oxidase inhibitors, care should be exercised if it is proposed to administer an MAO inhibitor concurrently with Alupent, one of the constituents of Alupent Expectorant.

In patients with gastric ulceration relative caution should be observed in the use of Bisolvon, one of the constituents of Alupent Expectorant.

Although Alupent Expectorant has been in wide general use for many years, there is no definite evidence of ill-consequence during human pregnancy. Only in doses much higher than the equivalent maximum therapeutic dose in man were effects on foetal development seen in animals. Alupent Expectorant treatment may result in the prolongation of pregnancy and inhibition of labour. Medicines should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

Beta-adrenergic blocking agents may antagonise Alupent and reduce its bronchodilator effect if administered concurrently.

Side-effects: Transitory sympathomimetic side-effects, such as tremor, palpitation, tachycardia and headache, have occasionally been reported with Alupent, as have nausea and abdominal discomfort.

Occasional gastro-intestinal side-effects may be caused by Bisolvon, but these are almost invariably mild. In a very few patients a transitory rise in serum transaminase levels may be seen during treatment with Bisolvon. With continuation of the drug transaminases return to pre-treatment levels, even in those patients in whom there was pre-existing impairment of hepatic function.

Overdosage: Orciprenaline may cause tachycardia, palpitation, increase in systolic blood pressure, decrease in diastolic blood pressure, tremor and anxiety. These should be treated symptomatically, but care should be taken if beta-adrenergic blocking agents are used in patients liable to bronchospasm. Toxic effects following overdosage with bromhexine have not been reported, but animal studies suggest that these may include listlessness, anorexia, ataxia, cyanosis, pulmonary rales, hypothermia, diuresis, respiratory failure, convulsions or coma.

Pharmaceutical precautions Alupent Expectorant Tablets and Mixture should be protected from heat, light and air.

Legal category POM.

Package quantities *Tablets:* 50 and 250.

Mixture: 250 ml and 2 litres.

Further information Nil.

Product licence numbers

Alupent Expectorant Tablets	0015/0022
Alupent Expectorant Mixture	0015/0025

ATROVENT®

Presentation *Metered dose inhaler:* 10 ml vial (200 metered doses) available as complete unit with mouthpiece. Each metered dose contains ipratropium bromide 0.02 mg of which 0.018 mg is available to the patient.

Nebuliser solution: an aqueous solution of ipratropium bromide 0.025% (0.25 mg/ml) for administration by inhalation.

Uses *Action:* Atrovent is an anticholinergic drug with bronchodilator properties.

Indications: Atrovent metered dose inhaler is indicated in the treatment of chronic reversible airways obstruction, particularly in chronic bronchitis.

Atrovent nebuliser solution is indicated in the treatment of reversible airways obstruction.

Dosage and administration *Metered dose inhaler:* *Adults:* Usually 1 or 2 puffs three or four times daily, although some patients may need up to 4 puffs at a time to obtain maximum benefit during early treatment.

Children: 6–12 years: usually 1 or 2 puffs three times daily. Under 6 years: usually 1 puff three times daily.

In order to ensure that the inhaler is used correctly, administration should be supervised by an adult.

Nebuliser solution: Atrovent nebuliser solution may be administered from an intermittent positive pressure ventilator or from suitable nebulisers.

The recommended dose per inhalation ranges from 0.1–0.5 mg and this can be achieved by nebulising 0.4–2.0 ml solution. These volumes may be suitably measured using the integral dropper (20 drops are approximately equivalent to 1 ml) and diluted with sterile sodium chloride 0.9% solution or sterile distilled water for ease of administration.

Adults: 0.1–0.5 mg up to 4 times daily. Single doses of 2.0 mg have been safely given.

Children: (3–14 years) 0.1–0.5 mg up to 3 times daily. Single doses of 1.0 mg have been safely given.

Contra-indications, warnings, etc

Contra-indications: Known hypersensitivity to atropine.

Precautions: Patients must be instructed in the correct use of a metered dose inhaler or nebuliser solution and warned against the accidental release of the contents into the eye. Generally, caution is advocated in the use of anticholinergic agents in patients with glaucoma and prostatic hypertrophy. However, specific studies with Atrovent in patients with glaucoma showed that inhaling cumulative doses of 0.16 mg had no effect on the eye.

Atrovent has been in general use for several years and there is no definite evidence of ill-consequence during pregnancy; animal studies have shown no hazard. Nevertheless, medicines should not be used in pregnancy, especially during the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

If a reduced response to Atrovent becomes apparent, the patient should seek medical advice.

Side-effects: Anticholinergic side-effects are unlikely at therapeutic doses, but some patients may complain of a dry mouth. Urinary retention and constipation have only rarely been reported with Atrovent. There is no evidence that in the therapeutic dose range Atrovent has any adverse effect on bronchial secretion.

Overdosage: Inhaled doses of 5.0 mg produce an increase in heart rate and palpitation. Single doses of

ipratropium bromide 30 mg by mouth cause anti-cholinergic side-effects but these are not severe and do not require specific reversal.

Pharmaceutical precautions *Atrovent metered dose inhaler:* Protect from heat including the sun. The vials should not be punctured or incinerated even when empty.

Atrovent nebuliser solution: Store at room temperature. Protect from heat and light. Once the bottle has been opened, the contents should not be kept for longer than 1 month. Following dilution, Atrovent nebuliser solution should be used within 24 hours.

Legal category POM.**Package quantities**

Atrovent metered dose inhaler: 10 ml vial (200 metered doses) complete with mouthpiece.

Atrovent nebuliser solution: 20 ml in amber glass bottle complete with integral dropper.

Further information There is evidence that the concurrent administration of Atrovent and sympathomimetic drugs produces a greater relief of bronchospasm than either drug given alone.

Atrovent has been shown to produce effective bronchodilation in patients receiving beta-adrenergic blocking agents.

Product licence numbers

Atrovent metered dose inhaler	0015/0043
Atrovent nebuliser solution	0015/0078

BISOLVOMYCIN®

Presentation Turquoise blue/grey capsules imprinted with the Company symbol. Each capsule contains bromhexine hydrochloride 8 mg and oxytetracycline hydrochloride 250 mg.

Uses *Action:* Bisolvomycin provides the dual action of the mucolytic agent Bisolvon (bromhexine hydrochloride) and the bacteriostatic antibiotic oxytetracycline hydrochloride.

Bisolvon stimulates the mucous glands to produce a secretion which is less viscous and has a reduced content of acid glycoprotein fibres.

Oxytetracycline is effective against a wide range of both Gram-positive and Gram-negative organisms.

Indications: Those conditions of the upper or lower respiratory tract associated with the retention of viscid mucoid secretions and complicated by the presence of tetracycline-sensitive organisms, e.g. bronchitis, infective asthma, bronchiectasis, sinusitis. Other treatment for bronchospasm should be given as appropriate.

Dosage and administration *Adults and children over 12 years:* 1 capsule four times daily. *Children under 12 years:* oxytetracycline is not recommended as it may cause staining of teeth.

Contra-indications, warnings, etc

Contra-indications: As oxytetracycline is one of the active constituents, Bisolvomycin should not be given in pregnancy or in the presence of renal or hepatic dysfunction. The concurrent administration of antacids should be avoided.

Precautions: Caution should be observed in patients with gastric ulcer.

Side-effects: Bisolvon may cause occasional gastro-intestinal side-effects, but these are almost invariably mild. In a very few patients a transient rise in serum transaminase levels has been seen with Bisolvon. With continued treatment transaminases usually return to pretreatment levels, even in those patients in whom there was pre-existing hepatic dysfunction.

Nausea, diarrhoea and symptoms from the overgrowth of resistant organisms have been reported with oxytetracycline.

Overdosage: Toxic effects following overdosage with bromhexine have never been reported, but animal studies suggest that these might include listlessness, anorexia, ataxia, cyanosis, pulmonary rales, hypothermia, diuresis, respiratory failure, convulsions or coma.

Animal studies suggest that toxic effects following overdosage with oxytetracycline may include gastro-intestinal irritation, anorexia, epigastric burning, nausea, vomiting, diarrhoea, headache and symptoms of raised intracranial pressure, jaundice and azotaemia. Management should be symptomatic with appropriate treatment for liver or renal failure if present.

Pharmaceutical precautions Bisolvomycin Capsules should be protected from air, light and moisture.

Legal category POM.

Package quantities Packs of 20 and 250.

Further information Nil.

Product licence number 0015/5003.

BISOLVON*

Presentation *Bisolvon Tablets:* Yellow, compressed tablets, impressed with the letter B on one side and with the Company symbol on the reverse. Each tablet contains bromhexine hydrochloride 8 mg.

Bisolvon Elixir: Clear, yellow liquid. Each 5 ml contains bromhexine hydrochloride 4 mg.

Bisolvon Ampoules: Ampoules for injection. Each ampoule contains bromhexine hydrochloride 4 mg in 2 ml.

Uses *Action:* Bisolvon is a mucolytic expectorant whose action is to stimulate the mucous glands to produce a secretion which is less viscous and has a reduced content of acid glycoprotein fibres.

Indications: Those conditions of the upper and lower respiratory tract associated with retention of viscid mucoid secretions, e.g. bronchitis, asthma, bronchiectasis, sinusitis. Other treatment for infection or bronchospasm should be given as appropriate.

Dosage and administration *Orally:*

	Adults	Children 5-10 years	Children under 5 years
<i>Tablets</i> 8 mg	1 three times daily to 2 four times daily	$\frac{1}{2}$ four times daily	$\frac{1}{2}$ twice daily
<i>Elixir 4 mg</i> <i>in 5 ml</i>	2 x 5 ml three times daily to 4 x 5 ml four times daily	1 x 5 ml four times daily	1 x 5 ml twice daily

By injection: Adults only, not generally recommended for children under 12 years.

Ampoules 4 mg in 2 ml: 2-6 ampoules daily. The ampoules should be given by slow intravenous or deep intramuscular injection. Alternatively 1-5 ampoules may be added to 250-500 ml of 5% dextrose solution or 1-10

ampoules to 250-500 ml of sodium chloride 0.9% solution and given by slow intravenous infusion.

Diluents: Bisolvon Elixir may be diluted with either water or Sorbitol Solution BPC.

Contra-indications, warnings, etc

Contra-indications: There are no absolute contra-indications to the use of Bisolvon.

Precautions: In patients with gastric ulceration caution should be observed with the use of Bisolvon.

Although Bisolvon has been in wide general use for many years, there is no evidence of ill-consequence during human pregnancy; animal studies have shown no hazard. Medicines should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

Side-effects: Occasional gastro-intestinal side-effects may be caused, but these are almost invariably mild. In a very few patients a transitory rise in serum transaminase levels may be seen during treatment with Bisolvon. With continuation of the drug, transaminases return to pretreatment levels, even in those patients in whom there was pre-existing impairment of hepatic function.

Overdosage: Toxic effects following overdosage have never been reported, but animal studies suggest that these might include listlessness, anorexia, ataxia, cyanosis, pulmonary rales, hypothermia, diuresis, respiratory failure, convulsions or coma. These should be treated symptomatically.

Pharmaceutical precautions Bisolvon Tablets, Elixir and Ampoules should be protected from light and heat.

Legal category POM.

Package quantities *Tablets:* Packs of 50, 250 and 1,000.

Elixir: Packs of 250 ml and 1 litre.

Ampoules: Packs of 5.

Further information Nil.

Product licence numbers

Bisolvon Tablets 0015/0021

Bisolvon Elixir 0015/0019

Bisolvon Ampoules 0015/5004

BUSCOPAN*

Presentation *Buscopan Tablets:* White, sugar-coated tablets, printed on one side with the Company symbol. Each tablet contains hyoscine-N-butylbromide 10 mg.

Buscopan Ampoules: Ampoules for intramuscular or intravenous injection, each containing hyoscine-N-butylbromide 20 mg in 1 ml.

Uses *Action:* Buscopan is an antispasmodic agent, which relaxes smooth muscle of the organs of the abdominal and pelvic cavities. It is believed to act predominantly on the intramural parasympathetic ganglia of these organs.

Indications: Buscopan Tablets are indicated in spasm of the gastro-intestinal tract or the genito-urinary tract, and in spasmodic dysmenorrhoea.

Buscopan Ampoules are indicated in acute spasm, as in renal or biliary colic; in radiology for differential diagnosis of obstruction and to reduce spasm and pain in pyelography, and in other diagnostic procedures where spasm may be a problem, e.g. gastro-duodenal endoscopy.

Dosage and administration *Adults: Orally:* 2 tablets four times daily. In spasmodic dysmenorrhoea, treatment should commence two days before the expected onset of the period and continue for three days after menstruation has begun.

By injection: 1 ampoule intramuscularly or intravenously repeated after half-an-hour if necessary. When used in endoscopy this dose may need to be repeated more frequently.

Children 6–12 years: Orally: 1 tablet three times daily.

Diluent: Buscopan Injection Solution may be diluted with dextrose or with sodium chloride 0.9% injection solutions. It is also miscible and compatible with most of the commonly used aqueous radiological contrast media such as diodone, sodium acetate and sodium diatrizoate.

Contra-indications, warnings, etc

Contra-indications: Because of a possible mydriatic effect, Buscopan should not be administered to patients with glaucoma.

Precautions: Although Buscopan has been in wide general use for many years, there is no definite evidence of ill-consequence during human pregnancy; animal studies have shown no hazard. Medicines should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

Side-effects: Dryness of the mouth, temporary loss of accommodation and tachycardia have very occasionally been reported.

Overdosage: Oral doses of up to 1090 mg produced only tiredness. Other features which may be encountered are dry mouth, loss of accommodation, tachycardia, orthostatic hypotension and Cheyne-Stokes respiration.

Gastric lavage should be employed where appropriate. Parasympathetic agents, e.g. pilocarpine or neostigmine, should be used as necessary.

Pharmaceutical precautions Buscopan Tablets and Ampoules should be protected from light and heat.

Legal category POM.

Package quantities *Tablets:* Packs of 100 and 500.

Ampoules: Packs of 10.

Further information Nil.

Product licence numbers

Buscopan Tablets 0015/0047

Buscopan Ampoules 0015/5005

CATAPRES®

Presentation *Catapres Tablets 0.10 mg:* White compressed tablets impressed with the motif  on one side and with the Company symbol on the reverse. Each tablet contains clonidine hydrochloride 0.10 mg.

Catapres Tablets 0.30 mg: White, compressed tablets impressed with the motif  and with the Company symbol on the reverse. Each tablet contains clonidine hydrochloride 0.30 mg.

Catapres PL Perlongets: red/yellow gelatin capsules imprinted with the notation Catapres PL, 11P and the Company symbol. Each Perlonget contains 5 mini-

tablets constituting 0.25 mg clonidine hydrochloride in sustained release form.

Catapres Ampoules: Ampoules for injection. Each ampoule contains clonidine hydrochloride 0.15 mg in 1 ml.

Uses **Action:** Catapres has been shown to have both central and peripheral sites of action. With long-term treatment Catapres reduces the responsiveness of peripheral vessels to vasoconstrictor and vasodilator substances and to sympathetic nerve stimulation. Early in treatment, however, blood pressure reduction is associated with a central reduction of sympathetic outflow and increased vagal tone.

Clinically there may be reduced venous return and slight bradycardia resulting in reduced cardiac output. Although initially peripheral resistance may be unchanged it tends to be reduced as treatment continues. There is no interference with myocardial contractility. Studies have shown that cardiovascular reflexes, as shown by the lack of postural hypotension and exercise hypotension, are preserved.

Indications: Catapres is indicated for the treatment of all grades of essential and secondary hypertension, hypertension during pregnancy and hypertensive crises.

Catapres PL is indicated for all degrees of hypertension excluding hypertensive crises.

Dosage and administration *Catapres Tablets:* Oral treatment should commence with 0.05–0.10 mg three times daily.

This dose should be increased gradually every second or third day until control is achieved. Most patients will be controlled on divided daily doses of 0.30–1.2 mg. However, some patients may require higher doses, e.g. 1.8 mg or more.

Catapres PL Perlongets: most patients will be satisfactorily controlled on one Perlonget daily (usually given in the evening). This dosage can be increased if necessary up to 2 or 3 Perlongets daily (one in the morning and one or two at night).

Catapres may be added to an existing antihypertensive regimen where blood pressure control has not been satisfactorily achieved. If side-effects with existing therapy are troublesome the concomitant use of Catapres may allow a lower dose of the established regimen to be employed. Patients changing treatment should have their existing therapy reduced gradually whilst Catapres is added to their regimen.

Catapres Ampoules: In hypertensive crises 1 or 2 Catapres Ampoules should be given by slow intravenous injection.

An effect is usually seen within 10 minutes and reaches a maximum about 30 minutes to 1 hour after administration. The duration of effect depends upon the severity of the condition and is commonly of the order of 3–7 hours. Up to 5 ampoules may be given in 24 hours to achieve and maintain the desired blood pressure.

Patients undergoing anaesthesia should continue their Catapres treatment before, during and after anaesthesia, using oral or intravenous administration according to individual circumstances.

Diluent: Catapres Injection Solution is compatible with 0.9% sodium chloride solution and with 5% dextrose solution.

Contra-indications, warnings, etc

Contra-indications: There are no known absolute contra-indications to the use of Catapres.

Precautions: This product may cause drowsiness. Pa-

tients who are affected should not drive or operate machinery. Sedation due to the drug may be increased by the concomitant use of other central nervous depressants.

Sudden withdrawal of Catapres, particularly in those patients receiving high doses, may result in rebound hypertension. Termination of long-term therapy with Catapres for any reason should therefore be performed gradually. With Catapres PL this may be achieved by progressively increasing the interval between doses. If a hypertensive episode should nevertheless occur, reintroduction of oral or intravenous Catapres should reverse any such effect. If the use of Catapres is not practical then an alpha-adrenergic blocking drug, such as phentolamine, should be used.

Patients with a known history of depression should be carefully supervised while under long-term treatment with Catapres as there have been occasional reports of further depressive episodes during oral treatment in such patients.

Caution should be exercised in patients with Raynaud's disease or other occlusive peripheral vascular disease. As with all drugs used in hypertension, Catapres should be used with caution in patients with cerebrovascular, coronary or renal insufficiency.

Concomitant use of diuretics or other antihypertensive agents will usually result in an increased hypotensive effect.

Concomitant administration of tricyclic anti-depressants may reduce the hypotensive effect of Catapres.

Alpha-adrenergic blocking drugs antagonise the acute effects of Catapres.

Although clonidine has been in wide general use for many years, there is no definite evidence of hazard during human pregnancy. In animal studies involving doses higher than the equivalent maximum therapeutic dose in man, effects on foetal development were seen only in one species. Foetal malformations did not occur. Medicines should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

Catapres should only be given to breast-feeding women if considered essential by the physician. There is as yet insufficient experience to enable Catapres to be recommended for children.

Intravenous injection of Catapres should be given slowly to avoid a possible transient pressor effect. This is particularly important in patients already under treatment with other hypotensive agents such as guanethidine or reserpine.

Side-effects: Initially, sedation or dry mouth are encountered in a few patients. These effects usually subside as treatment continues. Other drug-related side-effects which have been mentioned in the literature include dizziness, headache, nocturnal unrest, nausea, euphoria, constipation, impotence (rarely) and agitation on withdrawal of long-term therapy.

There are occasional reports of fluid retention during initial stages of oral treatment. This is usually transitory and can be corrected by the addition of a diuretic.

Facial pallor has been noted following injection.

A single case of toxic hepatitis has been reported, but the authors commented that the role of Catapres in hepatotoxicity in this patient remains questionable.

Acute administration in animals or in man has occasionally induced a transient elevation of blood sugar. This is believed to be due to the initial pharmacological effect of alpha-adrenergic stimulation. Investigators

agree that this has no clinical significance. The inclusion of diabetic patients in many Catapres investigations has confirmed its suitability as an antihypertensive agent for such patients.

Overdosage: Accidental overdosage may cause hypotension, bradycardia, sedation and coma. Transient hypertension may be seen if the total dose is over 10 mg.

Gastric lavage should be performed where appropriate. In most cases all that is required are general supportive measures. Forced diuresis has been employed. Where bradycardia is severe atropine will increase the heart rate. If hypotension is giving rise to concern the administration of an alpha-adrenergic blocking drug such as phentolamine may help.

Pharmaceutical precautions Catapres Tablets and Ampoules should be protected from light and heat.

Legal category POM.

Package quantities Tablets 0.10 mg: Packs of 50 and 250.

Tablets 0.30 mg: Pack of 100.

Perlongets 0.25 mg: Pack of 56.

Ampoules 0.15 mg in 1 ml: Pack of 5.

Further information No adverse reaction has been reported with the concurrent administration of digoxin, aminophylline, anticonvulsants or antiarrhythmic preparations. Monitoring of haematological and hepatic status in large numbers of patients has revealed no drug-related adverse effects. Renal blood flow and glomerular filtration rates are maintained and there is no deterioration in renal function. There is evidence that plasma renin levels are reduced. Catapres does not affect the estimation of VMA levels.

Clonidine hydrochloride is also available as Dixarit 0.025 mg tablets (WB Pharmaceuticals Ltd) for the prophylactic management of migraine, recurrent vascular headache and menopausal flushing.

Product licence numbers

Catapres Tablets 0.10 mg	0015/5009
Catapres Tablets 0.30 mg	0015/5041
Catapres PL Perlongets 0.25 mg	0015/0072
Catapres Ampoules 0.15 mg in 1 ml	0015/5008

DULCODOS*

Presentation White, sugar-enteric-coated tablets printed on one side with the Company symbol. Each tablet contains bisacodyl (Dulcolax*) 5 mg and docusate sodium 100 mg.

Uses Action: Dulcodos combines the contact laxative effect of Dulcolax with the faecal softening action of docusate sodium. Dulcodos Tablets disintegrate in the small intestine, the two constituents being released simultaneously. In the colon, docusate sodium, by lowering surface tension, allows water to penetrate the faecal mass more readily, preventing normal faeces from becoming inspissated. At the same time Dulcolax on contact with the mucosa of the large bowel, initiates a general peristaltic movement which results in the evacuation of soft, well-formed stools. Neither substance depends for its effect on systemic absorption. Dulcodos Tablets, when taken after food, act in 10-12 hours.

Indications: Chronic constipation, or other conditions in which painful defaecation is a problem. Replacement of

the enema, prior to surgery, labour or radiological investigation, in conjunction with Dulcolax Suppositories.

Dosage and administration Dulcodos Tablets are suitable for routine use in adults, and children over 10 years.

In constipation, 2 tablets at night.

For complete bowel clearance, 2 tablets at night, followed by one Dulcolax Suppository next morning.

In radiology, 2 tablets on each of the two nights prior to the investigation, followed by 1 Dulcolax Suppository (if necessary) 1 hour before the investigation.

Contra-indications, warnings, etc

Contra-indications: Only those conditions where any laxative is contra-indicated.

Precautions: Because Dulcodos Tablets are enteric-coated for disintegration in the intestine, they should not be crushed or chewed. For the same reason antacids should not be given within 1 hour of administering Dulcodos Tablets.

Although Dulcodos has been in general use for many years, there is no evidence of ill-consequence during human pregnancy; animal studies have shown no hazard. Medicines should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

Side-effects: The mode of action of Dulcolax, and the addition of the faecal softener, docusate sodium, mean that side-effects, such as abdominal discomfort, should only rarely be encountered.

Overdosage: Colicky lower abdominal pain with possible signs of dehydration may be expected particularly in the elderly and the very young.

Gastric lavage should be performed where appropriate. Adequate hydration must be maintained and the serum potassium should be measured. Antispasmodics may be of some value. Particular care about fluid balance should be taken in the elderly and young.

Pharmaceutical precautions Dulcodos Tablets should be protected from heat and light.

Legal category P.

Package quantities Blister packs of 20 and 100.

Further information Nil.

Product licence number 0015/5013.

DULCOLAX®

Presentation *Dulcolax Tablets:* Yellow sugar-enteric-coated tablets printed on one side with the Company symbol. Each tablet contains bisacodyl 5 mg.

Dulcolax Suppositories: White, opaque, foil-wrapped suppositories, each containing bisacodyl 10 mg.

Dulcolax Children's Suppositories: White, opaque, foil-wrapped suppositories for children each containing bisacodyl 5 mg.

Dulcolax Rectal Solution: Buffered polyethylene glycol solution containing bisacodyl 2.74 mg/ml.

Uses **Action:** Dulcolax is a synthetic laxative which acts on contact with the mucosa of the large bowel. It is reliable and predictable in its action, producing in most cases a soft, formed stool without straining.

Dulcolax Tablets taken after food act in 10–12 hours.

A Dulcolax Suppository will produce a motion within 20 minutes to 1 hour of insertion.

Indications: Constipation, either chronic or of recent onset, whenever a stimulant laxative is required.

Bowel clearance before surgery, labour or radiological investigation. Replacement of the evacuant enema in all its indications.

The rectal solution is indicated specifically in radiological procedures, either as a preparatory measure when given as a miniature enema to reduce flatus and faecal shadow interference, or mixed with the barium enema.

Dosage and administration Dulcolax is suitable for routine use in adults of all ages, and in children.

1. In constipation

(a) *Adults and children over 10 years:* 2 tablets at night, or one 10 mg suppository in the morning. (Occasionally a higher tablet dosage is required: up to 3 or 4 may be given.)

(b) *Children under 10 years:* 1 tablet at night or one 5 mg suppository in the morning.

2. For replacement of the enema

(a) *Adults and children over 10 years:* 2 tablets at night followed by one 10 mg suppository in the morning.

(b) *Children under 10 years:* 1 tablet at night followed by one 5 mg suppository in the morning.

3. In preparation for radiological investigation

(a) *Adults and children over 10 years:* 2 tablets on each of the 2 nights before the investigation and one 10 mg suppository (if necessary) 1 hour before investigation. Where needed 2–3 ml of the rectal solution may be administered, as a miniature enema.

(b) *Children under 10 years:* 1 tablet on each of the 2 nights before the investigation and one 5 mg suppository (if necessary) 1 hour before the investigation. Where needed 1–2 ml of the rectal solution may be administered, as a miniature enema.

N.B. Dulcolax Rectal Solution may be administered together with a barium enema, at a dose of 2–5 ml in 1–3 litres of enema solution.

Contra-indications, warnings, etc

Contra-indications: Only those conditions where any laxative is contra-indicated.

Precautions: Because Dulcolax Tablets are enteric-coated for disintegration in the intestine, they should not be crushed or chewed. For the same reason, antacids should not be given within 1 hour of administering Dulcolax Tablets.

Dulcolax Solution is for rectal administration only.

Although Dulcolax has been in general use for many years, there is no evidence of ill-consequence during human pregnancy; animal studies have shown no hazard. Nevertheless, medicines should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

Side-effects: As with any effective laxative, griping has occasionally been reported after administration of Dulcolax Tablets. If this occurs, it can be minimised by dosage adjustment.

Overdosage: Colicky lower abdominal pain with possible signs of dehydration may be expected particularly in the elderly and the very young.

Gastric lavage should be performed where appropriate. Adequate hydration must be maintained and the serum potassium should be measured. Antispasmodics may be

of some value. Particular care about fluid balance should be taken in the elderly and young.

Pharmaceutical precautions All dosage forms should be protected from heat and light.

Legal category P.

Package quantities *Tablets*: Packs of 40, 200 and 1,000.

Suppositories 10 mg: Packs of 6, 50 and 200.

Children's Suppositories 5 mg: Packs of 6.

Rectal Solution: 250 ml bottles.

Further information Nil.

Product licence numbers

Dulcolax Tablets	0015/0048
Dulcolax Suppositories 10 mg	0015/0049
Dulcolax Children's Suppositories 5 mg	0015/0050
Dulcolax Rectal Solution	0015/5011

MEXITIL*

Presentation *Mexitil Capsules 200 mg*: red/red hard gelatin capsules imprinted with the notation 200 mg and the Company symbol. Each capsule contains mexiletine hydrochloride 200 mg.

Mexitil Capsules 50 mg: red/purple hard gelatin capsules imprinted with the notation 50 mg and the Company symbol. Each capsule contains mexiletine hydrochloride 50 mg.

Mexitil Ampoules: Ampoules for intravenous injection. Each ampoule contains mexiletine hydrochloride 250 mg in 10 ml.

Uses *Action*: Mexitil is an anti-arrhythmic agent which depresses the maximum rate of depolarisation with little or no modification of resting potentials or the duration of action potentials.

Indications: For the treatment of existing or anticipated ventricular arrhythmias and ectopic beats such as those found after myocardial infarction and in ischaemic heart disease. Also for ventricular arrhythmias induced by digitalis or other drugs and for idiopathic and other ventricular arrhythmic states. It has been given in conjunction with, or after, other anti-arrhythmic preparations and also other drugs acting on the cardiovascular system.

Dosage and administration

1. Intravenous Mexitil:

- (a) *Loading dose*: IV injection of 4–10 ml (100–250 mg) Mexitil given at a suggested rate of 1 ml per minute (25 mg per minute).

Then

add 500 mg (2 ampoules) Mexitil to 500 ml of a suitable infusion solution (see 'Pharmaceutical Precautions'). Administer the first 250 ml by IV infusion over 1 hour (4 ml per minute).

Then

administer the second 250 ml by IV infusion over 2 hours (2 ml per minute).

- (b) *Maintenance dose*: Add 250 mg (1 ampoule) Mexitil to 500 ml of a suitable infusion solution (see 'Pharmaceutical Precautions'). Administer by IV infusion at a suggested rate of 1 ml per minute (0.5 mg per minute), according to patient response. Continue for as long as required or until oral maintenance therapy is commenced.

2. Oral Mexitil

- (a) *Loading dose*: Give 400 mg Mexitil.
(b) *Maintenance dose*: Give 200–250 mg Mexitil three to four times daily commencing 2 hours after the loading dose. The usual daily dose is between 600–800 mg in divided doses.

Note: In acute myocardial infarction and particularly when opiates have been given, absorption may be delayed and therefore a larger loading dose e.g. 600 mg may be preferable.

3. Alternative loading dose regimes

- (a) *Combination IV Mexitil and Oral Mexitil loading dose*: IV injection of 8 ml (200 mg) Mexitil given at a suggested rate of 1 ml per minute. On completion of injection or infusion give 400 mg Mexitil orally.
Maintenance dose.
As in 2b.
(b) *Combination IV Lignocaine and Oral Mexitil loading dose*: Give IV lignocaine according to manufacturer's instructions.
On completion of injection give 400 mg Mexitil orally.
Maintenance dose.
As in 2b.

4. *Change over from IV to Oral Mexitil maintenance*: On discontinuing the IV infusion commence the maintenance dose. Give 200–250 mg Mexitil orally three or four times a day.

Notes:

1. The loading dose regime is designed to compensate for the rapid phase of tissue distribution which occurs especially with IV loading.

2. Side-effects are more likely to be encountered during the initial tissue loading phase in which case the rate of infusion should be reduced.

3. If the optimum therapeutic effect is not achieved the rate of infusion or oral dosage may be increased, side-effects permitting.

4. Gastric emptying time may be delayed in patients with myocardial infarction and/or to whom opiates have been given and thus it may be necessary to titrate the dose against therapeutic effects and side-effects.

5. The 50 mg capsule is available in order that a more precise dose titration may be undertaken should this be required. Smaller increments will also reduce the incidence of side-effects.

Contra-indications, warnings, etc

Contra-indications: In view of the conditions in which ventricular arrhythmias may be encountered there are no specific exclusions or contra-indications. However, if the drug is used in the following situations, the patient should be carefully monitored: sinus node dysfunction, conduction defect, bradycardia, hypotension or cardiac, renal or hepatic failure. There may be potentiation of tremor in patients with Parkinsonism.

Precautions: Because of the conditions in which Mexitil is used, patients will usually be under observation with particular regard to ECG and blood pressure. Routine laboratory monitoring is also advisable although disturbance of renal and hepatic function or appearance of anti-nuclear factor have not been a feature even of long-term treatment.

The duration of treatment required in any patient is of necessity variable, and although no precise guide can be given, withdrawal of treatment may be attempted after

a suitable period free of arrhythmia. Gradual withdrawal, i.e. over 1–2 weeks, is preferable as arrhythmias which have been satisfactorily controlled may recur.

Although Mexilit has been in general use for several years, there is no definite evidence of ill-consequence during human pregnancy; animal studies have shown no hazard. Medicines should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

Side-effects: Side-effects are mainly related to blood concentration and may therefore be seen during the initial phases of both IV and oral treatment when fluctuation may occur before the blood and tissue concentrations reach equilibrium. Reducing the rate of injection or infusion or delaying the next oral dose allows the blood concentration to fall and usually reduces side-effects. Generally side-effects are of three types:

Gastro-intestinal – nausea, vomiting, indigestion, unpleasant taste, hiccoughs.

Central nervous system – light-headedness, drowsiness, confusion, dizziness, diplopia, blurred vision, nystagmus, dysarthria, ataxia, tremor, paraesthesiae, convulsion.

Cardiovascular – hypotension, sinus bradycardia, atrial fibrillation, palpitation.

Side-effects can usually be reversed by reducing dosage. When hypotension has occurred this has tended to be in patients with severe illness who have already been given a variety of anti-arrhythmic or other preparations and, if associated with bradycardia, may be reversed by the use of atropine. Animal studies using toxic doses have shown that benzodiazepines (diazepam) reduce the CNS effects.

Overdosage: The minimum fatal dose is unknown but 4.40 g proved fatal in a healthy young adult.

The clinical features include nausea, vomiting, drowsiness, confusion, ataxia and convulsions. Blurred vision and paraesthesiae have also been reported. Hypotension, sinus bradycardia, atrial fibrillation and cardiac arrest are more specific effects.

Gastric lavage should be performed where appropriate and the patient should be transferred to an intensive/coronary care unit for possible cardiopulmonary support. Arrhythmias should be treated as appropriate and diazepam may be useful to control convulsions.

Pharmaceutical precautions Mexilit solution for injection is known to be compatible with the following infusion solutions: sodium chloride 0.9%; sodium chloride 0.9% with potassium chloride 0.3% or 0.6%; dextrose 5%; sodium bicarbonate 1.4%; sodium lactate (M/6).

Legal category POM.

Package quantities

Capsules 200 mg: pack of 100.

Capsules 50 mg: pack of 100.

Ampoules 250 mg in 10 ml: pack of 5.

Further information Mexilit has been used successfully within a few hours of myocardial infarction. Concomitant IV therapy with other local anaesthetic type anti-arrhythmic agents such as lignocaine or procainamide is not recommended, although no problems have been encountered using oral mexiletine in conjunction with these drugs. Mexilit may be used concurrently with digoxin and beta-adrenergic blocking drugs.

Product licence numbers

Mexilit Capsules 200 mg 0015/0064

Mexilit Capsules 50 mg 0015/0062

Mexilit Ampoules 250 mg in 10 ml 0015/0065

PERSANTIN®

Presentation A white sugar-coated tablet with the Company symbol on one side, containing dipyridamole 100 mg.

Uses Action: Dipyridamole has an antithrombotic action based on its ability to modify various aspects of platelet function, such as platelet aggregation, adhesion and survival, which have been shown to be factors associated with the initiation of thrombus formation.

Dipyridamole modifies platelet function by enhancing prostacyclin effect through a strong inhibition of phosphodiesterase and mild stimulation of adenylyl cyclase formation. It has also been shown to inhibit the formation of thromboxane A₂ which is known to cause platelet adhesion and aggregation.

Indications: For diseases or conditions where modification of platelet function may be beneficial.

Dosage and administration Adults: Three to six tablets (300–600 mg) daily in three or four doses.

Children: The normal total daily dose is 5 mg/kg in divided doses.

Persantin should usually be taken before meals.

Contra-indications, warnings, etc

Contra-indications: There are no absolute contra-indications to the administration of Persantin.

Precautions: Persantin is a potent vasodilator and should therefore be used with caution in patients with rapidly worsening angina, sub-valvular aortic stenosis or haemodynamic instability associated with a recently sustained myocardial infarction.

Although Persantin has been in wide general use for many years there is no evidence of ill-consequence during human pregnancy; animal studies have shown no hazard. Medicines should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

Side-effects: If these occur it is usually during the early part of treatment and they are often dose-related. The vasodilating properties of Persantin may occasionally produce a vascular headache which normally disappears with dosage reduction. Dyspepsia has occasionally been reported. Mild diarrhoea is rarely encountered.

Overdosage: Overdosage may lead to headache, gastro-intestinal symptoms and hypotension. Coronary vasodilation may cause chest pain in patients with ischaemic heart disease.

General supportive measures should be employed. Coronary vasodilation may be reversed by administering aminophylline by slow IV injection.

Pharmaceutical precautions Protect from heat, light and moisture.

Legal category POM.

Package quantities Packs of 100 tablets.

Further information There is evidence that the effects of aspirin and dipyridamole on platelet behaviour are synergistic. Persantin is also licensed as a coronary vasodilator in the form of 25 mg tablets and 10 mg/2 ml

ampoules for slow intravenous injection. The 25 mg tablets may be used where dose titration is required for the modification of platelet function in children.

Product licence number 0015/5016.

TRANXENE*

Presentation Pink/grey hard gelatin capsules imprinted with the notation 15 mg and the Company symbol. Each capsule contains potassium clorazepate 15 mg.

Uses *Action:* Tranxene is a tranquilliser exhibiting many characteristics of the benzodiazepine group of preparations. Particular features which distinguish Tranxene from other members of this group are the rapid appearance in the blood of the anxiolytic compound nordiazepam, the maintenance of satisfactory therapeutic effect with once daily administration and little sedation.

Indications: Relief of all forms of anxiety, tension and agitation in acute and chronic anxiety states. Tranxene is compatible with all antidepressants in the treatment of anxiety accompanied by depression.

Dosage and administration Adults only, not generally recommended for children under 12 years. 1 capsule daily, usually administered at night.

Contra-indications, warnings, etc

Contra-indications: There are no absolute contra-indications to the use of Tranxene.

Precautions: As sole treatment, Tranxene is not recommended for acute primary depressive states or major psychoses.

The action of Tranxene may potentiate other preparations with central nervous system depressant effects such as barbiturates, narcotics, phenothiazines and alcohol.

Although sedation has not proved to be a problem with Tranxene, in accordance with general principles patients should be advised that their ability to drive or to operate dangerous machinery may be impaired.

Although Tranxene has been in wide general use for many years, there is no definite evidence of ill-consequence during human pregnancy; animal studies have shown no hazard. Medicines should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

Tranxene and its metabolites are excreted in human milk in minimal quantities.

Side-effects: Side-effects which have been reported only rarely are dizziness, gastro-intestinal upset, nervousness, blurred vision, dry mouth, headache and mental confusion. Drowsiness has occasionally been reported but does not constitute a major problem.

Overdosage: An overdose of 900 mg (60 capsules) has been reported causing drowsiness, ataxia, respiratory depression and coma. Treatment should include gastric lavage and/or induced vomiting and general supportive therapy.

Pharmaceutical precautions Tranxene Capsules should be protected from heat, light and moisture.

Legal category POM.

Package quantities Packs of 100 in aluminium foil strips.

Further information In common with other benzodiazepines Tranxene has a central muscle-relaxant effect, and synergism with peripherally acting muscle relaxants is a theoretical possibility.

Product licence number 0015/0057.

VILLESCON* LIQUID

Presentation Red, raspberry-flavoured liquid. Each 5 ml contains:

Prolintane hydrochloride	2.5 mg
Thiamine hydrochloride	1.67 mg
Riboflavin-5-phosphate sodium	1.36 mg
Pyridoxine hydrochloride	0.5 mg
Nicotinamide	5.0 mg

Uses *Action:* The principal ingredient of Villescon, prolintane hydrochloride, is a sympathomimetic amine with two main actions. It stimulates appetite and has a mild central action which produces an increased feeling of well-being in debilitated patients.

Indications: Villescon is indicated as a tonic after illness, surgery or labour, for apathy and anorexia in elderly patients, for institutional neuroses and for anorexia and lassitude following radiotherapy.

Dosage and administration *Adults:* 2 × 5 ml twice daily.

Children 5–12 years: $\frac{1}{2}$ × 5 ml twice daily to 2 × 5 ml twice daily.

The normal course of treatment is from 1–2 weeks.

It is recommended that the second daily dose be taken before four o'clock in the afternoon.

Diluent: Villescon Liquid may be diluted with purified water.

Contra-indications, warnings, etc

Contra-indications: Thyrotoxicosis, epilepsy.

Precautions: Although no interaction between Villescon and MAO inhibitors has ever been demonstrated, the theoretical possibility of such an interaction should be borne in mind if these preparations are co-prescribed. It should be noted that even in very small quantities pyridoxine hydrochloride (vitamin B₆) inhibits the activity of levodopa.

There exists a proportion of patients whose ill-defined symptoms reflect a basic inadequacy of personality. Such patients are liable to misuse any drug with central activity, and it is advised that in these cases the recurrent prescription of Villescon should be avoided.

Although Villescon Liquid has been in wide general use for many years, there is no definite evidence of ill-consequence during human pregnancy; animal studies have shown no hazard. Medicines should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

Side-effects: Tachycardia, nausea and colicky abdominal pains have been reported. Sleeplessness may be caused if Villescon is taken late in the day.

Overdosage: Accidental overdosage has been reported only rarely and may give rise to restlessness, insomnia, tachycardia and increase of blood pressure. An overdose of 300 mg prolintane has been reported in a young female who made a full recovery. Treatment should include gastric lavage and general supportive measures. Sedation may be required to treat restlessness and insomnia.

Pharmaceutical precautions Villescon preparations should be protected from heat, light and moisture.

Legal category POM.

Package quantities Bottles of 250 ml and 1 litre.

Further information Nil.

Product licence number 0015/0054.

VILLESCON* TABLETS

Presentation Orange, sugar-coated tablets, with the Company symbol on one side. Each tablet contains:

Prolintane hydrochloride	10.0 mg
Thiamine mononitrate	5.0 mg
Riboflavin	3.0 mg
Pyridoxine hydrochloride	1.5 mg
Nicotinamide	15.0 mg
Ascorbic acid	50.0 mg

Uses Action: The principal ingredient of Villescon, prolintane hydrochloride, is a sympathomimetic amine with two main actions. It stimulates appetite and has a mild central action which produces an increased feeling of well-being in debilitated patients.

Indications: Villescon is indicated as a tonic after illness, surgery or labour, for apathy and anorexia in elderly patients, for institutional neuroses and for anorexia and lassitude following radiotherapy.

Dosage and administration *Adults:* 1 tablet twice daily.

Children over 8 years: 1 tablet after breakfast.

The normal course of treatment is from 1–2 weeks. It is recommended that the second daily dose be taken before four o'clock in the afternoon.

Contra-indications, warnings, etc

Contra-indications: Thyrotoxicosis, epilepsy.

Precautions: Although no interaction between Villescon and MAO inhibitors has ever been demonstrated, the

theoretical possibility of such an interaction should be borne in mind if these preparations are co-prescribed. It should be noted that even in very small quantities pyridoxine hydrochloride (vitamin B₆) inhibits the activity of levodopa.

There exists a proportion of patients whose ill-defined symptoms reflect a basic inadequacy of personality. Such patients are liable to misuse any drug with central activity, and it is advised that in these cases the recurrent prescription of Villescon should be avoided.

Although Villescon Tablets have been in wide general use for many years there is no definite evidence of ill-consequence during human pregnancy; animal studies have shown no hazard. Medicines should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

Side-effects: Tachycardia, nausea and colicky abdominal pains have been reported. Sleeplessness may be caused if Villescon is taken late in the day.

Overdosage: Accidental overdosage has been reported only rarely and may give rise to restlessness, insomnia, tachycardia and increase of blood pressure. An overdose of 300 mg prolintane has been reported in a young female who made a full recovery. Treatment should include gastric lavage and general supportive measures. Sedation may be required to treat restlessness and insomnia.

Pharmaceutical precautions Villescon preparations should be protected from heat, light and moisture.

Legal category POM.

Package quantities Packs of 20 and 100.

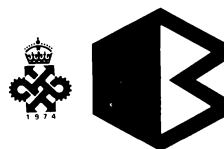
Further information Nil.

Product licence number 0015/0055.

* Trade Mark

The Boots Company PLC

1 Thane Road West
Nottingham NG2 3AA



ABICOL*

Presentation Abicol is presented as pink, scored tablets, each containing Reserpine BP 0.15 mg and Bendrofluzide BP 2.5 mg.

Uses Abicol is indicated for all grades of hypertension, either alone or in conjunction with other hypotensive agents.

Dosage and administration For most cases of hypertension, half to one tablet morning and evening. If necessary, dosage may be increased up to two tablets morning and evening. When Abicol is added to an existing regimen of antihypertensive drugs, the dosage of the latter should be reduced initially.

Contra-indications, warnings, etc

Electrolyte imbalance: All the thiazide diuretics can produce some degree of electrolyte imbalance, especially in patients with renal or hepatic impairment, or when dosage is high or prolonged. Serum electrolyte levels should be checked for abnormalities, particularly hypokalaemia, this being corrected by the addition of a potassium supplement to the regimen.

Digitalis intoxication: Sensitivity to digitalis may be increased by the kaliuretic effect of concurrent bendrofluzide and patients should be observed for signs of digitalis intoxication. Should these appear, the dosage of digitalis should be reduced temporarily and a potassium supplement given to restore stability.

Uric acid retention: Thiazide diuretics may raise serum uric acid levels with consequent exacerbation of gout in susceptible subjects.

Diabetes: Thiazide derivatives sometimes lower carbohydrate tolerance and it may be necessary to adjust the insulin dosage of the diabetic patient. Care is also necessary when bendrofluzide is administered to those with a known pre-disposition to diabetes.

Pregnancy: Thiazides cross the placental barrier and it is, therefore, reasonable to assume that side-effects occurring in the adult may also develop in the foetus.

Other side-effects which may be encountered are those associated with reserpine, i.e. lethargy, vertigo, tremor, gastro-intestinal upset and nasal congestion.

Treatment of overdosage: Symptomatic and supportive; there is no specific antidote.

Pharmaceutical precautions Recommended storage conditions: 5°C to 20°C.

Legal category POM.

Package quantities Containers of 100 and 500 tablets.

Further information Bendrofluzide is an oral diuretic and antihypertensive agent which augments the antihypertensive activity of reserpine, thus allowing a smaller dose of the latter to be used. In this way, the side-effects

associated with the normal therapeutic dose of reserpine are less likely to occur or are reduced in severity.

Product licence number 0014/5126.

APRINOX*

Presentation Aprinox is Bendrofluzide BP, an oral diuretic of the benzothiadiazine group. Aprinox is available as white tablets in two strengths, 2.5 mg and 5 mg.

Uses Aprinox is indicated in all cases where the reduction of fluid retention by diuresis is required – oedema of cardiac, renal or hepatic origin; premenstrual, iatrogenic and all other types of oedema.

Aprinox will produce a moderate but usefully prolonged fall of blood pressure in hypertensive patients and often gives adequate control when used alone; if necessary, Aprinox can be administered concurrently with other specific hypotensive agents, allowing a reduction in the dosage of the latter.

Aprinox will effectively inhibit lactation without the hormonal effects attendant upon stilboestrol or other oestrogens.

Dosage and administration *Diuretic:* Initially 5–10 mg once daily or on alternative days. Maintenance: 5–10 mg once or twice weekly. The dose should be taken early in the morning so as to complete diuresis by bedtime.

Hypotensive: 2.5–5 mg once daily. When Aprinox is used concurrently with other specific hypotensive agents the dose of the latter should be halved.

A suggested dosage for inhibition of lactation is 5 mg in the morning and 5 mg at midday for about five days.

Dosage in children should be at the discretion of the attending physician.

Contra-indications, warnings, etc **Electrolyte imbalance:** All the thiazide diuretics can produce a degree of electrolyte imbalance, especially in patients with renal or hepatic impairment, or when dosage is high or prolonged. Serum electrolyte levels should be checked for abnormalities, particularly hypokalaemia, and the latter corrected by the addition of a potassium supplement to the regimen.

Note: Aprinox does not contain a potassium supplement.

Digitalis intoxication: Sensitivity to digitalis may be increased by the kaliuretic effect of concurrent bendrofluzide. Patients should be observed for signs of digitalis intoxication; if these appear, the dosage of digitalis should be temporarily reduced and a potassium supplement given to restore stability.

Uric acid retention: The thiazide diuretics may raise serum uric acid levels with consequent exacerbation of gout in susceptible subjects.

Diabetes: Thiazide derivatives sometimes lower carbohydrate tolerance and the insulin dosage of the diabetic patient may require adjustment. Care is necessary when bendroflumazide is administered to those with a known predisposition to diabetes.

Pregnancy: Thiazides cross the placental barrier; therefore it is reasonable to assume that side-effects occurring in the adult may also appear in the neonate.

Pharmaceutical precautions Recommended storage conditions: 5–20°C.

Legal category POM.

Package quantities Bottles of 100 and 500 tablets.

Further information A single dose of Aprinox will induce a diuresis extending over 12–18 hours – a period which can be contained within the patient's normal working day, leaving the night undisturbed. Simple dosage schedules, a low incidence of side-effects and economy in prescribing have established Aprinox as one of the most useful general-purpose diuretics.

Product licence numbers

Aprinox 2.5 mg 0014/5117

Aprinox 5 mg 0014/5118

BRUFEN®

Presentation Brufen is available as Brufen 400, sugar-coated tablets each containing 400 mg of Ibuprofen BP. The tablets are light-magenta in colour and bear the overprint 'Brufen 400' in black.

Brufen is available also as sugar-coated tablets each containing 200 mg of Ibuprofen BP. These are also light-magenta in colour and are overprinted 'Brufen' in black.

For children, and for adults who have difficulty in swallowing tablets, Brufen is presented as Brufen Syrup, an orange flavoured liquid containing 100 mg of Ibuprofen BP in each 5 ml.

Uses Brufen is indicated for its analgesic and anti-inflammatory effect in the treatment of rheumatoid arthritis (including juvenile rheumatoid arthritis or Still's disease) ankylosing spondylitis, osteoarthritis and other non-rheumatoid (seronegative) arthropathies.

In the treatment of non-articular rheumatic conditions, Brufen is indicated in periarticular conditions such as frozen shoulder (capsulitis), bursitis, tendinitis, tenosynovitis and low-back pain; Brufen can also be used in soft-tissue injuries such as sprains and strains.

Brufen is also indicated for its analgesic effect in the relief of mild to moderate pain such as dysmenorrhoea, dental and post-operative pain.

Dosage and administration *Adult:* The recommended dosage of Brufen is 1,200 mg daily in divided doses. Some patients can be maintained on 600–1,200 mg daily.

In severe conditions it can be advantageous to increase the dosage to 1,600 mg daily in divided doses until the acute phase is brought under control.

For the relief of mild to moderate pain the following dosages are recommended:

Dysmenorrhoea: 1,200 mg per day in three divided doses

Analgesia 1,200 to 1,600 mg daily given in divided doses

In cases of dental or post-operative pain an initial dose of 400 mg may be given.

The total daily dose of Brufen should not exceed 2,400 mg.

Children: The dosage of Brufen is 20 mg per kg of body weight daily except that in children weighing less than 30 kg the total dose given in 24 hours should not exceed 500 mg.

Contra-indications, warnings, etc Brufen should not be given to patients with severe or active peptic ulceration. Whilst no teratogenic effects have been demonstrated in animal experiments, the use of Brufen during pregnancy should, if possible, be avoided. Brufen should be prescribed with caution for those with asthma and especially for patients who have developed bronchospasm with other nonsteroidal agents.

Adverse effects reported include dyspepsia, gastrointestinal intolerance and bleeding, and skin rashes of various types. Less frequently, thrombocytopenia has occurred. Toxic amblyopia has occurred very rarely but, in those cases reported, recovery occurred on cessation of treatment.

Treatment of overdosage: Gastric lavage and, if necessary, correction of blood electrolytes. There is no specific antidote to Brufen.

Pharmaceutical precautions Brufen Syrup should be stored below 25°C.

Legal category POM.

Package quantities *Brufen 400 (400 mg tablets):* Pack of 100, pack of 250.

Brufen Tablets (200 mg): Pack of 100, pack of 500.

Brufen Syrup: Bottle of 200 ml.

Further information Taken on an empty stomach, peak serum levels of Brufen occur 45 minutes after ingestion, whereas, taken after a meal, the peak is delayed up to 90 minutes. Since most people can take Brufen on an empty stomach without gastric discomfort, the initial dose of the day will be more rapidly effective if taken before food. This is particularly valuable in providing relief of the morning stiffness associated with arthritis.

Product licence numbers

Brufen 400 Tablets: 0014/0158

Brufen Tablets 200 mg 0014/5132

Brufen Syrup 0014/0217

CHLORPROPAMIDE – BOOTS

Presentation Chlorpropamide – Boots is available as white, scored tablets each containing either 100 mg (7 mm diameter) or 250 mg (9.5 mm diameter) of Chlorpropamide BP.

Uses Chlorpropamide is indicated for the treatment of mild or moderately severe uncomplicated diabetes mellitus of the stable, non-ketotic, maturity-onset or adult type. It should not be used to replace dietetic therapy in the obese diabetic patient.

Dosage and administration Generally, chlorpropamide should be given as a single dose each morning before breakfast. The initial dose is 250–500 mg daily and this should be reduced to a maintenance level as soon as possible. In elderly patients, a smaller dose is advisable.

In establishing the optimal dosage for a particular patient, it should be borne in mind that it may take four to seven days for the hypoglycaemic response to become

maximal. It may take several weeks to achieve adequate control.

Note: The daily dosage of chlorpropamide should not exceed 500 mg.

Contra-indications, warnings, etc Chlorpropamide is contra-indicated in juvenile diabetes mellitus and in unstable or severely 'brittle' type diabetes; in maturity-onset type diabetes when complicated by ketosis, fever, trauma, gangrene, or by serious impairment of renal, hepatic or thyroid function. It is also contra-indicated in pregnancy.

Caution: Chlorpropamide may cause hypoglycaemic reactions, which should be treated similarly to those occurring during insulin therapy. The hypoglycaemic effects of chlorpropamide are enhanced by dicoumarol, monoamine oxidase inhibitors, beta-blockers and salicylates; conversely, the action may be diminished by adrenalin, corticosteroids, oral contraceptives and thiazide diuretics. Alcohol should be avoided since it may cause a disulfiram-like reaction.

Side-effects: These include skin sensitisation, gastro-intestinal disturbance, paraesthesias, tinnitus and headache. A rare reaction to chlorpropamide is impairment of liver function. Isolated cases of bone-marrow aplasia, including aplastic anaemia and agranulocytosis have been reported.

Treatment of overdosage: Hypoglycaemia should be treated by infusion of dextrose; treatment may have to be prolonged.

Pharmaceutical precautions None.

Legal category POM.

Package quantities 100 mg Tablets: Bottle of 500.
250 mg Tablets: Bottle of 500.

Product licence numbers

100 mg Tablets 0014/0175

250 mg Tablets 0014/0176

CORTISTAB*

Presentation Cortistab is available as tablets and as an injection. The tablets are Cortisone Tablets BP, containing Cortisone Acetate BP, 5 mg and 25 mg; the injection is Cortisone Injection BP containing Cortisone Acetate Injection BP 25 mg per ml.

Uses Cortisone Acetate has both glucocorticoid and mineralocorticoid properties and is used mainly for replacement therapy in chronic adrenocortical insufficiency. It can be used for other conditions requiring corticosteroid therapy.

Dosage and administration As with other corticosteroids, the dosage of Cortistab should be adjusted according to the severity, prognosis and anticipated duration of the disease, and the response of the individual patient.

In replacement therapy, the normal daily requirement is 12.5–50 mg of cortisone acetate by mouth in divided doses increased during infectious trauma or stress. In other conditions, a suggested regimen is 100 to 300 mg daily by intramuscular injection or 25 to 75 mg four times daily by mouth. When the desired degree of response has been achieved, reduce the dosage *gradually* to the lowest dose which maintains remission, usually from 25 mg to 100 mg daily. In chronic conditions, it is often better to maintain a sub-optimal response with small

doses than to give high doses and produce signs of hormonal excess. After prolonged corticosteroid treatment, the function of the patient's own adrenal cortices is often suppressed. To allow normal adrenal function to be restored, Cortistab dosage should be reduced gradually, e.g. by 5 to 12.5 mg every few days. Cortisone acetate is ineffective when injected into joint capsules.

Contra-indications, warnings, etc The contra-indications to Cortistab therapy are those common to all forms of corticosteroid therapy. These include severe infections (unless there is adequate chemotherapy), peptic ulcer, osteoporosis, a history of recent psychotic illness and chronic renal insufficiency.

Caution is necessary in patients with diabetes mellitus, congestive heart failure or hypertension. During treatment, the patient should be observed for psychotic reactions, muscular weakness, electrocardiographic changes, hypertension and untoward hormonal effects.

Side-effects: Corticosteroids exert hormonal and metabolic effects and prolonged treatment may be attended by such side-effects as moonface, hirsutism, psychosis and gastro-intestinal disturbance.

Treatment of overdosage: Treatment is symptomatic but is unlikely to be required.

Pharmaceutical precautions Cortistab Tablets should be protected from light. Cortistab injection should be kept at a temperature not exceeding 25°C, it should not be allowed to freeze. Protect from light.

Legal category POM.

Package quantities Cortistab Tablets 5 mg: Bottle of 100. Cortistab Tablets 25 mg: Bottle of 100. Cortistab Injection: Ampoule of 10 ml.

Further information Nil.

Product licence numbers

Cortistab Tablets, 5 mg: 0014/5044.

Cortistab Tablets, 25 mg: 0014/5045.

Cortistab Injection: 0014/5408.

DELTASTAB* INJECTION

Presentation Deltastab Injection is a sterile suspension of 25 mg per ml of Prednisolone Acetate BP 1963.

Uses Deltastab Injection is intended primarily for the local treatment by intra-articular or peri-articular injection of arthritic conditions such as rheumatoid arthritis and osteoarthritis when few joints are involved, and in traumatic arthritis, except when associated with fractures into the joint. In addition to articular use, Deltastab Injection injected into inflamed tendon sheaths and bursae will provide symptomatic treatment.

Deltastab Injection is suitable for parenteral administration by the intramuscular route in conditions requiring systemic corticosteroids.

Dosage and administration For articular use, 5 to 25 mg depending upon the size of the joint; the injection may be repeated when relapse occurs. Not more than three joints should be treated in any one day.

For parenteral use by intramuscular injection, the dosage of Deltastab Injection will depend upon the clinical circumstances and the judgement of the physician.

Suggested dosage: 25 to 100 mg once or twice weekly

Contra-indications, warnings, etc Intra-articular and peri-articular injections of Deltastab Injection are

contra-indicated when the joint or surrounding tissues are infected. The presence of infection also precludes injection into tendon sheaths and bursae. Deltastab Injection must not be injected directly into tendons, nor should it be injected into the spinal joints or any other than true diarthrodial joints.

Precautions: It should be borne in mind that joints and tissues injected with corticosteroids have an increased susceptibility to infection and full aseptic precautions should be observed when making local injections of Deltastab.

Side-effects: With intra-articular and other local injections, the principal side-effect encountered is a temporary local exacerbation with increased pain and swelling. Normally, this subsides after a few hours. Particularly after high or prolonged local administration corticosteroids can be absorbed in amounts sufficient to produce systemic effects.

Note: When being given by intramuscular injection, the precautions, side-effects, contra-indications and withdrawal symptoms associated with the systemic use of corticosteroids become relevant to Deltastab Injection.

Treatment of overdosage: Treatment is symptomatic, but is unlikely to be required.

Pharmaceutical precautions Store between 15°C to 20°C. Protect from light. Shake well before use.

Legal category POM.

Package quantities Vial of 5 ml.

Further information Nil.

Product licence number 0014/5137.

DIALAFLEX* SOLUTIONS 61, 62, 63

Presentation Dialaflex Solutions 61, 62 and 63 are sterile solutions specially formulated for peritoneal dialysis and are available in transparent, collapsible plastic containers of 1 litre.

The formulae of the solutions are as follows:

	<i>Dialaflex 61 g/litre</i>	<i>Dialaflex 62 g/litre</i>	<i>Dialaflex 63 g/litre</i>
Dextrose BP	13.6	63.6	13.6
Sodium Lactate	5.0	5.0	5.0
Sodium Chloride BP	5.6	5.6	5.0
Calcium Chloride BP	0.26	0.26	0.26
Magnesium Chloride for Dialysis BP	0.15	0.15	0.15
Sodium Metabisulphite (antioxidant)	0.05	0.05	0.05

The following table gives the solutions in terms of mEq/litre and mmol/litre:

	<i>mEq/litre</i>	<i>g/litre</i>	<i>mmol/litre</i>
Dialaflex 61			
Sodium	140.92		140
Calcium	3.6		1.8
Magnesium	1.5		0.75
Total Chloride	100.8		100
Lactate	44.6		45
Dextrose		13.6	75
Total			364.37

Dialaflex 62		
Sodium	140.92	140
Calcium	3.6	1.8
Magnesium	1.5	0.75
Total Chloride	100.8	100
Lactate	44.6	45
Dextrose		353

Total		642.91
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Dialaflex 63		
Sodium	130.52	130
Calcium	3.6	1.8
Magnesium	1.5	0.75
Total Chloride	90.5	90
Lactate	44.6	45
Dextrose		75

Total		343.67
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Dialaflex Solutions are colourless.

Indications Dialaflex Solutions are indicated only for use in peritoneal dialysis. This is employed as an alternative to haemodialysis in: Acute renal failure, chronic renal failure, prolonged post-operative anuria, intractable oedema, chronic congestive heart failure, poisoning due to ingestion of dialysable poisons.

Dialaflex 61 Solution is slightly hypertonic to avoid the dangers of increased hydration by absorption of water from the peritoneal cavity. It is indicated for routine dialyses which are not intended to remove excessive fluid from the body. Dialaflex 62 Solution is markedly hypertonic and is indicated when rapid removal of oedematous fluid is indicated. Dialaflex 63 Solution has a lower sodium content than Dialaflex 61. It is indicated for use in maintenance dialysis where removal of sodium is often desirable.

Dosage and administration Administration of Dialaflex Solutions necessitates the use of a special giving set to allow delivery of the solutions to and from the peritoneal cavity. This is done through a peritoneal catheter which is generally advised to be inserted in the mid-line between the umbilicus and the symphysis pubis at the junction of the middle and lower thirds.

Adults: For each dialysis 2 litres of Dialaflex Solution, ready warmed to body temperature, should be allowed to flow into the peritoneal cavity. After 20 minutes the solution is syphoned out and the procedure is repeated as often as is warranted by the situation and the condition of the patient.

Children: Each dialysis is usually performed with a volume of 1 litre of Dialaflex Solution.

Contra-indications, warnings, etc

Contra-indications: Peritoneal dialysis should not be employed if there has been recent injury to abdominal organs or in the presence of severe peritonitis.

Precautions: If full aseptic precautions are observed the danger of infection during peritoneal dialysis is slight. However, additional precautions against this possibility may be achieved by addition of antibiotics to the dialysis solution or by parenteral antibiotic administration.

Introduction of the trocar to enable the insertion of the catheter may carry the rare possibility of intestinal perforation.

Protein loss has been reported following prolonged period of peritoneal dialysis.

In patients with normal or depleted plasma potassium levels oral potassium supplements should be given or four millimoles potassium added to each litre of Dialaflex Solution.

Side-effects: Selection of the most suitable Dialaflex Solution and proper supervision of the peritoneal dialysis should ensure no untoward effects occur.

Overdosage: As peritoneal dialysis is invariably performed under supervision the question of overdosage is unlikely to arise.

Pharmaceutical precautions *Storage:* Dialaflex Solutions should be stored at 2°C–25°C. The shelf-life is two years.

Legal category POM.

Package quantities Plastic containers of 1 litre of Dialaflex Solutions are available in packs of 10.

Further information The volume of fluid recovered after dialysis should usually exceed the volume administered. The latter can be calculated by weighing the bags before and after dialysis. The weight per ml of solution is 1.009 g for Dialaflex 61 and Dialaflex 63, and 1.028 g for Dialaflex 62. Any deficiency in fluid balance may be corrected by either the oral or intravenous routes.

Product licence numbers

61 0014/0198
62 0014/0199
63 0014/0200

DIMERCAPROL INJECTION

Presentation Dimercaprol Injection BP (B.A.L. Injection) is a sterile solution of dimercaprol in arachis oil containing 10% V/V benzyl benzoate. It is presented in 2 ml ampoules, and each ml of the injection contains 50 mg of Dimercaprol BP.

Uses Dimercaprol Injection is indicated in the treatment of acute poisoning by certain heavy metals – arsenic, mercury, gold, bismuth, thallium and antimony. Although dimercaprol has not been successful in the treatment of lead poisoning when used alone, there is evidence that, used in conjunction with sodium calciumedetate, it can be used successfully in the treatment of lead poisoning, particularly in children.

Dosage and administration By intramuscular injection:

Adults: 400 to 800 mg, in divided doses, on the first day.
200 to 400 mg, in divided doses, on second and third days.
100 to 200 mg, in divided doses, on subsequent days.

Within the above dose range, individual dosage should be calculated on a body-weight basis, and will depend upon the severity of symptoms and the causative agent. As a general guide, single doses should not exceed 3 mg/kg; however, in severe acute poisoning, single doses up to 5 mg/kg may be required initially.

Children: Dimercaprol Injection is well tolerated by children and dosage should be calculated on the basis of body-weight, using the same unit dose per kilogram of body-weight as for an adult under similar clinical circumstances.

Precautions: The use of Dimercaprol Injection does not eliminate the need for the general treatment of poisoning due to the particular heavy metal. Any abnormal reaction (e.g. pyrexia) occurring after the initial injection of dimercaprol should be assessed before continuing treatment.

Contra-indications, warnings, etc Dimercaprol Injection is contra-indicated in poisoning by iron and cadmium.

Dimercaprol Injection is contra-indicated in the presence of extensive hepatic insufficiency or damage.

Dimercaprol Injection should be used with caution in the hypertensive patient.

Side-effects are relatively frequent, but, at the therapeutic dosage usually employed, are seldom severe enough to warrant cessation of treatment and are almost invariably reversible. There is some evidence to indicate that 30–60 mg of ephedrine sulphate, by mouth, given half an hour before each injection of dimercaprol, will reduce these reactions. Also, a minimum interval of four hours between doses appears to reduce side-effects.

Dimercaprol Injection may cause the following side-effects particularly at the higher dosage levels:

Elevation of blood pressure accompanied by tachycardia; nausea and possibly vomiting; a burning sensation of the lips, mouth, throat and eyes; salivation and lachrymation; conjunctivitis; rhinorrhoea; muscle pain and spasm; abdominal pain; headache; tingling of the hands and other extremities; a feeling of constriction in the chest and throat; sweating of the forehead and hands.

Local pain may occur at the site of injection, and gluteal abscess has occasionally been encountered.

A side-effect apparently peculiar to children is a fever which develops after the second or third injection, and persists until treatment with dimercaprol is terminated.

Pharmaceutical precautions Dimercaprol Injection may become cloudy in cold weather; if this occurs, warm slightly before use.

Protect from light.

Legal category POM.

Package quantities 12 ampoules of 2 ml.

Further information Nil.

Product licence number 0014/5509.

FREAMINE® II

Presentation FreAmine II is a sterile, non-pyrogenic solution containing crystalline amino acids and electrolytes. Each 100 ml contains FreAmine II Amino Acid Mixture (Lysine Acetate and Cysteine Hydrochloride, H₂O added) 8.5 g, Phosphoric Acid NF 0.115 g, Sodium Bisulphite USP less than 0.10 g and Water for Injection USP to 100 ml.

The approximate concentration of amino acids in grams per 100 ml is:

Essential amino acids: L-Isoleucine 0.59, L-Leucine 0.77, L-Lysine Acetate 0.87 (free base 0.62), Methionine 0.45, L-Phenylalanine 0.48, L-Threonine 0.34, L-Tryptophan 0.13, L-Valine 0.56.

Non-essential amino acids: L-Alanine 0.60, L-Arginine 0.31, L-Histidine 0.24, L-Proline 0.95, L-Serine 0.50, Aminoacetic Acid (Glycine) 1.7, L-Cysteine Hydrochloride

ride H_2O less than 0.02, Alpha amino nitrogen greater than 80% of total nitrogen present.

The concentration of electrolytes in mmols per litre is: Sodium 10, Phosphate 10. The pH of the solution is approximately 6.6 and the calculated osmolarity is approximately 850 mOsm per litre.

A 500 ml unit of FreAmine II provides 39 g of protein equivalent and 6.25 g of sodium.

Uses FreAmine II provides, in concentrated form, a physiological ratio of biologically utilisable amino acids for protein synthesis. Given with concentrated sources of calories such as hypertonic dextrose or fat emulsions and with electrolytes, vitamins and minerals, it provides total parenteral nutrition. Administered peripherally, alone as an isotonic solution (2.8%) or with minimum caloric supplementation such as 5% dextrose, FreAmine I provides nutritional support and spares body protein.

Parenteral nutrition with FreAmine II is indicated when there is a requirement to prevent nitrogen loss or to treat negative nitrogen balance in patients where

- a) by the oral, gastrostomy or jejunostomy routes, the alimentary tract should not or cannot be used
- b) gastro-intestinal absorption of protein is impaired
- c) protein requirements are substantially increased, as with extensive burns.

Dosage and administration The total daily dose of FreAmine II will depend upon protein requirements and the response of the patient as determined by clinical judgement and laboratory data such as nitrogen balance and serum protein levels.

The recommended daily allowance of protein for healthy adults is approximately 0.9 g/kg of body weight and, for healthy, growing infants and children, 2.2 g/kg of body weight. However, it must be borne in mind that, in traumatised or under-nourished patients, the protein and caloric requirements may be substantially increased. In such cases, daily amino acid doses of approximately 0.0–1.5 g/kg of body weight for adults and 2–3 g/kg of body weight for children are generally adequate to satisfy protein needs and to promote positive nitrogen balance. Higher doses may be required in severely catabolic states but, particularly with infants, should be accompanied by frequent laboratory assessment. For protein sparing in the well-nourished patient who is not receiving significant additional calories, amino acid doses 1.0–1.7 g/kg/day will reduce nitrogen loss and spare body protein but, if rises in blood urea nitrogen exceed 20 mg% in 48 hours, the rate of administration should be reduced or infusion discontinued.

Central venous nutrition: For severely catabolic, depleted patients or those requiring long-term total parenteral nutrition, administration of FreAmine II with hypertonic dextrose solutions by central venous infusions should be considered.

Peripheral parenteral nutrition: For the moderately catabolic or depleted patient for whom the central venous route of administration is not indicated, FreAmine may be mixed with dextrose 5% solutions and infused by peripheral vein, supplemented, if necessary, by fat emulsion.

Protein sparing nutrition: In the well-nourished, mildly catabolic subject (such as the routine post-surgical patient requiring short-term parenteral nutrition only) protein sparing can be achieved by peripheral infusion of FreAmine II with or without dextrose.

Contra-indications, warnings, etc FreAmine II is contra-indicated in patients with renal failure, severe liver disease or hypersensitivity to amino acids.

Warnings: The administration of amino acids to a patient with hepatic insufficiency may result in a rise in blood ammonia; administration in the presence of impaired renal function may augment an increasing blood urea nitrogen and also presents the dangers associated with retention of electrolytes. The safety of the use of amino acid solutions in pregnant women has not been established.

Precautions: Frequent evaluation and laboratory determinations should be carried out during parenteral nutrition. Studies should include blood sugar, serum proteins, kidney and liver function tests, electrolytes, haemogram carbon dioxide content, serum osmolarities, blood cultures and blood ammonia levels. Should hyperammonaemia develop, administration of amino acids should be discontinued and the patient's clinical state re-evaluated. (This is particularly important in infants.) Care should be taken to avoid circulatory overload, particularly in patients with cardiac insufficiency. In myocardial infarction, amino acids should be given with dextrose.

Strongly hypertonic amino acid solutions and associated hypertonic dextrose solutions should be administered only by continuous infusion through a central venous catheter with the tip located in the vena cava.

Side-effects: Prolonged infusion of hypertonic solutions may cause phlebotrombosis extending from the site of infusion.

Pharmaceutical precautions Avoid freezing and excessive heat; store at temperatures between 2°C and 25°C. Protect from light. Do not use a solution unless clear and a vacuum is present.

Legal category POM.

Package quantities FreAmine II: 500 ml Intravenous Infusion Bottle.

FreAmine II Hyperalimentation Kit (50% Dextrose): Consisting of one 500 ml bottle of FreAmine II and one 1,000 ml bottle containing 500 ml of 50% Dextrose Injection with Transfer Set and Additive Cap.

Further information FreAmine II is a concentrated source of naturally occurring, biologically available amino acids for intravenous nutrition. When used as total parenteral nutrition in conjunction with adequate calories and other nutrients, FreAmine II is life-supporting – promoting anabolism and tissue synthesis, even over extended periods. No peptides or glutamic or aspartic acid, which can cause nausea and vomiting, are included in the formulation.

Product licence numbers

FreAmine II 2737/0001

FreAmine II Hyperalimentation Kit

(50% Dextrose): 2737/0003

FreAmine II is McGaw product from The Boots Company Ltd, Nottingham.

FROBEN*

Presentation Light yellow, sugar-coated tablets containing either 50 mg or 100 mg of flurbiprofen. The

50 mg tablets are overprinted 'F50' in black; the 100 mg tablets are overprinted 'F100', also in black.

Uses Froben is a nonsteroidal anti-inflammatory agent which has significant anti-inflammatory, analgesic and antipyretic properties and is indicated in the treatment of rheumatoid disease, osteoarthritis, ankylosing spondylitis.

Dosage and administration The recommended daily dosage is 150–200 mg in three or four divided doses.

In patients with severe symptoms or disease of recent origin, or during acute exacerbations, the total daily dosage may be increased to 300 mg in divided doses.

Contra-indications, warnings, etc Froben should not be given to patients with peptic ulceration. Care should be taken when administering the drug to patients with asthma or who have experienced bronchospasm with other anti-inflammatory or analgesic agents. The safety of Froben during pregnancy or lactation has not been established. In animal experiments, no teratogenic effects were demonstrated but parturition was delayed and prolonged.

Side-effects: Dyspepsia, heartburn and headache are the commonest side-effects encountered. Occasional skin rashes have been reported.

Treatment of overdose: Gastric lavage and, if necessary, correction of serum electrolytes. There is no specific antidote to flurbiprofen.

Pharmaceutical precautions No special storage requirements are necessary.

Legal category POM.

Package quantities 50 mg Tablets: Packs of 100 and 500.

100 mg Tablets: Packs of 100.

Further information Froben is a potent non-steroidal anti-inflammatory agent which has significant anti-inflammatory, analgesic and antipyretic properties. It is a highly potent inhibitor of prostaglandin synthetase enzymes which are known to be associated with inflammation, pain and fever.

Studies in the treatment of rheumatoid disease, osteoarthritis and ankylosing spondylitis have indicated that Froben is as effective as the more potent of the established nonsteroidal anti-inflammatory agents and, in many patients, better tolerated. Long-term clinical studies have not revealed any evidence of significant effects upon the hepatic, renal or haemopoietic systems.

Because of the flexible dosage range, Froben is available as 50 mg tablets and 100 mg tablets, the higher strength preparation providing a convenient dose-form for those patients requiring 300 mg daily in divided doses.

Product licence numbers

Froben 50 mg Tablets 0014/0167

Froben 100 mg Tablets 0014/0168

FURAMIDE*

Presentation Furamide is presented as white, uncoated tablets, scored and embossed with the letters E.F. on one side. Each tablet contains Diloxanide Furoate BP 0.5 g.

Uses Furamide is used for the treatment of acute and chronic amoebic dysentery. It is rapidly effective in intestinal amoebiasis, but where there is liver involvement, specific treatment is recommended.

Dosage and administration *Adults:* 1 tablet 3 times daily for 10 days.

Children: Approx. 20 mg/kg body-weight (9 mg/lb) daily in divided doses for 10 days.

If required, a second course of treatment may be prescribed.

No special diets or enemas are required, and bed-rest is not necessary unless the clinical condition of the patient warrants it.

Contra-indications, warnings, etc There is no known contra-indication to the use of Furamide. The bacterial flora of the gut is not upset, and no serious side effects have been reported. Flatulence sometimes occurs but may usually be disregarded. More rarely, an urticaria rash may be seen.

Pharmaceutical precautions No special storage conditions are necessary.

Legal category POM.

Package quantities Packs of 15 and 250 tablets.

Further information Nil.

Product licence number 0014/5121.

FURAMIDE* COMPOUND

Presentation Furamide Compound is presented in tablets containing Furamide (Diloxanide Furoate BP 250 mg, Streptomycin Sulphate BP 150 mg and Chloroquine Phosphate BP 50 mg).

Uses Furamide Compound is indicated for the treatment of bacillary and amoebic dysentery.

It is intended for use in the treatment of diarrhoea when time or other circumstances does not allow for identification of the pathogen. The spectrum of streptomycin extends to all *Shigella* organisms, including *Shigella sonnei*, *flexneri* and *dysenteriae* (*shiga*), as well as to *Escherichia coli*. Furamide is specific against *Entamoeba histolytica*, and will destroy both vegetative and cyst forms of this parasite. Chloroquine phosphate is an acknowledged treatment for the hepatic complications of amoebic infection.

Dosage and administration *Adults:* 2 tablets 3 times daily for 5 days.

Children: 1 tablet 3 times daily for 5 days.

If considered necessary by the physician, treatment may be continued for a second 5 day period.

Contra-indications, warnings, etc There are no absolute contra-indications to the use of Furamide Compound. Side effects are uncommon. The Furamide component may cause flatulence in some patients but this may usually be disregarded. Headache, pruritus, blurring of vision and gastrointestinal disturbance may rarely be caused by chloroquine, but should disappear on withdrawal of the drug. As the streptomycin is not appreciably absorbed, toxic effects are unlikely and sensitivity reactions are rarely encountered.

Pharmaceutical precautions No special storage conditions are necessary.

Legal category POM.

Package quantities Pack of 15 tablets.

Further information Nil.

Product licence number 0014/5785.

HYDRENOX*

Presentation Hydrenox Tablets are Hydroflumethiazide Tablets BP each containing 50 mg of Hydroflumethiazide BP, oral diuretic of the thiazide group.

Uses Hydrenox is indicated in all cases where the reduction of fluid retention by diuresis is required, i.e. oedema of cardiac, renal or hepatic origin; premenstrual, iatrogenic and all other types of oedema. Hydrenox is also indicated in the treatment of hypertension, either used alone or in combination with a hypotensive agent.

Dosage and administration *Diuretic:* 50 to 200 mg daily, depending upon the severity of the oedema, as a single dose in the morning. The daily use should be given early enough to complete diuresis by bedtime. Doses of 25 to 50 mg on alternate days are usually adequate for maintenance therapy.

Hypotensive: 25 to 50 mg daily; when given as an adjunct to a specific hypotensive agent, the dose of the latter should be halved.

Dosage in children will be at the discretion of the physician; 1 mg per kg of body-weight daily has been suggested as suitable for most cases.

Contra-indications, warnings, etc

Electrolyte imbalance: All thiazide diuretics can produce a degree of electrolyte imbalance, especially in patients with renal or hepatic impairment or when dosage is high or prolonged. Serum electrolyte levels should be checked for abnormalities, particularly hypokalaemia which should be corrected by the addition of a potassium supplement to the regimen. Hydrenox does not contain a potassium supplement.

Digitalis intoxication: Sensitivity to digitalis may be increased by the kaliuretic effect of concurrent hydroflumethiazide. Patients should be observed for signs of digitalis intoxication and, if these appear, the dosage of digitalis reduced and a potassium supplement added to restore stability.

Jritic acid retention: Thiazide diuretics may raise serum uric acid levels with consequent exacerbation of gout in susceptible patients.

Diabetes: Thiazide diuretics sometimes lower carbohydrate tolerance and the insulin dosage of the diabetic patient may require adjustment.

Care is necessary when hydroflumethiazide is given to those with a known predisposition to diabetes.

Pregnancy: Thiazides cross the placental barrier; therefore it is reasonable to assume that side-effects occurring in the adult may also appear in the neonate.

Treatment of overdosage: Monitor blood pressure and renal electrolytes. Treatment is symptomatic.

Pharmaceutical precautions Recommended storage conditions, 5° to 20°C.

Legal category POM.

Package quantities Bottle of 100, bottle of 500.

Further information Nil.

Product licence number 0014/5119.

HYDROCORTISTAB* INJECTION

Presentation Hydrocortistab Injection is Hydrocortisone Acetate Injection BP, containing 25 mg of Hydrocortisone Acetate BP per ml.

Uses Hydrocortistab Injection is indicated for the local treatment, by intra-articular or peri-articular injection of arthritic conditions such as rheumatoid arthritis and osteoarthritis when few joints are involved and in traumatic arthritis, except when associated with fractures into the joint. It is also suitable for the symptomatic treatment, by the local injection, of certain non-articular inflammatory conditions such as inflamed tendon-sheaths and bursae.

Hydrocortistab Injection is not suitable for the production of systemic effects.

Dosage and administration By intra-articular or peri-articular injection, 5 mg to 50 mg depending upon the size of the joint. Not more than three joints should be treated in one day.

Contra-indications, warnings, etc As with all corticosteroids, the administration of Hydrocortistab Injection is contra-indicated when the affected site is infected. It should not be injected directly into tendons, nor should it be injected into spinal or any other than true diarthrodial joints.

Caution: Since joints and tissues injected with corticosteroids have an increased susceptibility to infection, local injections of Hydrocortistab should be carried out with full aseptic precautions.

Side-effects: The principal side-effect encountered with local injections of corticosteroids is a temporary local exacerbation, with increased pain and swelling. This usually subsides after a few hours. In certain circumstances, particularly after high or prolonged local dosage, corticosteroids can be absorbed in amounts sufficient to produce systemic effects.

Treatment of overdosage: Treatment is symptomatic but is unlikely to be required.

Pharmaceutical precautions Store between 15°C to 20°C; protect from light.

Legal category POM.

Package quantities Vial of 5 ml.

Further information Nil.

Product licence number 0014/5510.

LIGNOSTAB*

Presentation Lignostab is injection of lignocaine hydrochloride 2%. It is supplied in glass cartridges designed for use with dental-type cartridge syringes. Each cartridge contains 2.0 ml of solution.

Uses Lignostab is a local anaesthetic. It is mainly for use in dental procedures where the addition of a vasoconstrictor is either contra-indicated or not required. Since Lignostab contains no vasoconstrictor, the local anaesthetic effect is of relatively short duration.

Dosage and administration Lignostab is given by

injection, in dental procedures, into the gum. The amount of Lignostab required to produce adequate anaesthesia must be determined on an individual basis, bearing in mind that it is desirable to use the minimal effective dose.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to lignocaine. Injection into inflamed or infected areas is to be avoided.

Caution: Care should be taken to avoid the accidental intravenous injection of Lignostab.

Side-effects: Provided the correct injection technique is used and the lowest effective dose employed, side-effects with Lignostab are extremely rare. However, idiosyncratic reactions to local anaesthetics have been reported in some patients.

Toxic effects: Transient drowsiness and amnesia proceeding to severe central nervous system depression may sometimes occur, but excitation of the central nervous system is uncommon.

Pharmaceutical precautions *Recommended storage conditions:* 2–25°C; protect from light.

Legal category POM.

Package quantities Jars of 50 cartridges.

Further information Shelf-life of at least two years.

Product licence number 0014/5368.

LIGNOSTAB*-A LIGNOSTAB*-A100

Presentation Lignostab-A is injection of lignocaine hydrochloride 2% with adrenaline 1: 80,000. Lignostab-A100 is injection of lignocaine hydrochloride 2% with adrenaline 1: 100,000. Both are supplied in glass cartridges designed for use with dental-type syringes. Each cartridge contains 2.0 ml of solution.

Uses Lignostab-A and Lignostab-A100 are local anaesthetics, mainly for use in dental procedures.

Both these preparations include a vasoconstrictor (adrenaline), the effect of which is to prolong the local anaesthesia by delaying the diffusion of the anaesthetic into the surrounding tissues.

Dosage and administration Lignostab-A and Lignostab-A100, in dental procedures, are injected into the gum. The amount of either preparation needed to provide adequate anaesthesia must be determined on an individual basis, bearing in mind that it is desirable to use the minimal effective dose.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to lignocaine. Lignostab-A and -A100 should not be injected into inflamed or infected areas. Because of their adrenaline content, these preparations should be used with caution in patients with hypertension. Lignostab-A and -A100 are contra-indicated in patients taking antidepressants of the tricyclic group.

Caution: Care should be taken to avoid the accidental intravenous injection of Lignostab-A or -A100. Lignostab-A and -A100 should not be injected into extremities.

Side-effects: Provided the correct injection technique is used and the lowest effective dose employed, side-effects with Lignostab-A and -A100 are extremely rare. However, idiosyncratic reactions to local anaesthetics have been reported in some patients. The injection of

excessive amounts of Lignostab-A or -A100 may, due to the adrenaline content, cause ischaemia. This can be followed by a reactive hyperaemia resulting in post-extraction bleeding.

Toxic effects: Transient drowsiness and amnesia proceeding to severe central nervous system depression may occur, but excitation of the central nervous system is uncommon.

Treatment of overdosage: Respiratory failure may need assisted respiration. The circulation can be controlled with electrolyte or plasma infusions. If convulsions develop, these can be controlled by a short-acting barbiturate.

Pharmaceutical precautions *Recommended storage conditions:* 2–25°C. Protect from light.

Legal category POM.

Package quantities Jars of 50 Boxes of 500.

Further information Shelf-life of at least two years.

Product licence numbers

Lignostab-A 0014/5384

Lignostab-A100 0014/5385

LIGNOSTAB*-N

Presentation Lignostab-N is injection of lignocaine hydrochloride 2% with noradrenaline 1:80,000. It is supplied in glass cartridges designed for use with dental-type cartridge syringes. Each cartridge contains 2.0 ml of solution.

Uses Lignostab-N is a local anaesthetic, mainly for use in dental procedures. Lignostab-N includes the vasoconstrictor noradrenaline, the effect of which is to prolong the local anaesthesia by delaying the diffusion of the anaesthetic into the surrounding tissues.

Lignostab-N provides an alternative to local anaesthetics which contain adrenaline as a vasoconstrictor.

Dosage and administration Lignostab-N is given by injection, in dental procedures, into the gum. The amount required to provide adequate anaesthesia must be determined on an individual basis, bearing in mind that it is desirable to use the minimal effective dose.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to lignocaine. Injection into inflamed or infected areas is to be avoided. Because of the noradrenaline content, Lignostab-N should be used with caution in patients with hypertension. Lignostab-N is contra-indicated in patients taking antidepressants of the tricyclic group.

Caution: Care should be taken to avoid the accidental intravenous injection of Lignostab-N.

Side-effects: Provided the correct injection technique is used and the lowest effective dose employed, side-effects are extremely rare with Lignostab-N.

However, idiosyncratic reactions to local anaesthetics have been reported in some patients. The injection of excessive amounts of Lignostab-N may, due to the vasoconstrictor, cause ischaemia. This can be followed by a reactive hyperaemia and result in post-extraction bleeding.

Toxic effects: Transient drowsiness and amnesia proceeding to severe central nervous system depression may sometimes occur, but excitation of the central nervous system is uncommon.

Treatment of overdosage: Respiratory failure may need assisted respiration. The circulation can be maintained with electrolyte or plasma infusions. Should convulsions develop, these can be controlled with a short-acting barbiturate.

Pharmaceutical precautions *Recommended storage conditions:* 2–25°C. Protect from light.

Legal category POM.

Package quantities Jars of 50 and boxes of 500.

Further information Shelf-life of at least two years.

Product licence number 0014/5386.

MUSTINE HYDROCHLORIDE FOR INJECTION BP

Synonyms: Nitrogen Mustard. Mechlorethamine Hydrochloride USP, Mustargen Hydrochloride, Chlorethazine Hydrochloride, Chloromethine Hydrochloride INN, 'HN₂'.

Presentation Mustine hydrochloride is supplied in sterile vials each containing 10 mg of the powder. The injection is prepared by dissolving this in Sodium Chloride Injection BP 0.9% w/v or Water for Injections BP.

Mustine hydrochloride is di (2-chloroethyl) methylamine hydrochloride. It is a white or almost white hygroscopic, vesicant, crystalline powder or mass and is very soluble in water. A 0.2% solution in water has a pH of 3 to 5.

Uses The principal use of mustine hydrochloride is as part of combination treatment for Hodgkin's disease. It is also sometimes used in non-Hodgkin's lymphomas and carcinoma of bronchus, ovary and breast. It may be injected into pleural or peritoneal cavities for the treatment of malignant effusions. It may be applied locally for the treatment of mycosis fungoides.

Dosage and administration *Malignancy:* The normal intravenous dose of mustine hydrochloride is 0.1 mg per kg body-weight daily for three or four days. In selected cases, larger doses of 0.2 to 0.3 mg per kg body-weight daily may be given, but the course should then be limited to two injections. Alternatively, a single treatment using 3.4 mg per kg body-weight (15 mg per square metre body surface area) can be administered. The term 'body-weight' is defined, in this case, as the actual body-weight at the time of treatment except in cases where the weight has been artificially increased by oedema, ascites, or other fluid collections. The weight of the body before the increase is used in such cases.

UNDER NO CIRCUMSTANCES SHOULD MUSTINE BE GIVEN INTRAMUSCULARLY.

A repeat course of mustine therapy should not be undertaken for at least 6 weeks or until the bone-marrow has recovered its haemopoietic activity.

Preparation of intravenous injection: A fresh solution is prepared by dissolving 10 mg of mustine hydrochloride in 10 ml of Sodium Chloride Injection BP 0.9% w/v, or Water for Injections BP. The best method of administration is to set up an intravenous drip of Sodium Chloride Injection BP 0.9% w/v or Dextrose Injection BP 5% w/v; the required dose of mustine prepared as above, is then injected into the tubing. This avoids the hazard of extravasation during injection. The drip rate should be 10 drops per minute and the injection of mustine should

be carried out over 2 minutes. The drip should then be reduced to 20 drops per minute.

Alternatively the concentrated solution of mustine hydrochloride is freshly prepared as above and transferred aseptically to 500 ml of Sodium Chloride Injection BP 0.9% w/v.

Pleural effusions: Mustine is sometimes injected into the peritoneal or pleural cavities. There are minor variations in the techniques. Half an hour before the injection a short acting barbiturate such as oral quinalbarbitone 0.2 g, and chlorpromazine 25 mg should be given to reduce the nausea. Most articles advise the use of paracentesis to remove as much fluid as possible. Mustine hydrochloride may be injected into the cavity in a simple dose up to 0.4 mg/kg body-weight (15 to 30 mg of mustine in about 100 to 200 ml of normal saline).

The quinalbarbitone and chlorpromazine may be repeated if there is further nausea.

Mycosis fungoides: Mycosis fungoides may be treated by topical application of a dilute solution of mustine hydrochloride. Various strengths of mustine hydrochloride have been used but 20 mg in 100 ml of 0.9% w/v sodium chloride solution or water is frequently recommended. The solution is applied to the affected cutaneous areas using a gauze pad. The person applying the solution should wear polyvinylchloride gloves to give protection. Some patients develop an allergic contact dermatitis after topical application of mustine hydrochloride.

Contra-indications, warnings, etc

Warning: To prevent blistering, gloves should be worn when handling mustine hydrochloride, and because of its irritating powers the drug should be kept well away from the nose and eyes. Polyvinylchloride gloves give adequate protection but rubber and polyethylene gloves have been shown to be ineffective. Mustine hydrochloride accidentally spilled on the skin should be washed away immediately with large amounts of water or, if at hand, sodium carbonate solution or an isotonic solution of sodium thiosulphate. If mustine is accidentally splashed into the eye it should be immediately washed out for a long period of time with large amounts of water and, if available, irrigated with isotonic solution of sodium thiosulphate. The person concerned then should be seen by an ophthalmologist.

After treatment with mustine all apparatus, including PVC gloves, should be washed thoroughly. A 2.5% solution of sodium carbonate is particularly suitable for the lavage.

Adverse reactions and precautions: Nausea and vomiting often occur during the eight hours following injection. The administration of chlorpromazine, either alone or with a suitable barbiturate such as quinalbarbitone, often helps to control this and should be given thirty to sixty minutes before injection, repeated if necessary.

Transient anorexia, occasional diarrhoea and fever may occur. Peptic ulcers have been reported.

Severe haemopoietic depression may follow mustine therapy, with lymphocytopenia, granulocytopenia and occasionally agranulocytosis. It may lead to severe anaemia and thrombocytopenia. Leucocytes and platelet counts in peripheral blood start to fall about one week after treatment with a nadir between 14 and 18 days. During the same period there is a fall in haemoglobin level. Both leucocyte and platelet counts return to normal before the end of the fourth week. Mustine should not be used in patients with severe leucopenia, thrombocy-

topenia or anaemia and in coexistent or suspected granuloma. Extravasation during injection should be avoided as this may cause severe local reactions and even local tissue necrosis. If extravasation does occur during injection the involved area should be infiltrated with isotonic sodium thiosulphate solution followed by the application of an ice compress intermittently for six to twelve hours.

This product should not normally be administered to patients who are pregnant or to mothers who are breast-feeding.

If considered for use in pregnancy the risk to the foetus should be weighed against the potential benefits to the patient. The drug possesses foetotoxic and teratogenic potential.

Thrombophlebitis and venous thrombosis are potential complications to mustine therapy.

In non-pregnant women delayed menstruation or temporary amenorrhoea may follow the treatment. In males a reduction of active spermatogenesis has been reported. Hyperuricaemia may develop in patients with large tumour masses.

Treatment of overdose: Sodium thiosulphate will neutralise an injection of mustine hydrochloride BUT ONLY IF GIVEN IMMEDIATELY AFTERWARDS. Each 10 mg mustine requires 640 mg sodium thiosulphate given as an isotonic solution. This is equivalent to approximately 1.5 ml of a 50% solution of sodium thiosulphate diluted with 20 ml 0.9% sodium chloride solution or approximately 21 ml of 3% sodium thiosulphate solution.

Stability: An early study of the stability of mustine hydrochloride in saline solution at room temperature, using a colorimetric assay method, showed that the solution lost 7% of alkylating potential per hour. A later study indicated that solutions of mustine hydrochloride stored at room temperature lost approximately 50% of activity in one to two months.

Studies in Boots' laboratories storing 10 mg mustine hydrochloride in 20 ml Water for Injections showed no significant loss of activity over the first 10 days. Thereafter a slow but steady loss of activity occurred until the 40th day resulting in an overall loss of 20%.

Pharmaceutical precautions Store at 2° to 15°C.

Legal category POM.

Package quantities Pack of 10 vials.

Further information Nil.

Product licence number 0014/5512.

NEULENTE®

Presentation Neulente insulin injection is Insulin Zinc Suspension Injection BP (Purified), a cloudy neutral suspension of purified insulin consisting of 3 parts of insulin zinc suspension (amorphous) and 7 parts of insulin zinc suspension (crystalline). pH 7.2 ± 0.3

It is available in strengths of 40 and 80 units per ml.

This insulin is prepared from ox pancreas.

Uses For the management of diabetes mellitus.

Dosage and administration

Adults and children: The daily unit dosage of insulin is determined by the physician in accordance with the patient's requirements.

The site of each injection should be changed according to a suitable routine.

Insulin Zinc suspension should be well mixed by inverting the vial several times before use. It is administered by subcutaneous or intramuscular injection.

Subcutaneous: Onset of action occurs within 2 hours, with an overall duration of action which may extend to 28–30 hours.

Intramuscular: Onset of action is more rapid and overall duration of action shorter than with the subcutaneous route, assuming adequate vascular perfusion.

Insulin zinc suspension should not be given intravenously.

Contra-indications, warnings, etc Hypoglycaemia is an absolute contra-indication.

Insulin dosage requirement may change if the species of origin, type, or purity of insulin is changed.

Interactions: Insulin requirements may be affected by changes in life-style, pregnancy, infections, other medical conditions or certain drug therapies.

Insulin requirements may be increased by the concomitant use of corticosteroids, oral contraceptives, thyroid hormones, thiazide diuretics and may be decreased by beta-adrenergic blocking agents and monoamine oxidase inhibitors. Since the clinical effect is variable, diabetic patients should be carefully observed initially when any drug therapy is required.

Side-effects: The most important side-effect is hypoglycaemia. Reduction of hyperglycaemia in newly diagnosed diabetics may alter visual refraction.

Bovine insulin, like any other foreign protein, is potentially immunogenic.

Local reactions at the injection site may include transient erythema, induration, urticaria and oedema. These usually resolve with continuing usage of insulin.

True generalised hypersensitivity reactions approaching anaphylaxis are very rare.

Clinical evidence suggests that purified insulins are unlikely to cause localised lipodystrophies. However, at present, this possibility cannot be totally excluded.

Treatment of Overdosage: The symptoms and signs of hypoglycaemia depend on the patient's clinical state and on the rate and extent of the fall in blood glucose. If possible, dextrose, sucrose or rapidly available carbohydrate should be taken by mouth. Failing this, hypoglycaemia, should be reversed as rapidly as possible by intravenous injection of 50% Dextrose injection. Alternative emergency treatments include the subcutaneous injection of up to 1 ml of adrenaline injection 1: 1000, or the subcutaneous, intramuscular or intravenous injection of lyophilised glucagon 0.5–1.0 mg (1 unit = 1.0 mg). Both adrenaline and glucagon injections mobilise hepatic glycogen, but the effect is short-lived and must be supplemented by freely available carbohydrate as soon as possible.

Pharmaceutical precautions Store at 2°–10°C. Do not freeze. Avoid direct sunlight.

Legal category P.

Package quantities

40 units per ml: 10 ml vial.

80 units per ml: 10 ml vial.

Further information *Mixing in the Syringe:* Insulin zinc suspension (purified) should not be mixed with other insulins.

Product licence numbers

Neulente 40 units per ml: 0014/0224

Neulente 80 units per ml: 0014/0225

NEUPHANE®

Presentation Neuphane insulin injection is Isophane Insulin Injection BP (Purified), a cloudy neutral suspension of an insulin (purified)/protamine complex. pH 7.2 ± 0.3

It is available in strengths of 40 and 80 units per ml.
This insulin is prepared from ox pancreas.

Uses For the management of diabetes mellitus.

Dosage and administration

Adults and children: The daily unit dosage of insulin is determined by the physician in accordance with the patient's requirements.

The site of each injection should be changed according to a suitable routine.

Isophane insulin injection should be well mixed by inverting the vial several times before use. It is administered by subcutaneous or intramuscular injection.

Subcutaneous: Onset of action occurs within 2 hours, with an overall duration of action which may extend to 18–28 hours.

Intramuscular: Onset of action is more rapid and overall duration of action shorter than with the subcutaneous route, assuming adequate vascular perfusion.

Isophane insulin injection should not be given intravenously.

Contra-indications, warnings, etc Hypoglycaemia is an absolute contra-indication.

Insulin dosage requirements may change if the species of origin, type, or purity of insulin is changed.

Interactions: Insulin requirements may be affected by changes in life-style, pregnancy, infections, other medical conditions or certain drug therapies.

Insulin requirements may be increased by the concomitant use of corticosteroids, oral contraceptives, thyroid hormones, thiazide diuretics and may be decreased by beta-adrenergic blocking agents and monoamine oxidase inhibitors. Since the clinical effect is variable, diabetic patients should be carefully observed initially when any drug therapy is required.

Side-effects: The most important side-effect is hypoglycaemia. Reduction of hyperglycaemia in newly diagnosed diabetics may alter visual refraction.

Bovine insulin and protamine, like any other foreign proteins, are potentially immunogenic.

Localised reactions at the injection site may include transient erythema, induration, urticaria and oedema. These usually resolve with continuing usage of insulin.

True generalised hypersensitivity reactions approaching anaphylaxis are very rare.

Clinical evidence suggests that purified insulins are unlikely to cause localised lipodystrophies. However, at present, this possibility cannot be totally excluded.

Treatment of Overdosage: The symptoms and signs of hypoglycaemia depend on the patient's clinical state and on the rate and extent of the fall in blood glucose.

If possible, dextrose, sucrose or rapidly available carbohydrate should be taken by mouth. Failing this, hypoglycaemia should be reversed as rapidly as possible by intravenous injection of 50% Dextrose injection. Alternative emergency treatments include the subcutaneous injection of up to 1 ml of adrenaline injection 1:1000, or the subcutaneous, intramuscular or intravenous injection of lypophilised glucagon 0.5–1.0 mg (1 unit = 1.0 mg). Both adrenaline and glucagon injections mobilise hepatic glycogen, but the effect is short-

lived and must be supplemented by freely available carbohydrate as soon as possible.

Pharmaceutical precautions Store at 2°–10°C. Do not freeze. Avoid direct sunlight.

Legal category P.

Package quantities

40 units per ml: 10 ml vial.

80 units per ml: 10 ml vial.

Further information *Mixing in the Syringe:* Isophane insulin injection (purified) can be mixed with neutral insulin injection (purified).

If, on medical advice isophane insulin injection (purified) is to be mixed in the syringe with neutral insulin injection (purified), the following procedure should be adopted:—

1. Inject a volume of air equivalent to the dose of isophane insulin injection into the bottle of isophane insulin injection without inverting the bottle or withdrawing the dose.

2. Inject a volume of air equivalent to the dose of neutral insulin injection into the bottle of neutral insulin injection and withdraw the dose in the usual way.

3. Re-insert the needle into the isophane insulin injection and withdraw the appropriate dose.

Product licence numbers

Neuphane 40 units per ml 0014/0226

Neuphane 80 units per ml 0014/0227

NEUSULIN®

Presentation Neusulin insulin injection is Neutral Insulin Injection BP (Purified), a clear neutral solution of purified crystalline insulin. pH 7.15 ± 0.55.

It is available in strengths of 40 and 80 units per ml.

This insulin is prepared from ox pancreas.

Uses For the management of diabetes mellitus.

Dosage and administration

Adults and children: The daily unit dosage of insulin is determined by the physician in accordance with the patient's requirements.

The site of each injection should be changed according to a suitable routine. Neutral insulin injection is administered by subcutaneous, intramuscular or intravenous injection. Accidental intravascular injection should be avoided.

Subcutaneous: Onset of action occurs within 30–60 minutes, with an overall duration of action of approximately 6–8 hours. Consequently, 2 or 3 injections daily before meals may be appropriate if not used in combination with other insulins.

Intramuscular: Onset of action is more rapid and overall duration of action shorter than with the subcutaneous route, assuming adequate vascular perfusion.

Intravenous: Onset of action is most rapid and duration of action shortest with this route. It is usually reserved either for investigational purposes, or for the treatment of diabetic ketoacidosis.

Contra-indications, warnings, etc Hypoglycaemia is an absolute contra-indication.

Insulin dosage requirement may change if the species of origin, type or purity of insulin is changed.

Interactions: Insulin requirements may be affected by

changes in life-style, pregnancy, infections, other medical conditions or certain drug therapies.

Insulin requirements may be increased by the concomitant use of corticosteroids, oral contraceptives, thyroid hormones, thiazide diuretics and may be decreased by beta-adrenergic blocking agents and monoamine oxidase inhibitors. Since the clinical effect is variable, diabetic patients should be carefully observed initially when any drug therapy is required.

Side-effects: The most important side-effect is hypoglycaemia. Reduction of hyperglycaemia in newly diagnosed diabetics may alter visual refraction.

Bovine insulin, like any other foreign protein, is potentially immunogenic.

Local reactions at the injection site may include transient erythema, induration, urticaria and oedema. These usually resolve with continuing usage of insulin.

True generalised hypersensitivity reactions approaching anaphylaxis are very rare.

Clinical evidence suggests that purified insulins are unlikely to cause localised lipodystrophies. However, at present, this possibility cannot be totally excluded.

Treatment of overdosage: The symptoms and signs of hypoglycaemia depend on the patient's clinical state and on the rate and extent of the fall in blood glucose.

If possible, dextrose, sucrose or rapidly available carbohydrate should be taken by mouth. Failing this, hypoglycaemia should be reversed as rapidly as possible by intravenous injection of 50% Dextrose injection. Alternative emergency treatments include the subcutaneous injection of up to 1 ml of adrenaline injection 1:1000, or the subcutaneous, intramuscular or intravenous injection of lyophilised glucagon 0.5–1.0 mg (1 unit = 1.0 mg). Both adrenaline and glucagon injections mobilise hepatic glycogen, but the effect is short-lived and must be supplemented by freely available carbohydrate as soon as possible.

Pharmaceutical precautions Store at 2°–10°C. Do not freeze. Avoid direct sunlight.

Legal category P.

Package quantities

40 units per ml: 10 ml vial.

80 units per ml: 10 ml vial.

Further information If, on medical advice, isophane insulin injection (purified) is to be mixed in the syringe with neutral insulin injection (purified) the following procedure should be adopted:—

1. Inject a volume of air equivalent to the dose of isophane insulin injection (purified) into the bottle of long acting insulin, without inverting the bottle or withdrawing the dose.

2. Inject a volume of air equivalent to the dose of neutral insulin injection into the bottle of neutral insulin injection and withdraw the dose in the usual way.

3. Re-insert the needle into the long acting insulin injection and withdraw the appropriate dose.

Product licence numbers

Neusulin 40 units per ml 0014/0222

Neusulin 80 units per ml 0014/0223

OCUSOL* EYE DROPS

Presentation Ocusol Eye drops are a sterile preparation of Sulphacetamide Sodium BP 5% w/v, Zinc

Sulphate BP 0.1% w/v and Cetrimide BP 0.01% w/v in an aqueous base of adjusted tonicity, viscosity and pH.

Uses Ocusol Eye drops are indicated in the treatment of superficial eye infections such as blepharitis, conjunctivitis and infections of the cornea. They may also be used as a prophylactic measure against infection following eye injury or the removal of foreign bodies from the eye.

Dosage and administration One drop to be instilled into the affected eye three or four times daily.

Contra-indications, warnings, etc There are no known contra-indications to the use of Ocusol; no side-effects associated specifically with Ocusol have been reported.

Warning: Ocusol should not be used later than four weeks after the bottle has been opened.

Treatment of overdosage: There is no toxicological hazard even if the whole bottle is swallowed.

Pharmaceutical precautions None.

Legal category POM.

Package quantities 10 ml dropper-bottle.

Further information The formulation of Ocusol has an antibacterial activity equivalent approximately to that of a 30% solution of sulphacetamide sodium but is much less likely to cause local irritation than the latter more concentrated solution.

Product licence number 0014/5164.

POLYFUSOR* DEXTROSE INJECTIONS

Presentation Polyfusor Dextrose Injections are sterile, pyrogen-free solutions of Anhydrous Dextrose in Water for Injections prepared to British Pharmacopoeial standards. The solutions are enclosed in disposable, semi-rigid containers of pure polyethylene and are available in the following strengths:

Concentration of dextrose w/v (%)	Energy value in calories per litre	Concentration of anhydrous dextrose in grams per litre
2.5	94	25
5.0	188	50
10.0	375	100
20.0	750	200
40.0	1,500	400
50.0	1,875	500

Uses Polyfusor Dextrose Injections are given by intravenous infusion and are indicated in simple dehydration, carbohydrate depletion, hypoglycaemic coma. They can also be used to provide a temporary increase in blood volume in haemorrhage and shock.

Dosage and administration The volume, strength and rate of infusion of dextrose solutions given intravenously will depend upon the requirements of the patient and the judgement of the physician.

Contra-indications, warnings, etc

Contra-indications: Diabetes, except as a treatment for hypoglycaemia. The intravenous infusion of dextros:

solutions may be hazardous in patients with impaired hepatic or renal function.

Precautions: The intravenous infusion of dextrose solutions should not be too rapid or very prolonged. The rapid administration of large volumes of these solutions can cause water intoxication; conversely, infusion over a long period can cause dehydration.

Side-effects: Thrombosis of the chosen vein is always a possibility with intravenous infusion.

Treatment of overdosage: Introduce measures to correct water intoxication or dehydration as appropriate (see 'Precautions').

Pharmaceutical precautions Recommended storage conditions: 2–25°C. The shelf-life of Polyfusor Dextrose Injections is three years.

To prevent gross contamination of the outside surface of the Polyfusor, the outer envelope in which the Polyfusor is supplied should not be opened or removed until immediately before use.

Note: Immediately before use, the intact outer envelope in which the Polyfusor is supplied should be examined for moisture upon the inside surface; if moisture is observed, the integrity of the enclosed Polyfusor is suspect and it must be discarded. Unused solution remaining in a Polyfusor after use must also be discarded.

Legal category POM.

Package quantities Carton of 10 × 500 ml. Carton of 10 × 1,000 ml.

Further information Polyfusor Dextrose Injections provide a range of dextrose solutions designed to meet the many and varied requirements of intravenous carbohydrate therapy. Prepared to an exceptionally high standard, the solutions are supplied in disposable, semi-rigid containers made from a specially developed neutral plastic free from plasticisers, anti-oxidants and other additives likely to leach out and contaminate the enclosed solution. The intact wall of the Polyfusor is impervious to micro-organisms and virtually impermeable to water vapour, thus ensuring the stability of the contents for very long periods under normal storage conditions (see 'Shelf-life'). Polyfusor Dextrose Injections are part of the Polyfusor range of solutions for intravenous infusion – a range of solutions which, both in quality and extent, can meet the general and specific requirements of modern intravenous therapy.

Product licence numbers

1.5% 0014/5886
3% 0014/5245
10% 0014/5244
20% 0014/5884
50% 0014/5892
100% 0014/5893

POLYFUSOR* FRUCTOSE SOLUTIONS

Representation Polyfusor Fructose Solutions are sterile, hydrogen-free solutions of Laevulose in Water for Injections prepared to British Pharmacopoeial standards. The solutions are enclosed in disposable, semi-rigid containers of pure polyethylene and are available in the following strengths. (See table in next column.)

Uses Polyfusor Fructose Solutions are given by intravenous infusion and are indicated for conditions associated with carbohydrate deficiency. Fructose accelerates

Concentrations of laevulose w/v (%)	Energy value in calories per litre	Concentration of laevulose in grams per litre
10	375	100
20	750	200

ates the metabolism of ethyl alcohol and may be given in the treatment of acute ethanol poisoning. Fructose is a suitable source of calories in patients with renal failure unable to tolerate oral feeding. Neonatal hypoglycaemia occurring in newborn infants of diabetic mothers can be prevented by injection of fructose into the umbilical vein.

Dosage and administration The volume, strength and rate of infusion of fructose solutions given intravenously will depend upon the requirements of the patients and the judgement of the physician. Administration should be slow.

Contra-indications, warnings, etc

Contra-indications: Fructose should not be given to patients with fructose intolerance, or to patients with methyl alcohol poisoning as it enhances the oxidation of methyl alcohol to formaldehyde. Fructose should not be administered to patients in shock, with severe hepatic disease or uncontrolled diabetes mellitus.

Side-effects: Thrombosis of the chosen vein is always a possibility with intravenous infusion. Reported side-effects of large doses include facial flushing epigastric pain and sweating.

Treatment of overdosage: Treatment consists of withdrawal of the infusion.

Pharmaceutical precautions Recommended storage conditions: 2–25°C. The shelf-life of Polyfusor Fructose Solutions is one year. To prevent gross contamination of the outside surface of the Polyfusor, the outer envelope in which the Polyfusor is supplied should not be opened or removed until immediately before use.

Note: Immediately before use, the intact outer envelope in which the Polyfusor is supplied should be examined for moisture upon the inside surface; if moisture is observed the integrity of the enclosed Polyfusor is suspect and it must be discarded. Unused solution remaining in a Polyfusor after use also must be discarded.

Legal category POM.

Package quantities Carton of 10 × 500 ml.

Further information Prepared to an exceptionally high standard, Polyfusor Fructose Solutions are supplied in disposable, semi-rigid containers made from a specially developed neutral plastic, free from plasticisers, anti-oxidants and other additives likely to leach out and contaminate the enclosed solution. The intact wall of the Polyfusor is impervious to micro-organisms and virtually impermeable to water vapour, thus ensuring the stability of the contents for long periods under normal storage conditions (see 'Shelf-life'). Polyfusor Fructose Solutions are part of the Polyfusor range of solutions for intravenous infusion – a range of solutions which, both in quality, and extent, can meet the general and specific requirements of modern intravenous therapy.

Product licence numbers

10% 0014/5362
20% 0014/5363

POLYFUSOR* GLYCEROL AND SALINE INJECTION

Presentation Polyfusor Glycerol Solution is a sterile pyrogen-free solution of Glycerol and Sodium Chloride in Water for Injections prepared to British Pharmacopoeial standards. The solution contains Glycerol 10 parts (by weight) and Sodium Chloride 0.9% 100 parts (by volume). Approximate ion concentration in millimoles per litre: Sodium 143, Chloride 143.

Uses Polyfusor Glycerol Solution is used in the treatment of acute cerebral oedema.

Dosage and administration The volume and rate of infusion of Glycerol and Saline given intravenously will depend upon the requirements of the patient and the judgement of the physician. Glycerol has been given intravenously as a 10% solution in 0.9% Sodium chloride Solution in a dosage of 1.2 g per kg body weight and every 24 hours for up to six days.

Contra-indications, warnings, etc

Contra-indications: Cardiac or renal failure.

Precautions: The infusion must be given slowly.

Side-effects: Haemolysis, haemoglobinuria, and renal failure. Local phlebitis may occur.

Treatment of overdosage: Discontinue infusion.

Pharmaceutical precautions *Recommended storage conditions:* 2°C–25°C. The shelf-life of Polyfusor Glycerol and Saline Injection is three years.

To prevent gross contamination of the outside surface of the Polyfusor, the outer envelope in which the Polyfusor is supplied should not be opened before use.

Note: Immediately before use, the intact outer envelope in which the Polyfusor is supplied should be examined for moisture upon the inside surface; if moisture is observed, the integrity of the enclosed Polyfusor is suspect and it must be discarded. Unused solution remaining in a Polyfusor after use must also be discarded.

Legal category POM.

Package quantities Carton of 10 × 500 ml.

Further information Polyfusor Glycerol and Saline Injections is designed to meet the requirements of intravenous therapy. Prepared to an exceptionally high standard, the solution is supplied in disposable, semi-rigid containers made from a specially developed neutral plastic free from plasticisers, antioxidants and other additives likely to leach out and contaminate the enclosed solution. The intact wall of the Polyfusor is impervious to micro-organisms and virtually impermeable to water vapour, thus ensuring the stability of the contents for very long periods under normal storage conditions (see Shelf-life). Polyfusor Glycerol and Saline Injection is part of the Polyfusor range of solutions for intravenous infusion – a range of solutions which, both in quality and extent, can meet the general and specific requirements of modern intravenous therapy.

Product licence number 0014/5853.

POLYFUSOR* HARTMANN'S SOLUTION

Presentation Polyfusor Hartmann's Solution is a sterile pyrogen-free preparation of Compound Sodium Lactate Injection prepared to British Pharmacopoeial

standards. The solution is enclosed in disposable semi-rigid containers of pure polyethylene.

Approximate ion concentration in millimoles per litre Sodium, 131; Chloride, 111; Calcium, 2; Potassium, 5 Bicarbonate (as Lactate) 29.

Uses Polyfusor Hartmann's Solution is administered by intravenous infusion and is used for the treatment of dehydration with acidosis. It may also be used to expand extracellular fluids or restore extracellular electrolyte Hartmann's Solution may also be used in the treatment of diabetic coma and the fluid and electrolyte losses associated with infantile diarrhoea.

Dosage and administration The volume, strength and rate of infusion of compound sodium lactate solution given by intravenous infusion will depend upon the requirements of the patient and the judgement of the physician. A dosage of 300 ml per hour should not be exceeded.

Contra-indications, warnings, etc

Contra-indications: Hartmann's Solution should not be administered to patients with severe liver damage who would be unable to convert lactate to bicarbonate.

Precautions: Hartmann's Solution should be used with caution in patients with cardiac failure, hypertension impaired renal function, peripheral and pulmonary oedema, and in toxæmia of pregnancy.

Side-effects: Thrombosis of the chosen vein is always a possibility with intravenous infusion.

Treatment of overdosage: Administer a suitable diuretic

Pharmaceutical precautions *Recommended storage conditions:* 2–25°C. The shelf-life of Polyfusor Hartmann's Solution is three years.

To prevent gross contamination of the outside surface of the Polyfusor, the outer envelope in which the Polyfusor is supplied should not be opened or removed until immediately before use.

Note: Immediately before use, the intact outer envelope in which the Polyfusor is supplied should be examined for moisture upon the inside surface; if moisture is observed, the integrity of the enclosed Polyfusor is suspect and it must be discarded. Unused solution remaining in a Polyfusor after use must also be discarded.

Legal category POM.

Package quantities Carton of 10 × 500 ml. Carton of 10 × 1,000 ml.

Further information Polyfusor Hartmann's Solution is designed to meet the varied requirements of fluid therapy. Prepared to an exceptionally high standard, the solutions are supplied in disposable, semi-rigid containers made from a specially developed neutral plastic free from plasticisers, anti-oxidants and other additives likely to leach out and contaminate the enclosed solution. The intact wall of the Polyfusor is impervious to micro-organisms and virtually impermeable to water vapour, thus ensuring the stability of the contents for very long periods under normal storage conditions (see 'Shelf life'). Polyfusor Hartmann's Solution is part of the Polyfusor range of solutions for intravenous infusion – a range of solutions which, both in quality and extent, can meet the general and specific requirements of modern intravenous therapy.

Product licence number

Hartmann's Solution 0014/5410.

***OLYFUSOR* MANNITOL INJECTIONS**

Presentation Polyfusor Mannitol Injections are sterile, pyrogen-free solutions of Mannitol in Water for Injections prepared to British Pharmacopoeial standards. The solutions are enclosed in containers of pure polyethylene. Polyfusor Mannitol Injections are available as solutions of 10% and 20% w/v.

Uses Polyfusor Mannitol Injections are administered by intravenous infusion and are used as an osmotic diuretic alone or to supplement the action of other diuretics in order to promote renal function. Other uses include the treatment of oliguria and to assist the elimination of drugs such as aspirin and barbiturates which are excreted by the kidneys.

Dosage and administration The volume, strength and rate of infusion of mannitol solutions given in intravenous infusion will depend upon the requirements of the patient and the judgement of the physician. A dose of 200 g daily by intravenous infusion should not be exceeded.

Contra-indications, warnings, etc Mannitol is contra-indicated in cases of metabolic oedema associated with abnormal capillary fragility. If renal flow is inadequate, water intoxication is likely in patients receiving intravenous mannitol; therefore, its use in oedematous conditions associated with diminished cardiac reserve should only be considered if the advantages outweigh the risks. Patients with impaired renal function should be given a test dose of 200 mg/kg body weight administered over five minutes and, if 40 ml or more of urine is produced in an hour, mannitol may be given in therapeutic doses.

Solutions of mannitol given in intravenous infusion should be administered slowly and should not be mixed with blood in transfusion apparatus.

Side-effects: Rapid intravenous infusion of mannitol may produce headache, chills or chest pain. It may also depress respiration by altering the acid-base and electrolyte balance of the body fluids. Convulsions have been noted in patients administered excessive doses of mannitol solution.

Treatment of overdosage: Introduce measures to correct water and electrolyte imbalance.

Pharmaceutical precautions Recommended storage conditions: 20–30°C. Exposure to lower temperatures may cause deposition of crystals. Carefully examine the solution for crystals immediately before use. If necessary redissolve by raising the temperature to 60°C. Cool to blood heat before use. The shelf-life of Polyfusor Mannitol Injection is three years. To prevent gross contamination of the outside surface of the Polyfusor,

the outer envelope in which the Polyfusor is supplied should not be opened or removed until immediately before use.

Note: Immediately before use the intact outer envelope in which the Polyfusor is supplied should be examined for moisture upon the inside surface; if moisture is observed, the integrity of the enclosed Polyfusor is suspect and it must be discarded. Unused solution remaining in a Polyfusor after use must also be discarded.

Legal category POM.

Package quantities Carton of 10 × 500 ml.

Further information Polyfusor Mannitol Injections are designed to meet the many requirements of intravenous diuretic therapy. Prepared to an exceptionally high standard, the solution is supplied in disposable, semi-rigid containers made from a specially developed neutral plastic free from plasticisers, antioxidants and other additives likely to leach out and contaminate the enclosed solution. The intact wall of Polyfusor is impervious to micro-organisms and virtually impermeable to water-vapour, thus ensuring the stability of the contents for very long periods under normal storage conditions (see 'Shelf-life'). Polyfusor Mannitol Injections are part of the Polyfusor range of solutions for intravenous infusion – a range of solutions which, both in quality and extent, can meet the general and specific requirements of modern intravenous therapy.

Product licence numbers

10% 0014/5359

20% 0014/5360

***POLYFUSOR* PAEDIATRIC ELECTROLYTE**

Presentation Polyfusor Paediatric Electrolyte Solution is a sterile pyrogen-free solution prepared to British Pharmacopoeial standards. The solution is enclosed in disposable, semi-rigid containers of pure polyethylene.

Uses Polyfusor Paediatric Electrolyte Solution is given by intravenous infusion and is an electrolyte replacement solution for use in the treatment of infants, particularly where there is Potassium loss.

Dosage and administration The volume and rate of infusion of Polyfusor Paediatric Electrolyte Solution given intravenously will depend upon the requirements of the infant and the judgement of the physician.

Contra-indications, warnings, etc

Contra-indications: Severe liver damage, since such patients would be unable to convert lactate to bicarbonate; impaired renal or cardiac function.

Polyfusor Paediatric Electrolyte

Concentrations w/v (%)

Energy value in Calories per litre

Approximate ion concentrations in millimoles per litre

Sodium Lactate Molar Solution 1.825
Potassium Phosphate BPC 1949 0.130
Sodium Chloride BP 0.117
Potassium Chloride BP 0.149
Hydrochloric Acid BP 0.042% v/v
Anhydrous Dextrose 5

188 Calories provided by 50 g of
Anhydrous Dextrose

Sodium 38
Potassium 35
Chloride 45
Phosphate 7.5
Bicarbonate (as lactate) 18

Water for Injections BP to 100

Precautions: Because of the high potassium level, this infusion must be given slowly.

Side-effects: Thrombosis of the chosen vein is always a possibility with intravenous infusion.

Treatment of overdose: Discontinue infusion and treat symptomatically.

Pharmaceutical precautions *Recommended storage conditions:* 2°C–25°C. The shelf-life of Polyfusor Paediatric Electrolyte Solution is one-and-a-half years.

To prevent gross contamination of the outside surface of the Polyfusor, the outer envelope in which the Polyfusor is supplied should not be opened or removed until immediately before use.

Note: Immediately before use, the intact outer envelope in which the Polyfusor is supplied should be examined for moisture upon the inside surface; if moisture is observed, the integrity of the enclosed Polyfusor is suspect and it must be discarded. Unused solution remaining in a Polyfusor after use must also be discarded.

Legal category POM.

Package quantities Carton of 10 × 500 ml.

Further information Polyfusor Paediatric Electrolyte Solution is designed to meet the requirements of intravenous electrolyte replacement therapy. Prepared to an exceptionally high standard, the solution is supplied in disposable, semi-rigid containers made from a specially developed neutral plastic free from plasticisers, antioxidants and other additives likely to leach out and contaminate the enclosed solution. The intact wall of the Polyfusor is impervious to micro-organisms and virtually impermeable to water vapour, thus ensuring the stability of the contents for very long periods under normal storage conditions (see Shelf-life). Polyfusor Paediatric Electrolyte Solution is part of the Polyfusor range of solutions for intravenous infusion – a range of solutions which, both in quality and extent, can meet the general and specific requirements of modern intravenous therapy.

Product licence number 0014/5799.

POLYFUSOR* PHOSPHATES INJECTION

Presentation Polyfusor Phosphates Injection is a sterile, pyrogen-free solution of Sodium Phosphate and Potassium Acid Phosphate in Water for Injections prepared to British Pharmacopoeial standards. The solution is enclosed in disposable, semi-rigid containers of pure polyethylene.

<i>Concentrations w/v (%)</i>	<i>Approximate ion concentrations in millimoles per litre</i>
Sodium Phosphate 2.9	Sodium 162
Potassium Acid Phosphate 0.259	Phosphorus 100
	Potassium 19

Uses Polyfusor Phosphates Injection is given by intravenous infusion and is indicated in the treatment of severe hypercalcaemia, particularly that occurring in conjunction with cancer, hyperparathyroidism, hypervitaminosis-D, hyperthyroidism and sarcoidosis.

Dosage and administration The volume of phosphate solution given intravenously will depend upon the

requirements of the patient and the physician. No more than 100 millimoles of phosphorus should be given over 24 hours. The infusion must be given slowly.

Contra-indications, warnings, etc

Contra-indications: Intravenous phosphate therapy should not be used if the serum phosphorus concentration before therapy is raised.

Precautions: The patient must be carefully monitored. Rising blood urea nitrogen, elevation of serum phosphorus persisting more than 24 hours after therapy and normal or low serum calcium levels are among the contraindications to continued phosphate administration. Great caution should be undertaken during phosphate administration to patients with impaired renal function. In such patients 15–30 millimoles of phosphorus can be infused over 24 hours with constant monitoring of serum calcium and phosphorus.

Side-effects: Hypotension, tachycardia, pulmonary oedema, fever, hypocalcaemia and tetany, thrombophlebitis and calcification at infusion site.

Treatment of overdose: Discontinue infusion and give appropriate supportive treatment depending on electrolyte determination.

Recommended storage conditions: 2°C–25°C. The shelf life of Polyfusor Phosphates Injection is three years.

To prevent gross contamination of the outside surface of the Polyfusor, the outer envelope in which the Polyfusor is supplied should not be opened or removed until immediately before use.

Note: Immediately before use, the intact outer envelope in which the Polyfusor is supplied should be examined for moisture upon the inside surface; if moisture is observed, the integrity of the enclosed Polyfusor is suspect and it must be discarded. Unused solution remaining in a Polyfusor after use must also be discarded.

Legal category POM.

Package quantities Carton of 10 × 500 ml.

Further information Polyfusor Phosphates Injection is designed to meet the requirements of intravenous phosphate therapy. Prepared to an exceptionally high standard, the solution is supplied in disposable, semi-rigid containers made from a specially developed neutral plastic free from plasticisers, antioxidants and other additives likely to leach out and contaminate the enclosed solution. The intact wall of the Polyfusor is impervious to micro-organisms and virtually impermeable to water vapour, thus ensuring the stability of the contents for very long periods under normal storage conditions (see Shelf-life). Polyfusor Phosphate Injection is part of the Polyfusor range of solutions for intravenous infusion – a range of solutions which, both in quality and extent, can meet the general and specific requirements of modern intravenous therapy.

Product licence number 0014/0203.

POLYFUSOR* POTASSIUM CHLORIDE AND SODIUM CHLORIDE INJECTION

Presentation Polyfusor solution of Potassium Chloride and Sodium Chloride for intravenous infusion. Potassium Chloride 0.3% w/v and Sodium Chloride 0.9% w/v Injection BP in disposable containers of semi-rigid plastic. Each Polyfusor contains 500 ml of solution

Expressed in millimoles per litre, the electrolyte content of this solution is Sodium 150, Potassium 40 and Chloride 190.

Uses Polyfusor Potassium Chloride and Sodium Chloride Injection is given by intravenous infusion for the replacement of potassium loss.

Dosage and administration The amount of potassium administered by intravenous infusion depends upon the needs of the patient and the judgement of the physician; however, there are certain well-established principles concerned with potassium replacement.

1. The intravenous infusion of potassium solutions should be carried out slowly, i.e. at a rate not exceeding 20 millimoles of potassium per hour.

2. The concentration of potassium solutions given by intravenous infusion should not exceed 40 millimoles of potassium per litre.

3. An adult suffering from severe potassium loss may need up to 80 millimoles of intravenous potassium per day.

4. The administration of potassium (not necessarily by intravenous infusion) should be continued for at least three days after plasma potassium levels have returned to within normal levels.

Contra-indications, warnings, etc

Contra-indications: Addison's disease, adrenal insufficiency, acute or chronic renal disease, oliguria or anuria would preclude the giving of intravenous potassium.

Precautions: Before administering potassium by the intravenous route, it is essential to ensure that renal output is adequate and, by first giving a non-potassium hydrating solution, to ensure an adequate urine flow.

Side-effects: The adverse effects associated with the intravenous infusion of potassium solutions are almost invariably due to hyperkalaemia; these are listlessness, mental confusion, paraesthesia in extremities, weakness in the legs, hypotension, arrhythmias and, sometimes, cardiac arrest. Thrombosis of the selected vein is always a possibility with intravenous infusion.

Treatment of overdosage: Stop the infusion of potassium and, if there is persistent acidosis, replace with an infusion of sodium lactate or bicarbonate. Hyperkalaemia can be treated with an intravenous injection over a period of 145 minutes of Calcium Gluconate Injection BP.

Pharmaceutical precautions *Recommended storage conditions:* 2–25°C. The shelf-life of this product is 8 months.

To prevent gross contamination of the outside surface of the Polyfusor, the outer envelope in which the Polyfusor is supplied should not be opened or removed until immediately before use.

Note: Immediately before use, the intact outer envelope in which the Polyfusor is supplied should be examined for moisture upon its inside surface; if moisture is observed, the integrity of the enclosed Polyfusor is suspect and it must be discarded.

Legal category POM.

Package quantities Cartons of 10 × 500 ml.

Further information Polyfusor Potassium Chloride and Sodium Chloride Injection provides an immediately available source of intravenous potassium which obviates the inconvenient and somewhat hazardous use of

extemporaneously prepared potassium solutions. Other Polyfusor solutions for use in potassium replacement therapy include Potassium Chloride and Dextrose, Darrow's Solution, Hartmann's Solution and Ringer's Solution. These intravenous fluids are part of an extensive range of Polyfusor Solutions for Intravenous Infusion designed to meet almost every requirement in intravenous therapy. Polyfusor solutions are supplied in disposable, semi-rigid containers of a pure polyethylene free from plasticisers, stabilisers or other additives likely to leach out and contaminate the enclosed solution.

Product licence number 0014/5856.

POLYFUSOR* RINGER'S INJECTION

Presentation Polyfusor Ringer's Injection is a sterile, pyrogen free solution of Sodium Chloride, Potassium Chloride and Calcium Chloride in Water for Injections prepared to British Pharmacopoeial standards. The solution is enclosed in disposable, semi-rigid containers of pure polyethylene. The solution contains, in 1 litre, approximately 147 millimoles of sodium ions, 4 millimoles of potassium ions, 2 millimoles of calcium ions and 155 millimoles of chloride ions.

Uses Polyfusor Ringer's Injection is given by intravenous infusion and is used to correct the water and electrolyte depletion associated with dehydration.

Dosage and administration The volume and rate of infusion of Ringer's solution given by intravenous route will depend upon the requirements of the patient and the judgement of the physician.

Contra-indications, warnings, etc

Contra-indications: Intravenous Ringer's solution may be contra-indicated in patients with impaired renal or cardiac functions.

Precautions: Ringer's solution should not be administered rapidly or for prolonged periods. Rapid injection may cause sudden cardiac arrest or circulatory overloading.

Side-effects: Thrombosis of the chosen vein is always a possibility with intravenous infusion.

Treatment of overdosage: Discontinue the infusion. The use of a diuretic may be indicated.

Pharmaceutical precautions *Recommended storage conditions:* 2°C–25°C. The shelf-life of Polyfusor Ringer's Injection is three years.

To prevent gross contamination of the outside surface of the Polyfusor, the outer envelope in which the Polyfusor is supplied should not be opened or removed until immediately before use.

Note: Immediately before use, the intact outer envelope in which the Polyfusor is supplied should be examined for moisture upon the inside surface; if moisture is observed, the integrity of the enclosed Polyfusor is suspect and it must be discarded.

Legal category POM.

Package quantities Carton of 10 × 500 ml.

Further information Polyfusor Ringer's Injection is designed to meet the requirements of intravenous therapy. Prepared to an exceptionally high standard, the solutions are supplied in disposable, semi-rigid containers made from specially developed neutral plastic free from plasticisers, antioxidants and other additives

likely to leach out and contaminate the enclosed solution. The intact wall of the Polyfusor is impervious to micro-organisms and virtually impermeable to water vapour, thus ensuring the stability of the contents for very long periods under normal storage conditions (see shelf-life). Polyfusor Ringer's Injection is part of the Polyfusor range of solutions for intravenous infusion – a range of solutions which, both in quality and extent, can meet the general and specific requirements of modern intravenous therapy.

Product licence number 0014/5253.

POLYFUSOR* SODIUM CHLORIDE INJECTIONS

Presentation Polyfusor Sodium Chloride Injections are sterile, pyrogen-free solutions of Sodium Chloride in Water for Injections prepared to British Pharmacopoeial standards. The solutions are enclosed in disposable, semi-rigid containers of pure polyethylene and are available in the following strengths:

Concentrations of sodium chloride w/w	Approximate ion concentration in millimoles per litre	
	Sodium	Chloride
0.18%	31	31
0.45%	77	77
0.9%	150	150
1.8%	308	308
2.7%	460	460
5.0%	855	855

Uses Polyfusor Sodium Chloride Injections are administered by intravenous infusion and are used mainly as an immediate measure to correct the water and electrolyte depletion associated with dehydration. Hypertonic solutions are used in the treatment of acute sodium deficiency and of water intoxication. Other uses include maintenance saline therapy in secondary dehydration and in haemorrhage, as a means of temporarily increasing blood volume.

Dosage and administration The volume, strength and rate of infusion of saline solutions given by the intravenous route will depend upon the requirements of the patient and the judgement of the physician. The effect of saline therapy on dehydration can often be assessed from relief of symptoms, observation of blood pressure and measurement of the volume and concentration of urine output.

Contra-indications, warnings, etc

Contra-indications: Intravenous saline solutions may be contra-indicated in patients with impaired renal or cardiac function.

Precautions: Saline solutions should not be administered rapidly or for prolonged periods particularly in infants and the elderly. A too rapid injection of hypertonic saline may cause sudden cardiac arrest or circulatory overloading.

Side-effects: Thrombosis of the chosen vein is always a possibility with intravenous infusion.

Treatment of overdosage: An excess of sodium may be removed by the injection of a diuretic.

Pharmaceutical precautions Recommended storage conditions: 2–25°C. The shelf-life of Polyfusor Sodium Chloride Injections is three years.

To prevent gross contamination of the outside surface of the Polyfusor, the outer envelope in which the Polyfusor is supplied should not be opened or removed until immediately before use.

Note: Immediately before use, the intact outer envelope in which the Polyfusor is supplied should be examined for moisture upon the inside surface; if moisture is observed, the integrity of the enclosed Polyfusor is suspect and it must be discarded. Unused solution remaining in a Polyfusor after use must be discarded.

Legal category POM.

Package quantities Carton of 10 × 500 ml. Carton of 10 × 1,000 ml.

Further information Polyfusor Sodium Chloride Injections provide a range of saline solutions designed to meet the many and varied requirements of intravenous saline therapy. Prepared to an exceptionally high standard, the solutions are supplied in disposable, semi-rigid containers made from a specially developed neutral plastic free from plasticisers, antioxidants and other additives likely to leach out and contaminate the enclosed solution. The intact wall of the Polyfusor is impervious to micro-organisms and virtually impermeable to water vapour, thus ensuring the stability of the contents for very long periods under normal storage conditions (see 'Shelf-life'). Polyfusor Sodium Chloride Injections are part of the Polyfusor range of solutions for intravenous infusion – a range of solutions which, both in quality and extent, can meet the general and specific requirements of modern intravenous therapy.

Product licence numbers

0.18%	0014/5394
0.45%	0014/5696
0.9%	0014/5395
1.8%	0014/5738
2.7%	0014/5902
5.0%	0014/5906

POLYFUSOR* SODIUM CHLORIDE AND DEXTROSE INJECTION

Presentation Polyfusor solutions of saline and dextrose are sterile, pyrogen-free solutions of Sodium Chloride and Anhydrous Dextrose in Water for Injection prepared to British Pharmacopoeial standards. The solutions are enclosed in disposable semi-rigid containers of pure polyethylene and are available in the following strengths:

Concentrations of saline and dextrose w/v (%)	Energy value in calories per litre	Approximate ion concentration in millimoles per litre			
		Sodium	Chloride	Anhydrous dextrose in grams per litre	
Sodium chloride 0.18 and dextrose 4	150	30	30	40	
Sodium chloride 0.45 and dextrose 2.5	94	77	77	25	
Sodium chloride 0.45 and dextrose 5	188	77	77	50	
Sodium chloride 0.9 and dextrose 5	188	154	154	50	

Uses Polyfusor Saline and Dextrose Solutions are given by intravenous infusion and are indicated for the treatment of dehydration with carbohydrate loss.

Dosage and administration The volume, strength and rate of infusion of saline and dextrose solutions given by intravenous infusion will depend upon the requirements of the patient and the judgement of the physician.

Contra-indications, warnings, etc

Contra-indications: Intravenous saline and dextrose solutions may be contra-indicated in patients with impaired renal and cardiac function.

Precautions: Saline and dextrose solutions should not be administered rapidly or for prolonged periods – particularly in infants and the elderly.

Side-effects: Thrombosis of the chosen vein is always a possibility with intravenous infusion.

Treatment of overdose: Injection of a diuretic.

Pharmaceutical precautions Recommended storage conditions 2–25°C. The shelf-life of Polyfusor Sodium Chloride and Dextrose Solutions is 18 months. To prevent gross contamination of the outside surface of the Polyfusor, the outer envelope in which the Polyfusor is supplied should not be opened or removed until immediately before use.

Note: Immediately before use, the intact outer envelope in which the Polyfusor is supplied should be examined for moisture upon the inside surface, if moisture is observed, the integrity of the enclosed Polyfusor is suspect and it must be discarded. Unused solution remaining in a Polyfusor after use must also be discarded.

Legal category POM.

Package quantities Carton of 10 × 500 ml. Carton of 10 × 1,000 ml.

Further information Polyfusor Sodium Chloride and Dextrose Solutions are designed to meet the many and varied requirements of intravenous therapy. Prepared to an exceptionally high standard, the solutions are supplied in disposable, semi-rigid containers made from a specially developed neutral plastic free from plasticisers, anti-oxidants and other additives likely to leach out and contaminate the enclosed solution. The intact wall of the Polyfusor is impervious to micro-organisms and virtually impermeable to water vapour, thus ensuring the stability of the contents for very long periods under normal storage conditions (see 'shelf-life'). Polyfusor Sodium Chloride and Dextrose are part of the Polyfusor range of solutions for intravenous infusion – a range of solutions which, both in quality and extent, can meet the general and specific requirements of modern intravenous therapy.

Product licence numbers

Sodium Chloride 0.18% and Dextrose 4%	0014/5252
Sodium Chloride 0.45% and Dextrose 2.5%	0014/5869
Sodium Chloride 0.45% and Dextrose 5%	0014/5251
Sodium Chloride 0.9% and Dextrose 5%	0014/5250

POLYFUSOR[®] SODIUM LACTATE INJECTION

Presentation Polyfusor Sodium Lactate Injection is a sterile, pyrogen-free solution of Sodium Lactate prepared

to British Pharmacopoeial Standards. The solution is enclosed in disposable, semi-rigid containers of pure polyethylene. The injection is one-sixth molar and contains, in 1 litre, approximately 167 millimoles of sodium ions and 167 millimoles of bicarbonate ions (as lactate).

Uses Polyfusor, Sodium Lactate Injection is given by intravenous infusion and is used to treat acidosis and to alkalis the urine.

Dosage and administration The volume and rate of infusion of sodium lactate solution given intravenously will depend upon the requirements of the patient. It should be remembered that the conversion of sodium lactate to bicarbonate in the liver takes one to two hours so that for immediate correction of acidosis an injection of sodium bicarbonate should be given. The rate of infusion should not exceed 300 ml/hour.

Contra-indications, warnings, etc

Contra-indications: Intravenous sodium lactate solutions are contra-indicated in patients with severe liver damage.

Precautions: Sodium lactate solutions should not be administered rapidly or for prolonged periods – particularly in infants and the elderly.

Side-effects: Thrombosis of the chosen vein is always a possibility with intravenous infusion.

Treatment of overdose: Discontinue the infusion and treat symptomatically.

Pharmaceutical precautions Recommended storage conditions: 2°C–25°C. The shelf-life of Polyfusor Sodium Lactate Injection is three years.

To prevent gross contamination of the outside surface of the Polyfusor, the outer envelope in which the Polyfusor is supplied should not be opened or removed until immediately before use.

Note: Immediately before use, the intact outer envelope in which the Polyfusor is supplied should be examined for moisture upon the inside surface; if moisture is observed, the integrity of the enclosed Polyfusor is suspect and it must be discarded. Unused solution remaining in a Polyfusor after use must also be discarded.

Legal category POM.

Package quantities Carton of 10 × 500 ml.

Further information Polyfusor Sodium Lactate Injection is designed to meet the requirements of intravenous sodium lactate therapy. Prepared to an exceptionally high standard, the solution is supplied in disposable, semi-rigid containers made from a specially developed neutral plastic free from plasticisers, anti-oxidants and other additives likely to leach out and contaminate the enclosed solution. The intact wall of the Polyfusor is impervious to micro-organisms and virtually impermeable to water vapour, thus ensuring the stability of the contents for very long periods under normal storage conditions (see shelf-life). Polyfusor Sodium Lactate Injection is part of the Polyfusor range of solutions for intravenous infusion – a range of solutions which, both in quality and extent, can meet the general and specific requirements of modern intravenous therapy.

Product licence number 0014/5248.

PROTHIADEN*

Presentation Prothiaden is Dothiepin Hydrochloride BP, an antidepressant of the tricyclic group.

Prothiaden is available as sugar-coated tablets, each containing 75 mg of Dothiepin Hydrochloride BP. The tablets are red in colour and bear the overprint 'P75' in white. It is also available in hard gelatin capsules, each containing 25 mg of Dothiepin Hydrochloride BP. The capsules are red/brown in colour with the overprint 'P25' in white.

Uses Prothiaden is indicated in the treatment of depression and the anxiety frequently associated with depressive illness.

Dosage and administration Prothiaden should be given in a dosage of 75 to 150 mg daily. The following dosage schemes are suggested:

Mild to moderate depression: 25 mg three times daily or 75 mg at night.

Moderate to severe depression: 150 mg daily in divided doses, or as a single dose at night. (If the latter regimen is adopted, it is preferable to use a smaller dose for the first few days.)

*In certain circumstances, i.e. in hospital use, Prothiaden has been given at dosages up to 225 mg daily.

No dietary restrictions are necessary during treatment with Prothiaden.

Contra-indications, warnings, etc Prothiaden has anticholinergic properties; therefore, it may precipitate urinary retention in susceptible individuals and its use should be avoided in patients with existing or potential urinary retention. Patients with closed-angle glaucoma should not be given Prothiaden and the occurrence of a painful red eye in a patient receiving the drug may indicate acute closed-angle glaucoma; this requires urgent treatment. In patients with chronic simple glaucoma, the risk of Prothiaden causing a rise in intraocular pressure is relatively small provided adequate anti-glaucoma therapy is being used. Caution is advised when treating epileptic patients and those with cardiovascular disorders.

From studies in animals, it was concluded that Prothiaden had no teratogenic effects in the species tested. Nevertheless, as with any relatively new drug, the use of Prothiaden during pregnancy should be avoided if possible.

Use with other drugs: Prothiaden should not be given concurrently with MAO inhibitors; nor should it be given within 14 days of ceasing treatment with an MAO inhibitor. Prothiaden may alter the pharmacological effect of some concurrently administered drugs; CNS depressants, including alcohol and narcotic analgesics, will be potentiated, as will the effects of adrenaline and noradrenaline (it should be borne in mind that some local anaesthetic preparations contain these sympathomimetics). The hypotensive effect of certain antihypertensive agents (e.g. bethanidine, debrisoquine, guanethidine) may be reduced.

Side-effects: Generally, the side-effects associated with Prothiaden have been mild and controlled by reduced dosage. The following have been reported – dryness of mouth, constipation, disturbed accommodation, lassitude, dizziness, orthostatic hypotension, palpitations, somnolence, tremor, headache.

Overdosage: The symptoms of overdosage with Prothiaden may include sedation, dry mouth, blurring of vision,

tachycardia, tremor, sweating, nausea, vomiting, confusion. The main dangers from overdosage arise from unconsciousness, convulsions, abnormal cardiac rhythms, hypotension and depression of respiration. The smallest dose of Prothiaden alone which resulted in the death of an adult was reported to be 0.75–1.0 g. The largest dose from which recovery took place was reported to be 5.0 g. In view of the many factors which influence the outcome of an overdose, these figures should not be considered in isolation.

Treatment of overdosage: Gastric lavage; in the unconscious patient or where the cough reflex is depressed, the lungs should be protected by a cuffed endotracheal tube. Repeated gastric/intestinal aspiration may remove drug and metabolites excreted into the gut via the bile. General support of the circulation with continuous ECG monitoring is advised. Abnormalities of cardiac rhythm and epileptic convulsions may occur and should be treated accordingly. Forced diuresis and haemodialysis are not recommended. Bedrest is advisable, even after clinical recovery.

Pharmaceutical precautions *Recommended storage conditions:* 5°C–20°C.

Legal category POM.

Package quantities *Prothiaden Tablets (75 mg):* 28, 500.

Prothiaden Capsules (25 mg): 100, 600.

Further information Prothiaden exhibits the psychopharmacological properties common to the tricyclic antidepressants. It is used in the treatment of depression and to relieve the anxiety often associated with depressive illness.

Prothiaden is used in a wide variety of depressive states and, in clinical trials, has been shown to be as effective as imipramine and more effective than amitriptyline.

While Prothiaden exhibits the side-effects associated with tricyclic antidepressants, these are usually mild and rarely severe enough to warrant withdrawal of the drug. Adults of all age-groups tolerate Prothiaden well, an important aspect of therapy when treating old people and outpatients.

Because it is so well tolerated, Prothiaden allows a considerable flexibility of regimen with the recommended dosage levels. In certain cases of depression, it has been found that the daily dosage of Prothiaden given as a single night-time dose is more effective and even better tolerated than the conventional divided daytime dosage. There is evidence that the single bed-time dose improves the sleep pattern of the depressed patient.

Because of the anxiolytic effect, the response to Prothiaden in patients suffering from anxiety and depression can often be observed within a few days after starting treatment. The effect of the drug upon the depressive component of the condition usually becomes apparent after seven to ten days.

Product licence numbers

Prothiaden Capsules 0014/5941

Prothiaden Tablets 0014/0209

STABILLIN* V-K ELIXIRS AND TABLETS

Presentation Stabillin V-K Elixirs '62.5', '125' and '250' are preparations of dry granules which, when reconstituted with the specified volume of water, provide elixirs (Phenoxymethylpenicillin Elixir BPC) containing

respectively the phenoxymethylpenicillin potassium equivalent to 62.5, 125 and 250 mg of phenoxymethylpenicillin in each 5 ml.

Stabillin V-K Tablets are Phenoxymethylpenicillin Tablets BP 250 mg.

Uses Stabillin V-K preparations are indicated in the treatment of mild to moderate infections due to susceptible Gram-positive organisms and to prevent the recurrence of rheumatic fever.

Dosage and administration Phenoxymethylpenicillin should be taken 30 minutes before food.

Adult: 0.5 to 1.5 g daily in divided doses.

Children 6 to 12 years: 250 mg every 6 hours.

Children 1 to 5 years: 125 mg every 6 hours.

Children up to 1 year: 62.5 mg every 6 hours.

As a prophylactic: 1 tablet twice daily for adults; adjust dosage for children.

Contra-indications, warnings, etc Stabillin V-K is contra-indicated in patients with a known sensitivity to penicillin and should be given with caution to those with a history of allergy. Phenoxymethylpenicillin is secreted in the milk and should be used with caution in nursing mothers as it may cause an allergic reaction in the offspring.

Side-effects: Penicillins given by mouth sometimes produce transient diarrhoea and, occasionally, nausea, heartburn and pruritus ani.

Treatment of overdose: Treatment is symptomatic, but is unlikely to be required.

Pharmaceutical precautions Stabillin V-K Elixir and the reconstituted Elixir should be stored in a cool place; the latter should be used within one week of preparation.

Legal category POM.

Package quantities

Stabillin V-K Elixirs: Bottle of granules to make 100 ml.

Stabillin V-K Tablets: Bottle of 500.

Further information Nil.

Product licence numbers

Stabillin V-K Elixir '62.5': 0014/5341

Stabillin V-K Elixir '125': 0014/5342

Stabillin V-K Elixir '250': 0014/5343

Stabillin V-K Tablets: 0014/5082

STERIFLEX* No. 1

Presentation Steriflex No. 1 is Sodium Chloride Injection BP and is a sterile, colourless preparation of normal saline for infusion in a clear, collapsible container. Sodium Chloride Injection BP contains 9 g sodium chloride per litre; sodium 150 millimoles per litre; chloride 150 millimoles per litre.

Indications Steriflex No. 1 is used in the treatment of dehydration to correct water and electrolyte depletion. It is useful in the treatment of acute sodium deficiency or water intoxication.

Dosage and administration Intravenous infusions are preferably administered through a needle inserted into a superficial vein. However in obese patients or young children this may prove difficult and then it will be necessary to cut down to the vein and insert a cannula. During intravenous infusion the limb should be immo-

bilised, so there is less discomfort to the patient. If a leg vein is selected this may increase the incidence of thrombotic complications. Transfusion may be conducted under pressure, using the Martin or other suitable rotary pump, or by application of pressure to the Steriflex bag. The rate of administration and volume transfused will depend on the requirements of the individual patient. The correction of dehydration may be judged by relief of symptoms, restoration of blood pressure, reversal of haematoconcentration and the output of an adequate volume of urine of normal concentration.

Contra-indications, warnings, etc

Contra-indications: Patients with sodium overload. It is well known that this may occur with myocardial and renal damage, but it should also be appreciated that in the first five or six days after surgery or severe trauma there may be an inability to excrete unwanted sodium.

Precautions: Steriflex No. 1 is not suitable for protracted use unless there is heavy continued loss of electrolytes; even then, it should be used with care. In potassium-deficient patients administration of normal saline will increase potassium loss, so that if it is given, potassium supplements should also be given.

Side-effects: Thrombosis of the chosen vein is always a possibility with intravenous infusion. If infusion is protracted then another vein should be selected after 12-24 hours.

Treatment of overdose: An excess of sodium may be removed by the injection of a diuretic.

Pharmaceutical precautions **Storage:** Store at 2°C-25°C. The shelf-life is two years. The outer polythene bag is not sterilised but simply serves to protect the steriflex bag. Before use the pack should be inspected and rejected if it is not clear or if the inner container is damaged.

Legal category POM.

Package quantities Steriflex is packed in containers of 10, in volumes of 500 ml and 1,000 ml.

Product licence number 0014/0190.

STERIFLEX* No. 3

Presentation Steriflex No. 3 is a sterile, colourless preparation of Sodium Chloride and Dextrose Injection BP containing 5% of anhydrous dextrose in a clear, collapsible container and is intended for intravenous infusion. It contains 8 g per litre of sodium chloride, which represents 154 millimoles sodium and 154 millimoles chloride.

The anhydrous dextrose in Steriflex No. 3 provides 188 Calories per litre.

Indications Steriflex No. 3 is generally the standard solution for the correction of dehydration. In many conditions it is preferable to Sodium Chloride Injection BP (Steriflex No. 1), since the patient's carbohydrate store may be depleted. It is also of value in Addisonian crises and in dehydration with alkalosis.

Dosage and administration Intravenous infusions are preferably administered through a needle inserted into a superficial vein. However, in obese patients or young children this may prove difficult and then it will be necessary to cut down to the vein and insert a cannula. During intravenous infusion the limb should be immobilised so there is less discomfort to the patient. If a leg

is selected this may increase the incidence of thrombotic complications.

Transfusions may be conducted under pressure, using the Martin or other rotary pump, or by application of pressure to the Steriflex bag.

The rate of administration and volume transfused will depend on the requirements of the individual patient. The correction of dehydration may be judged by relief of symptoms, restoration of blood pressure, reversal of haemoconcentration and the output of an adequate volume of urine of normal concentration. Where acidosis is a feature, correction is indicated by the disappearance of hyperventilation.

Contra-indications, warnings, etc

Contra-indications: Patients with sodium overload. It is well known that this may occur with myocardial and renal damage, but it should also be appreciated that in the first five or six days after surgery or severe trauma there may be an inability to excrete unwanted sodium. Steriflex No. 3 is not suitable for the treatment of insulin coma.

Precautions: Steriflex No. 3 is not suitable for protracted use unless there is a heavy continued loss of electrolytes; even then, it should be used with care. In potassium-deficient patients administration of normal saline solution will increase potassium loss, so that if it is given, potassium should also be given.

Side-effects: Thrombosis of the chosen vein is always a possibility with intravenous infusion. If infusion is protracted then another vein should be selected after 12–24 hours.

Treatment of overdosage: Injection of a diuretic.

Pharmaceutical precautions *Storage:* Store at 2°C–25°C. The shelf-life is two years. The outer polythene bag is not sterilised but simply serves to protect the Steriflex bag. Before use the pack should be inspected and rejected if it is not clear or if the inner container is damaged.

Legal category POM.

Package quantities Steriflex is packed in containers of 10 in volumes of 500 ml and 1,000 ml.

Product licence number 0014/0191.

STERIFLEX* No. 6 STERIFLEX* No. 7

Presentation Steriflex Nos. 6 and 7 are sterile, colourless preparations of dextrose in water and are Dextrose Injection BP 5% and Dextrose Injection BP 10%, respectively. They are in clear, collapsible containers and are intended for intravenous infusion.

Steriflex No. 6 contains 50 g of anhydrous dextrose per litre providing 188 Calories per litre.

Steriflex No. 7 contains 100 g of anhydrous dextrose per litre, providing 375 Calories per litre.

Indications Steriflex No. 6 is an isotonic solution used for maintenance therapy of dehydration after electrolyte depletion has been corrected. It is also useful as a source of water and carbohydrate for patients who have undergone abdominal surgery and who are not able to take oral fluids. It may be used for the treatment of insulin coma. Steriflex No. 7 has the same uses as Steriflex No. 6, but it provides more carbohydrate per litre and it is hypertonic.

Dosage and administration Intravenous infusions are preferably administered through a needle inserted into a superficial vein. However, in obese patients or young children this may prove difficult and then it will be necessary to cut down to the vein and insert a cannula. During intravenous infusion the limb should be immobilised, so there is less discomfort to the patient. If a leg vein is selected this may increase the incidence of thrombotic complications.

Transfusion may be conducted under pressure, using the Martin or other suitable rotary pump, or by application of pressure to the Steriflex bag. The rate of administration and volume transfused will depend on the requirements of the individual patient.

Contra-indications, warnings, etc The administration of these solutions in diabetic patients must be conducted with caution.

Precautions: The infusion of these solutions should not be rapid or very prolonged. Large volumes of these solutions given too quickly may cause water intoxication, infusion over a long period can cause dehydration.

Side-effects: Thrombosis of the chosen vein is always a possibility with intravenous infusion. If infusion is protracted then another vein should be selected after 12–24 hours.

Pharmaceutical precautions *Storage:* Store at 2°C–25°C. The shelf-life is two years. The outer polythene bag is not sterilised but simply serves to protect the Steriflex bag. Before use the pack should be inspected and rejected if it is not clear or if the inner container is damaged.

Legal category POM.

Package quantities Steriflex is packed in containers of 10. Steriflex Nos 6 and 7 are available in volumes of 500 ml and 1,000 ml.

Product licence numbers

No. 6 0014/0193

No. 7 0014/0194

STERIFLEX* No. 9

Presentation Steriflex No. 9 is a sterile, colourless preparation of Ringer's Solution for Injection in clear, collapsible containers. It is intended for intravenous infusion. Each litre contains sodium chloride 8.6 g potassium chloride 0.3 g and calcium chloride 0.48 g, that is sodium 147 millimoles per litre, potassium 4 millimoles per litre, calcium 2 millimoles per litre and chloride 155 millimoles per litre.

Indications Steriflex No. 9 is used as an intravenous infusion when an isotonic solution is needed for the treatment of dehydration with salt depletion and where there has been some loss of intracellular potassium.

Dosage and administration Intravenous infusions are preferably administered through a needle inserted into a superficial vein. However, in obese patients or young children this may prove difficult and then it will be necessary to cut down to the vein and insert a cannula. During intravenous infusion the limb should be immobilised, so there is less discomfort to the patient. If a leg vein is selected this may increase the incidence of thrombotic complications. Transfusion may be conducted under pressure, using the Martin or other suitable rotary pump or by application of pressure to the Steriflex bag. The

rate of administration and volume transfused will depend on the requirements of the individual patient. The correction of dehydration may be judged by relief of symptoms, restoration of blood pressure, reversal of haemoconcentration and the output of an adequate volume of urine of normal concentration. Where acidosis is a feature, correction is indicated by the disappearance of hyperventilation.

Contra-indications, warnings, etc

Contra-indications: Patients with sodium overload. It is well known that this may occur with myocardial and renal damage, but it should also be appreciated that in the first five or six days after surgery or severe trauma there may be an inability to excrete unwanted sodium.

Precautions: Although Steriflex No. 9 contains potassium the quantity may be inadequate in the presence of intracellular potassium loss.

Side-effects: Thrombosis of the chosen vein is always a possibility with intravenous infusion. If infusion is protracted then another vein should be selected after 12–24 hours.

Treatment of overdosage: An excess of sodium may be removed by the injection of a diuretic.

Pharmaceutical precautions *Storage:* Store at 2°C–25°C. The shelf-life is two years. The outer polythene bag is not sterilised but simply serves to protect the Steriflex bag. Before use the pack should be inspected and rejected if it is not clear or if the inner container is damaged.

Legal category POM.

Package quantities Steriflex is packed in containers of 10 in volumes of 500 ml and 1,000 ml.

Product licence number 0014/0195.

STERIFLEX* No. 10

Presentation Steriflex No. 10 is a sterile, colourless preparation of Darrow's solution in a clear, collapsible container. It can be administered intravenously. Each litre of Steriflex No. 10 contains sodium chloride 4 g, potassium chloride 2.7 g, molar solution of sodium lactate 52.3 ml. The millimole concentrations per litre are sodium 121, potassium 35, chloride 103 bicarbonate (as lactate) 53.

Indications Metabolic acidosis with potassium deficiency. In cases of dehydration and shock there may be deficiency of intracellular potassium in the presence of normal or high serum potassium values. If dehydration is corrected without potassium supplementation hypokalaemia may occur.

Darrow's solution is frequently employed where acidosis is due to fluid loss from the alimentary tract, e.g. diarrhoea or excessive vomiting, or due to diabetic coma.

Dosage and administration Steriflex No. 10 should be used with caution. As with all solutions containing potassium, administration should be by slow intravenous infusion. Where there is established potassium depletion 3 litres per 24 hours will be required for adults. In infants and children a total of 80 ml per kg per 24 hours is a guide to maximum dosage.

Contra-indications, warnings, etc

Contra-indications: Potassium-containing solutions should not usually be given intravenously to correct

potassium depletion if potassium can be given by the oral route. Steriflex No. 10 should not be given to patients with cardiac arrhythmias.

Precautions: Particular care should be taken with patients who have oliguria or who have a plasma-sodium level below 120 millimoles per litre.

Side-effects: Untoward effects are likely to be due to hyperkalaemia and the first signs of this are shown in the electrocardiograph with the T wave becoming high and peaked. With increasing hyperkalaemia there is prolonged duration of the PR interval, leading to conduction defects, arrhythmias and possible cardiac arrest. Other symptoms include listlessness and mental confusion, numbness and tingling of the extremities, weakness of the legs, hypotension and, particularly in oliguric patients, an ascending flaccid paralysis.

Treatment of overdosage: When signs of hyperkalaemia are observed the infusion should be stopped and if acidosis persists replaced with a sodium bicarbonate or sodium lactate infusion. Hyperkalaemia may be treated by intravenous injection of 10 ml of calcium gluconate 10% solution with 50 ml or 50% dextrose solution and 10 units of soluble insulin.

Pharmaceutical precautions *Storage:* Store at 2°C–25°C. The shelf-life is two years. The outer polythene bag is not sterilised but simply serves to protect the Steriflex bag. Before use the bag should be inspected and rejected if it is not clear or if the inner container is damaged.

Legal category POM.

Package quantities Steriflex is packed in containers of 10, in volumes of 500 ml and 1,000 ml.

Product licence number 0014/0196.

STERIFLEX* No. 11

Presentation Steriflex No. 11 is a sterile, colourless preparation of Compound Sodium Lactate Injection BP in a clear, collapsible container. It is also known as Hartmann's Solution for Injection and as Ringer-Lactate Solution for Injection. It can be administered intravenously. Each litre of Steriflex No. 11 contains sodium chloride 6.0 g potassium chloride 0.4 g, calcium chloride 0.27 g, sodium lactate equivalent to 2.4 ml lactic acid. The millimole concentrations per litre are sodium 131, potassium 5, calcium 2, chloride 111, and bicarbonate (as lactate) 29.

Indications Steriflex No. 11 is indicated for the treatment of metabolic acidosis and dehydration with acidosis. It may be used to expand extracellular fluids or restore extracellular electrolyte in practically all patients.

The treatment of diabetic coma.

Dosage and administration Intravenous infusions are preferably administered through a needle inserted into a superficial vein. However, in obese patients or young children this may prove difficult and then it will be necessary to cut down to the vein and insert a cannula. During intravenous infusion the limb should be immobilised so there is less discomfort to the patient. If a leg vein is selected this may increase the incidence of thrombotic complications. Transfusion may be conducted under pressure, using the Martin or other suitable rotary pump, or by application of pressure to the Steriflex

bag. The rate of administration and volume transfused will depend on the requirements of the individual patient.

Contra-indications, warnings, etc

Contra-indications: Patients with sodium overload. It is well known that this may occur with myocardial and renal damage, but it should also be appreciated that in the first five or six days after surgery or severe trauma there may be an inability to excrete unwanted sodium.

Lactate-containing solutions are contra-indicated in patients with liver diseases.

Precautions: Although Steriflex No. 11 provides potassium this is only enough to maintain the potassium content of extracellular fluid and would be quite inadequate for patients with severe potassium loss. Under these circumstances potassium supplements must be given. Lactate overdose in patients with heart disease may provoke arrhythmias and heart failure. ECG monitoring is recommended if administering Steriflex No. 11 to such patients.

Side-effects: Thrombosis of the chosen vein is always a possibility with intravenous infusion. If infusion is protracted then another vein should be selected after 12–24 hours.

Treatment of overdose: Where facilities exist for control of water and electrolyte balance overdose should not occur. In less than ideal situations accidental over-administration can be treated with intravenous injection of a diuretic.

Pharmaceutical precautions *Storage:* Store at 2°C–25°C. The shelf-life is two years. The outer polythene bag is not sterilised but simply serves to protect the Steriflex bag. Before use the pack should be inspected and rejected if it is not clear or if the inner container is damaged.

Legal category POM.

Package quantities Steriflex is packed in containers of 10, in volumes of 500 ml and 1,000 ml.

Product licence number 0014/0197.

STERIFLEX* No. 18

Presentation Steriflex No. 18 is Sodium Chloride and Dextrose Injection BP, a sterile, colourless preparation of sodium chloride 0.18% and anhydrous dextrose 4.0% in a clear, collapsible container. Each litre of Steriflex No. 18 contains sodium chloride 1.8 g and anhydrous dextrose 40 g. In each litre there are 30 millimoles of sodium, 30 millimoles of chloride and 150 calories.

Indications Steriflex No. 18 is probably the most generally used isotonic solution for maintenance intravenous fluid replacement. It can be employed for maintenance therapy. It can be used for the treatment of moderate-prolonged dehydration due to water-loss, but in severe cases 1 or 2 litres of Steriflex No. 1 (Sodium Chloride Injection BP) should be given before continuing with Steriflex No. 18.

Dosage and administration Intravenous infusions are preferably administered through a needle inserted into a superficial vein. However, in obese patients or young children this may prove difficult and then it will be necessary to cut down to the vein and insert a cannula. During intravenous infusion the limb should be immobilised, so there is less discomfort to the patient. If a leg vein is selected this may increase the incidence of

thrombotic complications. Transfusion may be conducted under pressure, using the Martin or other suitable rotary pump, or by application of pressure to the Steriflex bag. The rate of administration and volume transfused will depend on the requirement of the individual patient.

Contra-indications, warnings, etc

Contra-indications: Patients with sodium overload. It is well known that this may occur with myocardial and renal damage, but it should also be appreciated that in the first five or six days after surgery or severe trauma there may be an inability to excrete unwanted sodium.

Precautions: In patients with potassium deficiency it may be necessary to add potassium supplements.

It should not be used as initial therapy for patients in diabetic coma.

Side-effects: Thrombosis of the chosen vein is always a possibility with intravenous infusion. If infusion is protracted then another vein should be selected after 12–24 hours.

Treatment of overdose: Injection of a diuretic.

Pharmaceutical precautions *Storage:* Store at 2°C–25°C. The shelf-life is two years. The outer polythene bag is not sterilised but simply serves to protect the Steriflex bag. Before use the pack should be inspected and rejected if it is not clear or if the inner container is damaged.

Legal category POM.

Package quantities Steriflex is packed in containers of 10, in volumes of 500 ml and 1,000 ml.

Product licence number 0014/0192.

STERIFLEX* No. 20

STERIFLEX* No. 21

STERIFLEX* No. 22

Presentation Steriflex No. 20 is Laevulose Injection BP 10%, Steriflex No. 21 is Laevulose Injection BP 20% and Steriflex No. 22 is Laevulose Injection BP 40%. These are sterile, colourless solutions of laevulose in water, available in clear, collapsible containers.

Steriflex No. 20 contains laevulose 100 g per litre.

Steriflex No. 21 contains laevulose 200 g per litre.

Steriflex No. 22 contains laevulose 400 g per litre.

Steriflex Nos. 20, 21 and 22 are available in volumes of 500 ml only.

Indications Laevulose is a carbohydrate which can be utilised or converted into glycogen in the absence of insulin. It is indicated for conditions associated with carbohydrate deficiency. In acute alcohol poisoning laevulose injection accelerates the metabolism of alcohol.

Neonatal hypoglycaemia can be prevented in the neonates of diabetic mothers by intravenous infusion of 250–500 mg per kilo of laevulose to the mother two to three hours before delivery and then administration of Steriflex No. 20 through the infant's umbilical vein to a total dosage of 1 g laevulose per kg of body weight, two to three hours after delivery.

Dosage and administration The dosage and choice of the concentration of laevulose solution will depend on the condition and needs of the patient. All infusions should be slow and not exceed 800 mg per kilo body weight laevulose per hour.

Intravenous infusions are preferably administered

through a needle inserted into a superficial vein. However, in obese patients or young children this may prove difficult and then it will be necessary to cut down to the vein and insert a cannula. During intravenous infusion the limb should be immobilised, so there is less discomfort to the patient. If a leg vein is selected this may increase the incidence of thrombotic complications. The rate of administration and volume transfused will depend on the requirements of the individual patient.

Contra-indications, warnings, etc

Contra-indications: Laevulose injection should not be given to patients known to be intolerant of laevulose, or to patients with methyl alcohol poisoning as it enhances the oxidation of methyl alcohol to formaldehyde.

Laevulose injections should not be administered to patients in shock, with severe hepatic or renal disease or uncontrolled diabetes mellitus.

Precautions: Rapid injection of laevulose injection can cause thrombotic complications.

Side-effects: Thrombosis of the chosen vein is always a possibility with intravenous infusion. Reported side-

effects of large doses include facial flushing, epigastric pain and sweating.

Treatment of overdosage: Treatment consists of withdrawal of the infusion.

Pharmaceutical precautions *Storage:* Store at 2°C–25°C. The shelf-life is two years. The outer polythene bag is not sterilised but simply serves to protect the Steriflex bag. Before use the pack should be inspected and rejected if it is not clear or if the inner container is damaged.

Legal category POM.

Package quantities Steriflex is packed in containers of 10 in volumes of 500 ml.

Product licence numbers

No. 20 0014/0187

No. 21 0014/0188

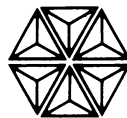
No. 22 0014/0189

* *Trade Mark*

Bristol-Myers Pharmaceuticals

Division of Bristol-Myers Company Limited

Langley Slough SL3 6EB



ALPHA KERI* BATH OIL ▼

Presentation Alpha Keri Bath Oil is a clear colourless water dispersible anti-pruritic bath additive.

The product contains the following active ingredients: mineral oil (91.7%) and lanolin oil (3.0%).

Uses Alpha Keri effectively deposits a thin uniform emulsified film of oil over the skin, and thus retards evaporation of moisture, helps to relieve itching, lubricates and softens the skin.

Alpha Keri is valuable as an aid in the management of dry pruritic skin, especially in senile pruritis, ichthyosis and other dermatoses where dermal hydration is an important part of the therapy (as in the prevention of decubitus ulcer).

Alpha Keri Bath Oil is particularly suitable for infant bathing. The preparation also overcomes the problem of cleansing the skin in conditions where the use of soaps, soap substitutes and colloid or oat-meal baths prove irritating.

Dosage and administration Alpha Keri should always be either added to water or rubbed onto wet skin.

Because of its inherent cleansing properties it is not necessary to use soap with Alpha Keri.

Bath: Add 1–2 capfuls to the bath water. Soak for 10–20 minutes.

Sponge bath: Add 1–2 capfuls to a basin of warm water. Apply over entire body with a sponge or flannel.

Infant bath: Add $\frac{1}{2}$ capful to bath water.

Skin cleansing: Rub a small amount onto wet skin, rinse and pat dry.

Shower: Pour a small amount onto a wet sponge or flannel and rub onto wet skin, rinse and pat dry.

Alpha Keri may also be used in Whirlpools or Hubbard tanks, add 30 ml to every 450 litres of water.

Contra-indications, warnings, etc As Alpha Keri deposits a film of oil over the skin, special care should be taken to guard against slipping, especially in the bath or shower.

Alpha Keri contains lanolin oil and is therefore contra-indicated in those patients allergic to this ingredient.

Pharmaceutical precautions Nil.

Expiry date: 3 years from date of manufacture.

Legal category P.

Package quantities Alpha Keri Bath Oil is available in bottles containing 240 ml.

Further information Nil.

Product licence number 0125/0141.

AMIKIN*

Presentation *Amikin Injection:* Each multidose vial contains in 2 ml, amikacin sulphate equivalent to ami-

kacin activity 500 mg (500,000 international units). The vial contains methyl and propyl paraben.

Amikin Paediatric Injection: Each ampoule contains in 2 ml, amikacin sulphate equivalent to amikacin activity 100 mg (100,000 international units). The ampoule contains no preservatives.

Uses AMIKIN is a semi-synthetic, aminoglycoside antibiotic which is active against a broad spectrum of Gram-negative organisms, including pseudomonas and some Gram-positive organisms.

Sensitive Gram-negative organisms include: pseudomonas spp., *Escherichia coli*, indole-positive and indole-negative proteus spp., klebsiella-enterobacter-serratia spp., *Citrobacter freundii*, salmonella, shigella, mima-herellea and providencia spp.

Many strains of these Gram-negative organisms resistant to gentamicin and tobramycin show sensitivity to Amikin *in vitro*.

The principal Gram-positive organism sensitive to Amikin is *Staphylococcus aureus*, including methicillin-resistant strains. Amikin has some activity against other Gram-positive organisms including *Streptococcus pyogenes*, *Diplococcus pneumoniae*, and certain strains of enterococci.

Amikin is indicated in the short-term treatment of serious infections due to susceptible strains of Gram-negative bacteria, including pseudomonas species. Although Amikin is not the drug of choice for infections due to staphylococci, at times it may be indicated for the treatment of known or suspected staphylococcal disease. These situations include: the initiation of therapy for severe infections when the organisms suspected are either Gram-negative or staphylococcal, patients allergic to other antibiotics, and mixed staphylococcal/Gram-negative infections.

Therapy with Amikin may be instituted prior to obtaining the results of sensitivity testing.

Surgical procedures should be performed where indicated.

Dosage and administration At the recommended dosage level, uncomplicated infections due to sensitive organisms should respond to therapy within 24 to 48 hours.

If clinical response does not occur within three to five days, consideration should be given to alternative therapy.

Intramuscular or intravenous administration: For most infections the intramuscular route is preferred, but in life-threatening infections, or in patients in whom intramuscular injection is not feasible, the intravenous route, either slow bolus (two to three minutes) or infusion (30 minutes) may be used.

If required, suitable diluents for intravenous use are: normal saline, 5% dextrose in water, lactated Ringer's injection and lactated Ringer's injection with 5% dex-

trose. Once the product has been diluted the solution must be used as soon as possible and NOT STORED.

Adults and Children: 15 mg/kg/day in two equally divided doses (equivalent to 500 mg b.i.d. in adults):

Use of the 100 mg/2 ml strength is recommended for children for the accurate measurement of the appropriate dose.

Neonates and Premature Infants: An initial loading dose of 10 mg/kg followed by 15 mg/kg/day in two equally divided doses.

Sufficient extensive clinical use has not been achieved to enable firm dosage guidelines to be given in premature infants.

Life-threatening infections and/or those caused by pseudomonas: The adult dose may be increased to 500 mg every eight hours but should neither exceed 1.5 g/day nor be administered for a period longer than 10 days. A maximum total adult dose of 15 g should not be exceeded.

Urinary tract infections: (other than pseudomonal infections): 7.5 mg/kg/day in two equally divided doses (equivalent to 250 mg b.i.d. in adults). As the activity of amikacin is enhanced by increasing the pH, a urinary alkalising agent may be administered concurrently.

Impaired renal function: In patients with impaired renal function, the daily dose should be reduced and/or the intervals between doses increased to avoid accumulation of the drug. A suggested method for estimating dosage in patients with known or suspected diminished renal function is to multiply the serum creatinine concentration (in mg/100 ml) by 9 and to use the resulting figure as the interval in hours between doses.

Serum Creatinine Concentration (mg/100 ml)		Interval between Amikin doses of 7.5 mg/kg/IM (hours)
1.5	} X9=	13.5
2.0		18
2.5		22.5
3.0		27
3.5		31.5
4.0		36
4.5		40.5
5.0		45
5.5		49.5
6.0		54

As renal function may alter appreciably during therapy, the serum creatinine should be checked frequently and the dosage regimen modified as necessary.

Intraperitoneal use: Following exploration for established peritonitis, or after peritoneal contamination due to faecal spill during surgery, Amikin may be used as an irrigant after recovery from anaesthesia in concentrations of 0.25% (2.5 mg/ml). It may also be instilled into the wound at closure. If instillation is desired in adults, a single dose of 500 mg is diluted in 20 ml of sterile distilled water and may be instilled through a polyethylene catheter sutured into the wound at closure. If possible, instillation should be postponed until the patient has fully recovered from the effects of anaesthesia and muscle-relaxing drugs.

Other routes of administration: Amikin in concentrations of 0.25% (2.5 mg/ml) may be used satisfactorily as an

irrigating solution in abscess cavities, the pleural space, the peritoneum and the cerebral ventricles.

Only the paediatric dosage form (which contains no preservatives) should be used for intraventricular administration.

Contra-indications, warnings, etc Patients should be well hydrated during Amikin therapy.

In patients with impaired renal function or diminished glomerular filtration, Amikin should be used cautiously. In such patients, renal function should be assessed by the usual methods prior to therapy and periodically during therapy. Daily doses should be reduced and/or the interval between doses lengthened in accordance with serum creatinine concentrations to avoid accumulation of abnormally high blood levels and to minimise the risk of ototoxicity.

If therapy is expected to last seven days or more in patients with renal impairment, or 10 days in other patients, a pre-treatment audiogram should be obtained and repeated during therapy. Amikin therapy should be stopped if tinnitus or subjective hearing loss develops, or if follow-up audiograms show significant loss of high-frequency response.

As with other aminoglycosides, ototoxicity and/or nephrotoxicity can result from the use of Amikin; precautions on dosage and adequate hydration should be observed.

If signs of renal irritation appear (such as albumin, casts, red or white blood cells), hydration should be increased and a reduction in dosage may be desirable. These findings usually disappear when treatment is completed. However, if azotaemia or a progressive decrease in urine output occurs, treatment should be stopped.

The use of Amikin in patients with a history of allergy to aminoglycosides or in patients who may have subclinical renal or eighth nerve damage induced by prior administration of nephrotoxic and/or ototoxic agents such as streptomycin, dihydrostreptomycin, gentamicin, tobramycin, kanamycin, bekanamycin, neomycin, polymyxin B, colistin, cephaloridine, or viomycin should be considered with caution, as toxicity may be additive. In these patients Amikin should be used only if, in the opinion of the physician, therapeutic advantages outweigh the potential risks.

The risk of ototoxicity is increased when Amikin is used in conjunction with rapidly acting diuretic drugs, particularly when the diuretic is administered intravenously. Such agents include frusemide and ethacrynic acid, which is itself an ototoxic agent. Irreversible deafness may result.

The intraperitoneal use of Amikin is not recommended in young children or in patients under the influence of anaesthetics or muscle-relaxing drugs (including ether, halothane, d-tubocurarine, succinylcholine and decamethonium) as neuromuscular blockade and consequent respiratory depression may occur.

Pregnancy: The safety of Amikin in pregnancy has not yet been established.

Side-effects: When the recommended precautions and dosages are followed the incidence of toxic reactions, such as tinnitus, vertigo, and partial reversible or irreversible deafness, skin rash, drug fever, headache, paraesthesia, nausea and vomiting is low. Urinary signs of renal irritation (albumin, casts, and red or white cells), azotaemia and oliguria have been reported.

Pharmaceutical precautions At times, Amikin may

be indicated as concurrent therapy with other antibacterial agents in mixed or superinfections. In such instances, Amikin should not be physically mixed with other antibacterial agents in syringes, infusion bottles or any other equipment. Each agent should be administered separately.

AMIKIN, as supplied, is stable at 25°C for a period of three years. At times, the solution may darken from colourless to a pale yellow but this does not indicate a loss in potency.

Expiry Date: 36 months from date of manufacture.

Legal category POM.

Package quantities *Amikin Injection:* 2 ml vials packed in cartons of 5.

Amikin Paediatric Injection: 2 ml ampoules packed in cartons of 5.

Further information Amikin is rapidly absorbed after intramuscular injection. Peak serum levels of approximately 11 mcg/ml and 23 mcg/ml are reached one hour after i.m. doses of 250 mg and 500 mg respectively. Levels 10 hours after injection are of the order of 0.3 mcg/ml and 2.1 mcg/ml respectively.

Twenty per cent or less is bound to serum protein and serum concentrations remain in the bactericidal range for sensitive organisms for 10 to 12 hours.

Amikin diffuses readily through extracellular fluids and is excreted in the urine unchanged, primarily by glomerular filtration. Half-life in individuals with normal renal functions is two to three hours.

Following intramuscular administration of a 250 mg dose, about 65% is excreted in six hours and 91% within 24 hours. The urinary concentrations average 563 mcg/ml in the first six hours and 163 mcg/ml over 6 to 12 hours. Mean urine concentrations after a 500 mg i.m. dose average 832 mcg/ml in the first six hours.

Single doses of 500 mg administered to normal adults as an intravenous infusion over a period of 30 minutes produce a mean peak serum concentration of 38 mcg/ml at the end of the infusion. Repeated infusions do not produce drug accumulation.

Amikin has been found in cerebrospinal fluid, pleural fluid, amniotic fluid and in the peritoneal cavity following parenteral administration.

Product licence numbers

Paediatric Injection 100 mg/2 ml 0125/0087
Injection 500 mg/2 ml 0125/0092

BiCNU* ▼

Presentation *BiCNU Injection:* each package contains a 30 ml vial containing 100 mg carmustine and a 5 ml vial containing 3 ml sterile ethanol diluent.

Uses BiCNU is indicated as palliative therapy as a single agent or in established combination therapy with other approved chemotherapeutic agents in the following:

1. Brain tumours – Glioblastoma, brainstem glioma, medulloblastoma, astrocytoma, ependymoma, and metastatic brain tumours.
2. Multiple myeloma – In combination with prednisone.
3. Hodgkin's Disease – As secondary therapy in combination with other approved drugs in patients who relapse while being treated with primary therapy, or who fail to respond to primary therapy.

4. Non-Hodgkin's lymphomas – As secondary therapy in combination with other approved drugs in patients who relapse while being treated with primary therapy, or who fail to respond to primary therapy.

5. BiCNU has also been used in the palliative management of other cancers such as malignant melanoma.

Dosage and administration

Intravenous administration: The recommended dose of BiCNU as single agent in previously untreated patients is 200 mg/m² intravenously every six weeks. This may be given as a single dose or divided into daily injections such as 100 mg/m² on two successive days.

When BiCNU is used in combination with other myelosuppressive drugs or in patients in whom bone marrow reserve is depleted the doses should be adjusted accordingly.

A repeat course of BiCNU should not be given until circulating blood elements have returned to acceptable levels (platelets above 100,000/mm³; leucocytes above 4,000/mm³) and this is usually in six weeks. Blood counts should be monitored frequently and repeat courses should not be given before six weeks because of delayed toxicity.

Doses subsequent to the initial dose should be adjusted according to the haematological response of the patient to the preceding dose. The following schedule is suggested as a guide to dosage adjustment.

<i>Nadir after Prior Dose</i>		<i>Percentage of prior dose to be given</i>
<i>Leucocytes (/mm³)</i>	<i>Platelets (/mm³)</i>	
> 4000	> 100,000	100
3000–3999	75,000–99,999	100
2000–2999	25,000–74,999	70
< 2000	< 25,000	50

Contra-indications, warnings, etc BiCNU should not be given to individuals who have demonstrated a previous hypersensitivity to it.

BiCNU should not be given to individuals with decreased circulating platelets, leucocytes, or erythrocytes either from previous chemotherapy or other causes.

BiCNU should not normally be administered to patients who are pregnant or mothers who are breast-feeding.

Safe use in pregnancy has not been established and therefore the benefit to risk of toxicity must be carefully weighed. BiCNU is embryotoxic and teratogenic in rats and embryotoxic in rabbits at dose levels equivalent to the human dose. BiCNU also affects fertility in male rats at doses somewhat higher than the human dose.

BiCNU is carcinogenic in rats and mice, producing a marked increase in tumour incidence in doses approximating those employed clinically.

BiCNU should be administered by individuals experienced in antineoplastic therapy. Since delayed bone marrow toxicity is the major toxicity, complete blood counts should be monitored frequently for at least six weeks after a dose. Repeat doses of BiCNU should not be given more frequently than every six weeks. The bone marrow toxicity of BiCNU is cumulative and therefore dosage adjustment must be considered on the basis of nadir blood counts from prior dose (see Dosage Adjustment Table under Dosage).

It is recommended that liver function tests also be monitored.

Adverse reactions: Haematological: The most frequent and most serious toxicity of BiCNU is delayed myelosuppression. It usually occurs four to six weeks after drug administration and is dose-related. Platelet nadirs occur at four to five weeks; leucocyte nadirs occur at five to six weeks post therapy. Thrombocytopenia is generally more severe than leucopenia. However both may be dose limiting toxicities. Anaemia also occurs, but is generally less severe.

Gastro-intestinal: Nausea and vomiting after i.v. administration of BiCNU are noted frequently. This reaction appears within two hours of dosing, usually lasting four to six hours and is dose-related. Prior administration of anti-emetics is effective in diminishing and sometimes preventing this side-effect.

Hepatic: When high doses of BiCNU have been employed, a reversible type of hepatic toxicity, manifested by increased transaminase, alkaline phosphatase and bilirubin levels, has been reported in a small percentage of patients.

Local: Burning at the site of injection is common but true thrombosis is rare.

Other: Rapid i.v. infusion of BiCNU may produce intense flushing of the skin and suffusion of the conjunctiva within two hours, lasting about four hours.

Pharmaceutical precautions *Preparation of intravenous solution:* Dissolve BiCNU with 3 ml of the supplied sterile diluent (absolute ethanol) and then aseptically add 27 ml of sterile water for injection to the alcohol solution. Each ml of the resulting solution will contain 3.3 mg of BiCNU in 10% ethanol and has a pH of 5.6 to 6.0.

Reconstitution as recommended results in a clear colourless solution which may be further diluted with sodium chloride for injection, or 5% dextrose for injection.

The reconstituted solution must be given intravenously and should be administered by i.v. drip over a one- to two-hour period. Injection of BiCNU over shorter periods of time may produce intense pain and burning at the site of injection.

Important note: The lyophilised dosage formulation contains no preservatives and is not intended as a multiple dose vial.

Stability: Unopened vials of the dry powder must be stored in a refrigerator (2°C–8°C). The recommended storage of unopened vials prevents significant decomposition for at least two years.

After reconstitution as recommended, decomposition of BiCNU at room temperature is linear with time. After three hours, approximately 6% of the solution has decomposed and after six hours, approximately 8%. Refrigeration (4°C) of the reconstituted BiCNU significantly increases the stability of the solution. After 24 hours, when protected from light, there is only 4% decomposition. Further dilution of the reconstituted solution with 500 ml of sodium chloride for injection or 5% dextrose for injection, results in a solution which is stable for 48 hours when protected from light and refrigerated.

Important note: BiCNU has a low melting point (approximately 27°C or 80.6°F). Exposure of the drug to this temperature or above will cause the drug to liquefy and appear as an oil film in the bottom of the vials. This is a sign of decomposition and vials should be discarded.

Legal category POM.

Package quantities BiCNU Injection packed in cartons of 10 units, each unit consisting of one vial of carmustine 100 mg and one vial of sterile absolute alcohol 3 ml.

Further information BiCNU alkylates DNA and RNA and has also been shown to inhibit several enzymes by carbamoylation of amino acids in proteins.

Intravenously administered BiCNU is rapidly degraded, with no intact drug detectable after 15 minutes. However, in studies with C¹⁴ labelled drug, prolonged levels of the isotope were observed in the plasma and tissue, probably representing radioactive fragments of the parent compound.

It is thought that the antineoplastic and toxic activities of BiCNU may be due to metabolites. Approximately 60 to 70% of a total dose is excreted in the urine in 96 hours and about 10% as respiratory CO₂. The fate of the remainder is undetermined.

Because of the high lipid solubility and the relative lack of ionisation at a physiological pH, BiCNU crosses the blood brain barrier.

Levels of radioactivity in the CSF are at least 50% higher than those measured concurrently in plasma.

Product licence number 0125/0108.

CeeNU* ▼

Presentation Blue-blue capsules printed BRISTOL 3030, containing 10 mg lomustine.

Blue-green capsules printed BRISTOL 3031, containing 40 mg lomustine.

Green-green capsules printed BRISTOL 3032, containing 100 mg lomustine.

Uses CeeNU is indicated as adjuvant therapy to surgery and radiotherapy or in combination with other chemotherapeutic agents in the following:

1. Brain tumours – Both primary and metastatic, in patients who have already undergone appropriate surgical procedures.

2. Lung cancer – Squamous cell, anaplastic large cell and adenocarcinoma. CeeNU has been used alone and in combination with appropriate antineoplastic drugs such as cyclophosphamide.

3. Malignant melanoma – Alone or in combination with other active drugs such as vincristine.

4. Hodgkin's Disease – Alone or in combination with other active drugs.

CeeNU has been used in renal cell carcinoma, although the response rate is low in this resistant cancer. Responses have also been observed with non-Hodgkin's lymphoma, ovarian and pancreatic carcinoma, but data are insufficient to make a definite recommendation.

Dosage and administration The recommended dose of CeeNU is 130 mg/m² as a single dose by mouth every six weeks.

In individuals with compromised bone marrow function, because of either disease or prior therapy, the dose should be reduced to 100 mg/m² every six weeks. A repeat course of CeeNU may be given when circulating blood elements have returned to acceptable levels (platelets above 100,000/mm³; leucocytes above 4,000/mm³) and this is usually in six weeks. Blood counts should be monitored frequently and repeat

courses should not be given before six weeks as haematological toxicity is delayed and cumulative.

Doses subsequent to the initial dose should be adjusted according to the haematological response of the patient to the preceding dose. The following schedule is suggested as a guide to dosage adjustment.

Nadir after Prior Dose		Percentage of prior dose to be given
Leucocytes (/mm ³)	Platelets (/mm ³)	
> 4,000	> 100,000	100
3,000-3999	75,000-99,999	100
2,000-2,999	25,000-74,999	70
< 2,000	< 25,000	50

When CeeNU is used in combination with myelosuppressive drugs, doses should be adjusted accordingly. It is recommended that liver and renal function be monitored frequently as well as blood counts.

Contra-indications, warnings, etc

Contra-indications: CeeNU should not be given to individuals who have demonstrated a previous hypersensitivity to it.

Warnings: CeeNU should be given with caution to individuals with depressed circulating platelets, leucocytes or erythrocytes.

Safe use in pregnancy has not been established. CeeNU is embryotoxic and teratogenic in rats and embryotoxic in rabbits at dose levels equivalent to the human dose. CeeNU also affects fertility in male rats at doses somewhat higher than the human dose. CeeNU is carcinogenic in rats and mice, producing a marked increase in tumour incidence in doses approximating to those employed clinically.

CeeNU should not normally be administered to patients who are pregnant or mothers who are breastfeeding.

Precautions: Since the major toxicity is delayed bone marrow suppression, blood counts should be monitored weekly for at least six weeks after a dose. At the recommended dosage, courses of CeeNU should not be given more frequently than every six weeks.

Adverse reactions: Haematological: Thrombocytopenia occurs at about four weeks after a dose of CeeNU and persists for one to two weeks.

Leucopenia occurs about six weeks after a dose of CeeNU and persists for one to two weeks.

CeeNU may produce cumulative myelosuppression, manifested by more depressed indices or longer duration of suppression after repeated doses.

Anaemia has been reported infrequently.

Gastro-intestinal: Nausea and vomiting may occur three to six hours after an oral dose and usually last less than 24 hours. The frequency and duration may be reduced by use of anti-emetics prior to dosing and by the administration of CeeNU to fasting patients.

Other toxicities: Stomatitis, alopecia and hepatic toxicity (manifested by transient reversible elevation of liver function tests) have been reported infrequently.

Neurological reactions such as disorientation, lethargy, ataxia and dysarthria have been noted in some patients receiving CeeNU.

Overdosage: In the case of overdosage, the patient should be treated symptomatically.

Pharmaceutical precautions Correct dosage may require the administration of more than one strength of capsule. The patient should be advised of the necessity of this to enhance compliance. CeeNU capsules should be stored at room temperature in a well closed container.

Expiry date: Three years from date of manufacture.

Legal category POM.

Package quantities CeeNU capsules are available in three strengths: 10 mg, 40 mg and 100 mg, each of which are supplied in screw-capped bottles containing 20 capsules.

Further information It is generally agreed that CeeNU acts as an alkylating agent, but as with other nitrosoureas, it may also inhibit several key enzymatic processes.

Following oral administration of radioactive CeeNU at doses ranging from 30 mg to 100 mg, about half the dosed radioactivity is excreted within 24 hours. The serum half-life of the drug and/or metabolites ranges from 16 hours to two days. Tissue levels are comparable to plasma levels at 15 minutes after intravenous administration.

Because of high lipid solubility and relative lack of ionisation at physiological pH, CeeNU crosses the blood brain barrier and radioactivity levels in the CSF are 50% or greater than those measured concurrently in plasma.

Product licence numbers

10 mg capsules 0125/0102

40 mg capsules 0125/0103

100 mg capsules 0125/0104

DEFENCIN CP*

Presentation Hard gelatin capsules (No. 4), having a pale pink cap and red body. Each capsule is coded Defencin VS40 and contains the equivalent of 40 mg isoxsuprine, in graded release form.

Uses Cerebral vascular disease including cerebral arteriosclerosis, cerebral vasospasm, and cerebral ischaemia.

Peripheral vascular disease including peripheral arteriosclerosis, Buerger's disease, Raynaud's disease and peripheral vasospasm.

Dosage and administration **Adults:** 1 capsule every 12 hours.

Children: The product is not intended for administration to children.

Contra-indications, warnings, etc Recent arterial bleeding or immediately post-partum.

Defencin is extremely well tolerated and side-effects are rare. Occasional hypotension, tachycardia, flushing or palpitations have been reported with preparations of isoxsuprine, but these are controlled by a reduction in dose.

Pharmaceutical precautions To be stored in a cool dry place, at temperatures generally not exceeding 20°C, protected from light.

Expiry date – 36 months from date of manufacture.

Legal category P.

Package quantities Blister strip of 14 capsules with 4 strips to a carton.

Further information Isoxsuprine (Defencin) is a myovascular relaxant which acts directly on vascular smooth muscle.

Product licence number 0125/0074.

KANTREX® CAPSULES

Presentation Yellow capsules containing kanamycin sulphate BP equivalent to kanamycin activity 250 mg.

Uses Kantrex is indicated in the treatment of the following, when due to sensitive organisms: Infections of the gastro-intestinal tract including Sonne dysentery and infectious diarrhoeas. Pre-operative bowel sterilisation. Elimination of carrier states. Adjunctive in the treatment of hepatic coma.

Dosage and administration *Adults: Intestinal infections:* 1–2 g per day in 4 divided doses for five to seven days.

Pre-operative bowel sterilisation: 1 g every hour for four hours followed by 1 g every six hours for 36–72 hours. The duration of therapy depends on the condition of the patient and the amount of concurrent mechanical cleansing.

Hepatic coma: 8–12 g per day in divided doses.

Children: Dosage appropriately reduced according to age and weight.

Contra-indications, warnings, etc The oral administration of Kantrex is remarkably free from side-effects. Overgrowth of yeasts is much less common than with neomycin. If superinfection occurs appropriate therapy should be instituted and the administration of Kantrex discontinued if necessary.

Although negligible amounts of kanamycin are absorbed through intact intestinal mucosa, the possibility of increased absorption from ulcerated or denuded areas should be considered.

Pharmaceutical precautions Expiry date – 48 months from date of manufacture.

There are no special directions for storage.

Legal category POM.

Package quantities Containers of 100 capsules.

Further information Kantrex (kanamycin sulphate) is a broad-spectrum antibiotic with a wide bactericidal action against pathogenic inhabitants of the gastro-intestinal tract.

When administered orally kanamycin is poorly absorbed from the gastro-intestinal tract. After oral administration of 6 g daily the serum activity is less than 2 mcg/ml.

Product licence number 0125/5002.

KANTREX® INJECTION

(For Single Dose Use Only.)

Presentation Kantrex Injection 1.0 g contains in 3 ml; kanamycin sulphate equivalent to kanamycin activity 1.0 g (1,000,000 international units).

Uses Kantrex is indicated in the treatment of the following infections due to susceptible organisms.

Respiratory tract infections (including tuberculosis). Genito-urinary tract infections (including gonorrhoea). Skin and soft-tissue infections. Bone and joint infections. Meningitis. Septicaemia and bacteraemia. Peritonitis. Post surgical infections.

Dosage and administration General recommendations:

Intramuscular route: For adults: 1 g administered daily in divided doses of 0.5 g every twelve hours or 0.25 g every six hours (15 mg/kg per day). The daily dose should not exceed 1.5 g even for heavier patients.

For children under 50 kg: 15 mg/kg per day in 2 divided doses every 12 hours. For premature infants weighing less than 2.5 kg, the recommended dose is 7.5–10 mg/kg per day.

Gonorrhoea: A single dose of 2.0 g is a most effective regimen.

Tuberculosis: 1–2 g should be given two or three times a week. Treatment may be prolonged for up to three or four months. In these cases a careful watch should be maintained against the possibility of ototoxicity developing.

Intravenous route: Only recommended when the intramuscular route is not feasible.

Adults and children: 15 mg per kg per day in 2 divided doses diluted with sterile, pyrogen-free, normal saline or 5% dextrose in water (or normal saline) by slow intravenous infusion (60–80 drops per minute). The preferred concentration of Kantrex for intravenous use is 0.25% (2.5 mg/ml).

Intraperitoneal route (following exploration for established peritonitis or after peritoneal contamination due to faecal spill during surgery):

Adults: 0.5 g Kantrex in 20 ml water for injection into the peritoneal cavity through a polyethylene catheter sutured into the wound at closure.

(It is generally recommended that instillation of Kantrex should be postponed until the patient has recovered from the effects of anaesthesia if muscle-relaxing drugs have been used.)

Aerosol treatment: 250 mg two to four times a day. Withdraw 0.75 ml from a 1 g vial, and dilute with 3.25 ml normal saline and nebulise. A bronchodilator and mucolytic can be included in the aerosol procedure.

Other routes of administration: Kantrex in concentrations of 0.25% has been used satisfactorily as an irrigating solution in abscess cavities, pleural spaces, peritoneal and ventricular cavities. Although solutions of 0.25% or less have been administered intrathecally (up to 25 mg in 10 ml during 24 hours) the intramuscular administration of 7.5 mg/kg Kantrex in infants with bacterial meningitis has produced peak mean CSF levels of 9 mcg/ml. This was approximately twice the concentration produced in normal infants and exceeds the MIC of many pathogenic organisms.

In patients with renal disease and impaired renal function, the daily dosage should be reduced in accordance with the serum creatinine concentration. A suitable dosage scheme is outlined below:

Serum creatinine concentration		Interval between Kanamycin doses of 7.5 mg/kg/IM (hours)
(mmol/litre)	(mg/100 ml)	
140	1.5	13½
180	2.0	18
230	2.5	22½
270	3.0	27
320	3.5	31½
360	4.0	36
410	4.5	40½
450	5.0	45
500	5.5	49½
550	6.0	54

This formula is based on two facts which have been demonstrated.

1. The half-life of Kantrex, in hours, is approximately three times the mg/100 ml serum creatinine concentration.

2. Dosage intervals of every third half-life, using a recommended intramuscular dose of Kantrex, will provide adequate antimicrobial levels and minimise risk of toxic drug accumulation.

Consequently, the appropriate Kantrex dosage interval in hours can be estimated by multiplying the serum creatinine in mg/100 ml by 9 or by dividing its value in mmol/litre by 10 as shown in the diagram above.

This method of adjusting the dose enables the serum concentration to be maintained at the correct non-toxic level despite impaired renal function and is an important measure in preventing side-effects.

Contra-indications, warnings, etc Patients should be well hydrated during kanamycin therapy.

In patients with renal disease and impaired renal function, the daily dosage should be reduced in accordance with the serum creatinine concentration.

Kanamycin therapy should be stopped if tinnitus, a sensation of fullness of the ears or subjective hearing loss develops, or if follow-up audiograms show significant loss of high-frequency response.

Use of antibiotics may occasionally result in overgrowth of non-sensitive organisms. If superinfection does appear, treatment should be discontinued and appropriate therapy instituted.

The incidence of side-reactions to kanamycin is low. In well-hydrated patients under 45 years of age with normal kidney function receiving the recommended dosage, the risk of ototoxic reactions is negligible. In cases of impaired kidney function where excretion of the drug may be affected, adjusting the dose in accordance with the creatinine clearance level will minimise any accumulation of kanamycin and reduce the risk of ototoxic reactions. However, older patients and patients receiving a total dose of more than 20 g of kanamycin should be carefully observed for signs of eighth-nerve involvement.

Urinary signs of renal irritation (casts, white or red cells and albumin) may appear, particularly in toxic, poorly hydrated patients. Where the renal function is not impaired, however, and there is no evidence of nitrogen retention, these signs are reversible and are not indications for stopping therapy.

Skin eruptions during therapy have rarely been noted and their relationship to Kantrex has not been established.

Liver, haematopoietic or cardiovascular toxicity has not been observed.

Pharmaceutical precautions Kantrex Injection retains its potency for at least three years from date of manufacture. No refrigeration or special storage facilities are necessary. Slight discoloration of the solution may occasionally be noticed. This discoloration does not affect the potency, tolerance or therapeutic effectiveness of the product.

Diluents – Sterile Normal Saline or 5% dextrose in water (or normal saline).

Kantrex should not be physically mixed with other antimicrobial agents.

Expiry date – 36 months from date of manufacture.

For single dose use only.

Legal category POM.

Package quantities Kantrex is supplied in rubber-capped vials as a ready-to-use sterile aqueous solution.

Kantrex 1.0 g (1,000,000 international units) in 3 ml.

Further information Nil.

Product licence number

Kantrex 1.0 g 0125/5004.

NEOPLATIN* ▼

Presentation *Neoplatin injection*: Vials containing 10 mg and 50 mg cisplatin (cis-diamminedichloroplatinum).

Uses Neoplatin is indicated as palliative therapy to be employed in addition to other modalities, or in established combination therapy with other approved chemotherapeutic agents in the management of neoplastic diseases, especially:

Metastatic Testicular Tumours – In patients who have already received appropriate surgical and/or radiotherapeutic procedures. The combination of Neoplatin, bleomycin and vinblastine has been reported to be highly effective. Other combinations have also been reported to be active.

Metastatic Ovarian Tumours – As secondary therapy in patients refractory to standard chemotherapy.

Dosage and administration

Single agent therapy: The recommended dose of Neoplatin in adults and children is 50–120 mg/m² as a single i.v. dose every three to four weeks, or 15–20 mg/m² i.v. daily for five days every three to four weeks.

Combination therapy: In general, current multiple drug treatment schedules including Neoplatin employ lower doses ranging from 20 mg/m² upwards, administered i.v. every three to four weeks.

Pretreatment hydration with 1–2 litres of fluid infused for 8–12 hours prior to a Neoplatin dose is recommended in order to initiate diuresis.

Reconstitute the 10 mg vial contents with 10 ml, and the 50 mg vial contents with 50 ml of Sterile Water for Injection PhEur. The resulting drug solution is then administered in 2 litres of a suitable diluent such as 0.9% saline, or a dextrose-saline solution. It is recommended that administration should be over a six–eight hour period. Diuresis may be aided by the addition to the infusion solution of 37.5 g mannitol.

Adequate hydration and urinary output must be maintained during the 24 hours following infusion.

A repeat course of Neoplatin should not be given until the serum creatinine is below 1.5 mg/100 ml (130 µmol/l) and/or the blood urea below 55 mg/100 ml (9 mmol/l). A repeat course should not be given until circulating blood elements are at an acceptable level. Subsequent doses of Neoplatin should not be given until an audiometric analysis indicates that auditory acuity is within normal limits.

Contra-indications, warnings, etc Neoplatin induces nephrotoxicity, myelosuppression, neurotoxicity and ototoxicity which may be additive to pre-existing dysfunctions. Consequently, the use of Neoplatin in patients with hearing or renal impairment or depressed bone marrow function may be associated with increased toxicities. Such conditions represent relative contra-indications.

Neoplatin is contra-indicated in patients with a history of hypersensitivity to Neoplatin or other platinum-containing compounds.

Warnings: Neoplatin produces cumulative nephrotoxicity. The serum creatinine, BUN or creatinine clearance should be measured prior to initiating therapy, and prior to each subsequent course.

Anaphylactic-like reactions to Neoplatin have been reported. These reactions have occurred within minutes of administration to patients with prior exposure to Neoplatin and have been alleviated by administration of adrenaline, steroids and antihistamines.

Safe use in pregnancy has not been established. This product should not normally be administered to patients who are pregnant or to mothers who are breast-feeding. Neoplatin is mutagenic in bacteria and produces chromosome aberrations in animal cells in tissue culture. Although carcinogenicity and teratogenicity have not been established, compounds with similar mechanisms of action and mutagenicity have been reported to be carcinogenic.

The influence of Neoplatin on human reproduction has not been determined. Neoplatin therapy might have an anti-fertility effect.

Precautions: Neoplatin should be administered by individuals experienced in the use of antineoplastic therapy.

Neurotoxicity appears to be cumulative. Prior to each course, the absence of symptoms of peripheral neuropathy should be established. (See Adverse Reactions.)

Since renal toxicity is cumulative, measurements of BUN, serum creatinine or creatinine clearance should be performed prior to initiating therapy and prior to each subsequent course. At the recommended dosage, Neoplatin should not be given more frequently than once every three to four weeks. (See Adverse Reactions.)

Since ototoxicity of Neoplatin is cumulative, audiometric testing should be performed prior to initiating therapy and prior to each subsequent course of the drug. (See Adverse Reactions.)

Peripheral blood counts should be monitored weekly. Liver function should be monitored periodically. Neurological examination should also be performed regularly. (See Adverse Reactions.)

Adverse reactions: Nephrotoxicity: Renal toxicity has been noted in about one third of patients given a single dose of Neoplatin when prior hydration has not been employed. It is first noted during the second week after dose and is manifested by elevations in BUN and serum creatinine, serum uric acid and/or a decrease in creatinine clearance.

Renal toxicity becomes more prolonged and severe

with repeated courses of the drug. Renal function must return to normal before another dose of Neoplatin can be given.

Renal function impairment has been associated with renal tubular damage. The administration of Neoplatin using a six to eight hour infusion with intravenous hydration and mannitol has been used to reduce nephrotoxicity. However, renal toxicity still can occur after utilisation of these procedures.

Neurotoxicity: Neurotoxicity, usually characterised by peripheral neuropathies, has occurred in some patients. Loss of taste and seizures have also been reported. Neuropathies resulting from Neoplatin treatment may occur after prolonged therapy (four to seven months); however, neurological symptoms have been reported to occur after a single dose.

Neoplatin therapy should be discontinued when the symptoms are first observed. Preliminary evidence suggests peripheral neuropathy may be irreversible in some patients.

Ototoxicity: Ototoxicity has been observed in patients treated with a single dose of Neoplatin, 50 mg/m², and is manifested by tinnitus and/or hearing loss in the high frequency range (4,000 to 8,000 Hz).

Decreased ability to hear normal conversational tones may occur occasionally. Ototoxic effects may be more severe in children receiving Neoplatin. Hearing loss can be unilateral or bilateral and tends to become more frequent and severe with repeated doses. It is unclear whether Neoplatin-induced ototoxicity is reversible. Careful monitoring by audiometry should be performed prior to initiation of therapy and prior to subsequent doses of Neoplatin.

Haematological: Myelosuppression may occur in patients treated with Neoplatin. The nadirs in circulating platelets and leucocytes occur between days 18 to 23 (range 7.5 to 45) with most patients recovering by day 39 (range 13 to 62). Leucopenia and thrombocytopenia are more pronounced at higher doses. Anaemia (decrease in haemoglobin level by 2 g/100 ml blood) occurs at approximately the same frequency and with the same timing as leucopenia and thrombocytopenia.

Gastro-intestinal: Marked nausea and vomiting occur in almost all patients treated with Neoplatin and are occasionally so severe that the drug must be discontinued. Nausea and vomiting usually begin within one to four hours after treatment and last up to 24 hours. Various degrees of nausea and anorexia may persist for up to one week after treatment.

Other toxicities: Hyperuricaemia: Hyperuricaemia has been reported to occur at approximately the same frequency as the increases in BUN and serum creatinine. It is more pronounced after doses greater than 50 mg/m², and peak levels of uric acid generally occur between three to five days after the dose. Allopurinol therapy for hyperuricaemia effectively reduces uric acid levels.

Anaphylactic-like reactions: Anaphylactic-like reactions, possibly secondary to Neoplatin therapy, have been occasionally reported in patients previously exposed to Neoplatin. The reactions consist of facial oedema, wheezing, tachycardia and hypotension within a few minutes of drug administration. All reactions may be controlled by intravenous adrenaline, corticosteroids or antihistamines. Patients receiving Neoplatin should be observed carefully for possible anaphylactic-like reactions and supportive equipment and medication should be available to treat such a complication.

Other toxicities reported to occur infrequently are cardiac abnormalities, anorexia and elevated SGOT.

Pharmaceutical precautions Neoplatin injection should be stored at room temperature.

Expiry date: 36 months from date of manufacture.

Preparation of intravenous solution: Reconstitute the 10 mg vial contents with 10 ml, and the 50 mg vial contents with 50 ml of Sterile Water for Injection PhEur. The resulting drug solution is then administered in 2 litres of a suitable diluent, such as 0.9% saline, or a dextrose-saline solution. It is recommended that administration should be over a six to eight hour period. Diuresis may be aided by the addition to the infusion solution of 37.5 g mannitol.

The reconstituted solution should be protected from light, kept at room temperature and is stable for 20 hours. Refrigeration will result in precipitation.

Legal category POM.

Package quantities Neoplatin injection is packed in cartons of 10 vials, each vial containing 10 mg or 50 mg lyophilised cisplatin.

Further information Cisplatin has biochemical properties similar to that of bifunctional alkylating agents producing inter-strand and intra-strand crosslinks in DNA. It is apparently cell-cycle non-specific. Following a single i.v. dose, cisplatin concentrates in liver, kidneys, and large and small intestines in animals and humans. Cisplatin apparently has poor penetration into the CNS.

Plasma levels of radioactivity decay in a biphasic manner after an i.v. bolus dose of radioactive cisplatin to patients. The initial plasma half-life is 25 to 49 minutes, and the post-distribution plasma half-life is 58 to 73 hours. During the post-distribution phase, greater than 90% of the radioactivity in the blood is protein-bound. Cisplatin is excreted primarily in the urine. However, urinary excretion is incomplete with only 27 to 43% of the radioactivity being excreted within the first five days post-dose in human beings. There are insufficient data to determine whether biliary or intestinal excretion occurs.

Product licence number 0125/0109.

PENTREXYL* CAPSULES

Presentation Pentrexyl Capsules (Ampicillin Capsules BP): Grey and scarlet capsules containing 250 mg or 500 mg (overprinted BRISTOL/BRISTOL) ampicillin as ampicillin trihydrate BP.

Uses Pentrexyl is a broad-spectrum antibiotic indicated for the treatment of infections due to susceptible Gram-positive organisms including streptococci, pneumococci, penicillin G sensitive staphylococci and enterococci and susceptible strains of Gram-negative bacteria including *H. influenzae*, *E. coli*, *Proteus mirabilis*, *N. gonorrhoeae*, *N. meningitidis*, *Shigellae*, *S. typhi* and other *Salmonellae*.

Typical indications include: ear, nose and throat infections, bronchitis, pneumonia, urinary tract infections, gonorrhoea, gynaecological infections, septicaemia, peritonitis, endocarditis, meningitis, enteric fever, gastro-intestinal infections.

Dosage and administration To ensure maximum

absorption Pentrexyl should be administered orally at least one hour before or after meals.

Usual adult dose: Ear, nose and throat infections: 250 mg four times a day.

Bronchitis: routine therapy – 250 mg four times a day; high dosage therapy – 1 g four times a day.

Pneumonia: 500 mg four times a day.

Urinary tract infections: 500 mg three times a day.

Gonorrhoea: 3.5 g orally with 1 g probenecid as a single dose. Repeated doses are recommended for the treatment of females.

Gastro-intestinal infections: 500–750 mg three to four times daily.

Enteric: acute – 1–2 g four times a day for two weeks; carriers – 1–2 g four times a day for four to twelve weeks.

Usual children's dose (under 10 years): Half adult dose.

All recommended dosages are given as a guide only and such dosages may be increased in severe infections. A minimum of 10 days' treatment is recommended for any infection caused by Group A Beta-Haemolytic Streptococci to help prevent the occurrence of acute rheumatic fever or acute glomerulonephritis.

Contra-indications, warnings, etc

Contra-indication: A history of hypersensitivity to any of the penicillins.

Side-effects: As with other penicillins side-effects are rare and usually of a mild, transient nature. It may be expected that untoward reactions will be essentially limited to the sensitivity phenomena. Side-effects are more likely to occur in individuals who have previously demonstrated hypersensitivity to penicillins and in those with a history of allergy, asthma, hay fever or urticaria. Rashes of two types have been recorded – an urticarial rash, which is usually indicative of true penicillin hypersensitivity, and an erythematous rash which is generally specific to ampicillin. The incidence of the latter is particularly high in patients with infectious mononucleosis. In such cases therapy should be discontinued.

Pharmaceutical precautions Pentrexyl should be stored in a cool, dry place. Expiry Date – 36 months from date of manufacture.

Legal category POM.

Package quantities *Pentrexyl 250 mg:* Containers of 500 capsules.

Pentrexyl 500 mg: Containers of 100 capsules.

Further information Nil.

Product licence numbers

Pentrexyl Capsules 250 mg 0125/0080

Pentrexyl Capsules 500 mg 0125/0081

QUESTRAN*

Presentation Questran sachets containing 9 g of orange-flavoured powder. Each sachet supplies 4 g of anhydrous cholestyramine (a basic anion-exchange resin).

Uses Questran is used for:

1. Reduction of plasma cholesterol in hypercholesterolaemia, particularly in those patients who have been diagnosed as Fredrickson's Type II (high plasma cholesterol with normal or slightly elevated triglycerides).

2. Relief of diarrhoea associated with ileal resection

Crohn's disease, vagotomy and diabetic vagal neuropathy.

3. Relief of pruritus associated with partial biliary obstruction.

4. Management of radiation-induced diarrhoea.

Dosage and administration *Adults:* As a precautionary measure, where concurrent drug therapy exists then such drugs should be administered 30 minutes to 1 hour before Questran.

1. To reduce cholesterol: After initial introduction, 3 to 6 Questran sachets per day, administered either as a single daily dose or in divided doses up to four times daily according to dosage requirement and patient acceptability. Dosage may be modified according to response and can be increased to 9 sachets per day if necessary.

2. To relieve diarrhoea: as for reduction of cholesterol, but it may be possible to reduce this dosage.

3. To relieve pruritus: 1 or 2 sachets daily are usually sufficient. Questran may be administered mixed with water, skimmed milk, fruit juice, soups, pulpy fruit, etc.

Children 6–12 years: The initial dose is determined by the following formula:

$$\text{child's weight in lb} \times \text{adult dose}$$

$$150$$

Subsequent dosage adjustment may be necessary.

Infants and children under 6 years: The dose has not been established.

Contra-indications, warnings, etc Questran is contra-indicated in patients with complete biliary obstruction, since Questran cannot be effective where bile is not secreted into the intestine.

Because it sequesters bile acids, Questran may interfere with normal fat absorption and prevent absorption of fat-soluble vitamins such as A, D and K. If Questran is to be administered in high dosage for a prolonged period, fat-soluble vitamins should be given daily in a water-miscible form, or, if preferred, administered parenterally.

Gastro-intestinal side-effects are those most frequently reported. The principal complaint is constipation, which may be controlled with the usual remedies, and frequently disappears on continued usage of Questran.

The use of Questran in pregnancy or lactation or by women of childbearing age requires that the potential benefits of drug therapy be weighed against the possible hazards to the mother and child. The safe use of Questran by pregnant women has not been established.

Pharmaceutical precautions Questran should not be taken in its dry form. The powder should be prepared immediately prior to administration.

There are no special directions for storage.

Expiry Date – 48 months from date of manufacture.

Legal category POM.

Package quantities Questran is available in cartons containing 40 sachets.

Further information The correlation between high blood cholesterol levels and ischaemic heart conditions has prompted the dietary control of patients who have shown signs or symptoms of coronary artery disease. With Questran it is possible to reduce cholesterol levels without recourse to excessively stringent dietary measures or systemically absorbed drugs.

Questran (cholestyramine) is a basic anion-exchange resin. It is not absorbed in the gut and its affinity for bile acids in the intestinal tract prevents their reabsorption. To compensate for the faecal loss of bile acids, their major precursor, cholesterol, is oxidised at an increased rate in the liver and plasma cholesterol levels are thus lowered.

Product licence number 0125/5009.

SOTACOR*

Presentation *Sotacor tablets:* Sotacor 80 mg tablets – pink, circular, tablets, engraved 'SOTACOR 80' on one face, each tablet containing 80 mg sotalol hydrochloride.

Sotacor 160 mg tablets – blue, circular, tablets, engraved 'SOTACOR 160' on one face, each containing 160 mg sotalol hydrochloride.

Sotacor injection: Ampoules containing sotalol hydrochloride 10 mg in each 5 ml of solution.

Uses Sotacor, the hydrochloride of 4-(2-isopropylamino-1-hydroxyethyl)-methanesulphonanilide, is a synthetic beta-adrenergic receptor blocking agent. Sotacor exerts a significant antihypertensive effect and additionally protects the heart from undesirable sympathetic drive. It is devoid of intrinsic sympathomimetic and local anaesthetic activity.

1. *Hypertension:* Sotacor produces smooth and gradual reduction of blood pressure on a long-term basis.

2. *Angina pectoris:* Sotacor reduces the frequency and severity of anginal attacks and increases exercise tolerance.

3. *Thyrotoxicosis:* Sotacor relieves the effect of adrenergic over-activity.

4. *Cardiac arrhythmias:* Sotacor tablets may be used prophylactically and as maintenance therapy in the management of cardiac arrhythmias. Sotacor Injection is used in the management of acute cardiac arrhythmias, especially following myocardial infarction, to restore normal rate and rhythm.

Dosage and administration When administering beta-blocking drugs to previously untreated patients it is desirable to start with a low dose and gradually increase the dose until optimum response has occurred. It is usually undesirable to reduce the heart rate below 55 beats per minute.

Sotacor Tablets: Sotacor may be administered daily in either single or divided doses.

Children: Sotacor is not intended for administration to children.

Adults: 1. *Hypertension:* Initial daily dose should be one 160 mg tablet. The majority of mild to moderate hypertensives will respond to one tablet daily and be adequately controlled at this level.

2. *Angina pectoris:* Initial daily dose should be one 160 mg tablet. The majority of anginal patients will be controlled at this dosage level.

N.B. A gradual transfer of therapy over a two-week period is recommended in patients receiving other anti-anginal therapy.

3. *Thyrotoxicosis:* Initial daily dose should be one 160 mg tablet.

4. *Arrhythmia:* In the management of cardiac arrhythmia.

mias, as prophylaxis or maintenance therapy, Sotacor dosage will normally be between 160 mg and 240 mg daily.

N.B. In all these indications dosage may be increased by increments of up to 160 mg per day – the rapidity with which this dosage increase takes place depends upon the patient's tolerance, particularly as measured by the degree of induced bradycardia and the clinical response.

Sotacor Injection should be administered slowly in doses of 20–60 mg intravenously over two to three minutes. Larger doses, up to 100 mg should be injected over three minutes or longer. Continuous ECG monitoring is recommended. Should repeated administrations be necessary, a 10-minute interval between injections is advised, remembering that additive effect and prolongation of effect may ensue.

Contra-indications, warnings, etc Sotacor should not be used where there is evidence of heart block; metabolic acidosis; history of bronchospasm; diabetic ketoacidosis. Beta-blockade may precipitate heart failure in subjects with poor cardiac reserve or may aggravate existing heart failure. Patients whose heart failure is well controlled with digitalis and diuretics may be given Sotacor.

Treated diabetes: Sotacor, like other beta-blocking drugs, may reduce or mask pre-hypoglycaemic warning signs.

Anaesthesia: It is not necessary to discontinue Sotacor prior to most forms of elective surgery, although there is some doubt as to whether beta-receptor blockers should be continued up to the time of surgery involving cardiopulmonary bypass. However, as with other beta-blockers, sudden withdrawal of Sotacor Tablets or Injection might expose the patient to severe angina, arrhythmias, and even myocardial infarction.

If the drug is to be discontinued prior to surgery, especially in patients with ischaemic heart disease, then the drug should be withdrawn over a period of one week. It is usual to discontinue Sotacor Injection 24 to 48 hours prior to elective surgery.

In the presence of Sotacor, anaesthesia may proceed provided that vagal dominance is counteracted by an intravenous injection of atropine sulphate (0.5–2 mg) immediately prior to induction of anaesthesia. Some anaesthetic agents such as ether, cyclopropane, trichloroethylene, methoxyflurane and enflurane appear to cause impairment of myocardial contractility in the presence of beta-receptor blockade. Caution is advised in the use of these agents in patients receiving Sotacor. No evidence of serious interaction has been found between nitrous oxide, halothane or isoflurane and beta-receptor blockers. Raised pCO_2 levels should be avoided in patients receiving Sotacor.

Pregnancy: Notice should be taken of current views on the undesirability of administering drugs during pregnancy. Animal studies with sotalol hydrochloride have shown no evidence of teratogenicity or other harmful effects on the fetus.

Side-effects: There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when the treatment was withdrawn. Discontinuance of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-adrenergic blocker should be gradual.

Sotacor tablets: At the recommended dosage side effects are uncommon. However, minor side effects such as bradycardia, nausea, insomnia, lassitude and diarrhoea have been reported. These are usually transient and can be avoided by gradual introduction of treatment and usually remit on reduction of dosage.

Sotacor Injection is usually well tolerated. Side effects due to beta-blockade, manifested as bradycardia and hypotension, should be treated, if necessary, as for overdosage.

Overdosage: In the rare event of profound cardiovascular effects such as excessive bradycardia or hypotension, atropine sulphate, 0.5–2 mg intravenously, should be administered. It may also be necessary to administer isoprenaline 5 mcg per minute, up to 25 mcg, by slow intravenous injection in order to reverse beta-receptor blockade.

Pharmaceutical precautions Sotacor Tablets should be protected from light.

Expiry Date:

Sotacor 80 mg	36 months	from	date of
	manufacture.		
Sotacor 160 mg	36 months	from	date of
	manufacture.		
Sotacor Injection	36 months	from	date of
	manufacture.		

Legal category POM.

Package quantities *Sotacor 80 mg tablets:* Units of 100 and 300.

Sotacor 160 mg tablets: Units of 28 – blister strips of 14 tablets with 2 strips to a carton.

Sotacor Injection is supplied as 10 mg sotalol hydrochloride in 5 ml ampoules, with 5 ampoules per box.

Further information The maximum dose of Sotacor is usually 320 mg daily. Where improved control of hypertension is required the addition of a diuretic will often give a more satisfactory response.

Product licence numbers

Sotacor 80 mg tablets	0125/0076
Sotacor 160 mg tablets	0125/0093
Sotacor Injection	0125/0078

SOTAZIDE*

Presentation *Sotazide tablets:* Pale blue, capsule-shaped, concave, upper bisected tablets containing 160 mg sotalol hydrochloride and 25 mg hydrochlorothiazide.

Uses In the management of mild or moderate hypertension. The combination product may be suitable for use when satisfactory control of arterial blood pressure cannot be obtained with either a diuretic or a beta-adrenoreceptor blocking drug used alone.

Dosage and administration *Initial dose:* One Sotazide tablet daily increasing to two if necessary.

The individual optimal dosage and the rapidity with which dosage increase occurs should be determined from blood pressure and pulse rate readings and by the degree of induced bradycardia.

Following a reduction in blood pressure the dosage should not be increased until the new blood pressure is stable.

A slight reduction in dosage will alleviate symptoms of

weakness and dizziness if blood pressure continues to fall after a month or two on the maintenance dose.

Contra-indications, warnings, etc

Contra-indications: Sotazide should not be used where there is evidence of heart block; history of bronchospasm; diabetic keto-acidosis; impending or uncontrolled cardiac failure; anaesthesia that produces myocardial depression; hypersensitivity to sotalol, hydrochlorothiazide or sulphonamide derivatives.

Since thiazides appear in breast milk, patients should stop nursing if the use of Sotazide is essential.

Warnings: *Pregnancy:* In animal studies Sotazide has been shown to have no adverse teratogenic effects in doses up to 25 times the recommended human dose. However, its safe use in human pregnancy has not been fully established.

Treated diabetes: Hypoglycaemic therapy may have to be altered in diabetics; Sotazide may potentiate the insulin hypoglycaemic effects and mask the symptoms of hypoglycaemia.

Hepatic/renal disease: Sotazide should be used with caution in patients with impaired hepatic function, liver disease or severe renal disease, since they are particularly sensitive to alterations of fluid and electrolyte balance. Thiazides may precipitate azotaemia. Cumulative effects of the hydrochlorothiazide may develop in patients with impaired renal function.

Anaesthesia: It is not necessary to discontinue Sotazide prior to most forms of elective surgery, although there is some doubt as to whether beta-receptor blockers should be continued up to the time of surgery involving cardiopulmonary bypass. However, sudden withdrawal of Sotazide might expose the patient to severe angina, arrhythmias, and even myocardial infarction.

If the drug is to be discontinued prior to surgery, especially in patients with ischaemic heart disease, then the drug should be withdrawn over a period of one week.

In the presence of Sotazide, anaesthesia may proceed provided that vagal dominance is counteracted by an intravenous injection of atropine sulphate (0.5–2 mg) immediately prior to induction of anaesthesia. Some anaesthetic agents such as ether, cyclopropane, trichloroethylene, methoxyflurane and enflurane appear to cause impairment of myocardial contractility in the presence of beta-receptor blockade. Caution is advised in the use of these agents in patients receiving Sotazide. No evidence of serious interaction has been found between nitrous oxide, halothane, or isoflurane and beta-receptor blockers. Raised pCO₂ levels should be avoided in patients receiving Sotazide.

Precautions: In view of the minimal myocardial depressant effect of sotalol and the lack of myocardial effect of hydrochlorothiazide, Sotazide has only a remote potential for precipitation or exacerbation of cardiac failure. Nevertheless, Sotazide should not be given to patients with cardiac decompensation unless incipient or established heart failure is controlled. At the first sign of impending cardiac failure or the progression of failure, Sotazide dosage should be reduced or discontinued.

The dosage of Sotazide should be decreased or therapy discontinued if the pulse rate falls below 50 beats/minute. Following a reduction in blood pressure, the dosage of Sotazide should not be increased before a stable level of blood pressure is attained.

Sudden withdrawal of treatment with beta-blockers in hypertensive patients with angina pectoris has induced severe and continuous angina in some cases. Although

this effect has not been observed with Sotazide, should such a reaction occur, Sotazide treatment should be reinstituted and then withdrawn gradually by reducing the dosage over a period of weeks.

All patients receiving hydrochlorothiazide (as in Sotazide) therapy should be checked periodically for clinical signs of fluid or electrolyte imbalance: hyponatraemia, hypochlorhaemic alkalosis and hypokalaemia. Hypokalaemia can sensitise or exaggerate the response of the heart to the toxic effects of cardiac glycosides. With the lower dose of hydrochlorothiazide present in Sotazide, the possibility of any imbalance becomes less likely.

With the use of hydrochlorothiazide (as in Sotazide), serum protein-bound iodine may decrease without producing symptoms of thyroid disturbance.

Side-effects: The overall incidence of side-effects with Sotazide is low. The few reported adverse reactions were largely the pharmacological effects seen with the use of beta-blocking agents and diuretics. These reactions are mild, or moderate in intensity, most often transitory, and usually do not require interruption or withdrawal of therapy.

Sotalol, when used alone, is generally well tolerated. Dyspnoea, tiredness, dizziness, light-headedness, headache, fever and excessive bradycardia have been reported. Most of these side-effects are transient or disappear when the dosage is reduced, e.g. with the use of Sotazide.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when the treatment was withdrawn. Discontinuation of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-adrenergic blocker should be gradual.

Hyperuricaemia has been observed with thiazides but clinical gout is rare. Other side-effects for thiazides are documented but uncommon. Photosensitivity, anaphylactic reactions and depression of the formed elements of the blood have been reported.

The relevance of these observations to Sotazide therapy has not yet been determined.

Overdosage: If excessive bradycardia (and/or hypotension) occurs, atropine 0.5–2.0 mg should be given intravenously, immediately followed, if necessary, by a beta-receptor stimulating agent, such as isoprenaline, intravenously, 5 mcg/minute up to 25 mcg initially.

Pharmaceutical precautions *Expiry data:* 24 months from date of manufacture.

Legal category POM.

Package quantities Units of 28 – blister strips of 14 tablets with 2 strips per carton.

Further information Sotazide is an effective anti-hypertensive which combines sotalol hydrochloride, a beta-adrenergic blocking agent, and hydrochlorothiazide, a diuretic/antihypertensive. The concomitant use of these agents frequently produces a more pronounced anti-hypertensive effect than if either is used alone. By using lower doses than would be required if each agent were used alone, side-effects, especially the hypokalaemia associated with diuretics, are minimised. In hypertensive patients, where sodium and water retention is frequently a problem, the diuretic component will help control fluid imbalance.

Product licence number 0125/0113.

STADOL* ▼

Presentation Vials containing 2 mg butorphanol tartrate in 1 ml solution. Vials containing 4 mg butorphanol tartrate in 2 ml solution.

Uses Stadol is a strong non-narcotic synthetic analgesic of the phenanthrene series.

Stadol is indicated for:

- (a) pre-anaesthetic medication;
- (b) intra-operative use;
- (c) relief of moderate to severe pain.

Dosage and administration *Adults: Intravenous:* The usual recommended single dose is 1 mg repeated every three to four hours as necessary. The effective dose range is 0.5–2 mg.

Intramuscular: The usual recommended single dose is 2 mg repeated every three to four hours as necessary. The effective dose range is 1–4 mg.

Children: Stadol is not at present recommended for administration to children.

Contra-indications, warnings, etc

Prior narcotic administration: Because of its antagonist properties, Stadol should not be given to patients physically dependent on narcotics. Caution should be exercised in the administration of Stadol to patients who have recently received narcotic medication.

Head injury: Stadol may produce miosis and this could obscure the clinical progress of patients with head injury.

Cardiovascular disease: Stadol increases cardiac work, especially in the pulmonary circuit, and is not at present recommended for use in patients with acute myocardial infarction.

Respiratory disease: Some respiratory depression may be produced by Stadol and it should thus be used with caution in patients with severely limited respiratory reserve or obstructive airways disease or in patients with pre-existing respiratory depression caused by other disease states or drug administration. Naloxone is a specific antagonist for Stadol-induced respiratory depression.

Renal and hepatic dysfunction: Though laboratory investigations have not indicated that Stadol causes or increases renal or hepatic impairment, extensive disease may predispose to greater activity and side-effects from usual clinical doses possibly as a result of decreased metabolism and excretion.

Biliary surgery: Clinical studies with Stadol have not been undertaken in patients about to undergo biliary tract surgery.

Pregnancy and labour: Stadol is not presently recommended for use in pregnancy or in nursing mothers. However, safety of Stadol administration in labour has been established.

Operating machinery, etc: As Stadol may produce sedation and dizziness, patients should be warned not to drive or operate machinery.

Side-effects: Sedation (ranging from mild drowsiness to actual sleep) is the most common side-effect. Vertigo, dizziness, and nausea may occur. Alteration of mood and vivid dreams are infrequent. Other side-effects are rare. All of these reactions occur more frequently in patients with recent narcotic experience.

Dependence liability: Human and animal studies conducted show that Stadol has a low physical dependence

liability. Nevertheless, caution should be used in prescribing Stadol to patients who have a history of drug abuse.

Pharmaceutical precautions *Expiry Date:* 24 months from date of manufacture.

Legal category POM.

Package quantities Stadol injections are available in packs of 25 vials per carton.

Further information *Analgesic activity:* Stadol is a strong analgesic. Analgesia occurs within 30 minutes of intramuscular injection and within two minutes of intravenous injection. Peak analgesic activity occurs at approximately 60 minutes after intramuscular and 30 minutes after intravenous administration.

Respiratory effects: At an analgesic dose of 2 mg Stadol depresses respiration to a degree equal to that seen with 10 mg morphine. There is no appreciable increase in the magnitude of respiratory depression with a 4 mg dose but the duration of depression is dose related. Stadol-induced respiratory depression is completely reversible by naloxone (which is a specific antagonist).

Product licence numbers

Injection 2 mg per 1 ml 0125/0100

Injection 4 mg per 2 ml 0125/0100

TETREX* CAPSULES

Presentation Capsules having an orange body and yellow cap, printed 'BRISTOL/BRISTOL' in green. Each capsule contains tetracycline phosphate compound equivalent to tetracycline activity 250 mg.

Uses The absorption of tetracycline may be inhibited in the presence of calcium ions in the intestinal contents. The phosphate component of Tetrex combines with calcium and leaves more free tetracycline available for absorption.

Tetrex is indicated in the treatment of the following infections when due to sensitive organisms:

- Infections of the respiratory tract.
- Infections of the gastro-intestinal tract.
- Infections of the genito-urinary tract.
- Infections of the skin and soft tissues.

Dosage and administration *Adults:* Usual dose 1 g per day in 4 divided doses of 250 mg each or 2 divided doses of 500 mg each.

Higher doses may be required to control acute episodes.

Acute gonococcal urethritis – 500 mg three times daily for one to two days. Female patients require more prolonged therapy.

Children: Usual dose 25 mg/kg/day in 4 divided doses. Children weighing more than 40 kg should be given the recommended adult dose.

Therapy for most infections should be continued for 24–48 hours after the patient has become asymptomatic or afebrile.

Contra-indications, warnings, etc This drug is contra-indicated in individuals who have shown serious hypersensitivity to tetracycline, unless the need for this therapy necessitates its use with proper safeguards.

If renal impairment exists, even usual oral doses of the drug may lead to excess systemic accumulation of tetracycline and possible liver toxicity. Under such

conditions, lower than usual doses are indicated, and if therapy is prolonged, tetracycline serum-level determinations may be advisable.

Tetracycline may form a stable calcium complex in any bone-forming tissue with no serious harmful effects reported thus far in humans. However, use of tetracycline during tooth development (last trimester of pregnancy, neonatal period, infancy and early childhood) may cause discoloration of the teeth (yellow-grey-brownish). This effect occurs mostly during long-term therapy, but it has also been observed following short treatment courses.

Enamel hypoplasia has been observed in a few children. If superinfection with non-susceptible organisms occurs proper measures should be taken.

Pharmaceutical precautions Expiry date – 36 months from date of manufacture.

There are no special directions for storage.

Legal category POM.

Package quantities Containers of 100 capsules.

Further information Tetracycline phosphate compound is absorbed rapidly from the gastro-intestinal tract providing reliable high tetracycline levels in the blood. It is serum bound to a much lesser degree than most other tetracyclines and therefore allows greater concentrations of active antibiotic to reach the site of infection.

Product licence number 0125/0066.

VEPESID* CAPSULES ▼

VEPESID* INJECTION ▼

Presentation Vepesid Injection-ampoules containing 100 mg etoposide in 5 ml.

Vepesid Capsules-soft gelatin capsules containing 100 mg etoposide.

Uses Vepesid is an anti-neoplastic drug for intravenous or oral use, which can be used alone or in combination with other oncologic drugs.

Present data indicate that Vepesid is applicable in the therapy of: small cell lung cancer, resistant non-seminomatous testicular carcinoma.

Dosage and administration The recommended course of Vepesid Injection is 60–120 mg/m², i.v., daily for five consecutive days. As Vepesid produces myelosuppression, courses may not be repeated more frequently than at 21 day intervals. In any case, repeat courses of Vepesid should not be given until the blood picture has been checked for evidence of myelosuppression and found to be satisfactory.

Immediately before administration, the required dose of Vepesid Injection must be diluted with 0.9% saline solution for injection to give a solution concentration of not more than 0.25 mg/ml of etoposide; it should then be given by intravenous infusion over a period of not less than 30 minutes.

Care should be taken to avoid extravasation.

If oral dosing is preferred, twice the relevant i.v. dose should be given daily, for five consecutive days. As Vepesid produces myelosuppression, courses may not be repeated more frequently than at 21 day intervals. In any case, repeat courses of Vepesid should not be given until the blood picture has been checked for evidence of myelosuppression and found to be satisfactory.

Contra-indications, warnings, etc Vepesid is contra-indicated in patients with severe hepatic dysfunction

or in those patients who have demonstrated hypersensitivity to the drug.

Vepesid must not be given by intra-cavity injection.

Warnings: Vepesid should not normally be administered to patients who are pregnant or to mothers who are breast feeding. Safe use in pregnancy has not been established.

Vepesid is teratogenic in rats at dose levels equivalent to those employed clinically.

The influence of Vepesid on human reproduction has not been determined.

In-vitro tests indicate that Vepesid is mutagenic.

Precautions: Vepesid should be administered by individuals experienced in the use of antineoplastic therapy.

When Vepesid is administered intravenously care should be taken to avoid extravasation.

If radiotherapy and/or chemotherapy has been given prior to starting Vepesid treatment, an adequate interval should be allowed to enable the bone marrow to recover. If the leucocyte count falls below 2,000/mm³, treatment should be suspended until the circulating blood elements have returned to acceptable levels (platelets above 100,000/mm³, leucocytes above 4,000/mm³), this is usually within 10 days.

Peripheral blood counts and liver function should be monitored. (See Adverse Reactions.)

Bacterial infections should be brought under control before treatment with Vepesid commences.

Adverse reactions: Haematological: The dose limiting toxicity of Vepesid is myelosuppression, predominantly leucopenia and thrombocytopenia. Anaemia occurs infrequently.

The leucocyte count nadir occurs approximately 21 days after treatment.

Alopecia: Alopecia occurs in approximately 50% of patients and is reversible on cessation of therapy.

Gastrointestinal: Nausea and vomiting are the major gastrointestinal toxicities and occur in approximately 30% of patients. Anti-emetics are useful in controlling these side effects. Abdominal pain, diarrhoea and anorexia occur infrequently.

Other Toxicities: Hypotension may occur following an excessively rapid infusion and may be reversed by slowing the infusion rate.

Anaphylactic-like reactions have been reported rarely following administration of Vepesid. Reactions respond to cessation of therapy and administration of an antihistamine.

No specific toxic effects have been observed with respect to the cardiovascular system, nervous system, the liver or kidney. However, Vepesid has been shown to reach high concentrations in the latter two organs, thus presenting a potential for accumulation in cases of functional impairment.

Pharmaceutical precautions Vepesid capsules and injection should be stored at room temperature. The injection should be protected from light.

Preparation of intravenous solution: Immediately before administration the required dose of Vepesid Injection must be diluted with 0.9% saline solution for injection to give a solution concentration of not more than 0.25 mg/ml of etoposide; it should then be given by intravenous infusion over a period of not less than 30 minutes. The infusion solution should be kept at room temperature and should be used within six hours of preparation. Solutions of concentration greater than

0.25 mg/ml may show signs of precipitation, and are therefore not recommended. Any solutions showing signs of precipitation should be discarded.

The intravenous solution is suitable for infusion in glass or PVC containers.

Vepesid should not be physically mixed with any other drug.

Expiry date: Vepesid injection: 5 years from date of manufacture. Vepesid capsules: 2 years from date of manufacture.

Legal category POM.

Package quantities Vepesid injection is packed in cartons of 10 ampoules, each ampoule containing 100 mg etoposide in 5 ml of solution.

Vepesid capsules are packed in bottles of 10 capsules, each capsule containing 100 mg etoposide.

Further information Etoposide is a semisynthetic derivative of podophyllotoxin.

Experimental data indicate that etoposide arrests the cell cycle in the G₂ phase. Etoposide differs from the

vinca alkaloids in that it does not cause an accumulation of cells in metaphase, but prevents cells from entering mitosis or destroys cells in the G₂ phase. The incorporation of thymidine into DNA is inhibited in-vitro by etoposide. Etoposide does not interfere with microtubule assembly. Etoposide is approximately 94% protein-bound in human serum. Plasma decay kinetics follow a bi-exponential curve and correspond to a two compartmental model. The mean volume of distribution is approximately 32% of body weight. Etoposide demonstrates relatively poor penetration into the cerebrospinal fluid. Urinary excretion is approximately 45% of an administered dose, 29% being excreted unchanged in 72 hours.

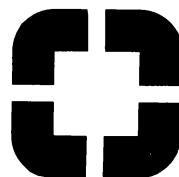
An information sheet on the storage, preparation and handling of the product is available

Product licence numbers

Vepesid Capsules	0125/0124
Vepesid Injection	0125/0121

**Trade Mark*

Brocades Great Britain Limited
Brocades House
Pyrford Road
West Byfleet, Surrey



AMFIPEN* CAPSULES
AMFIPEN* SYRUP
AMFIPEN* SYRUP FORTE
AMFIPEN* INJECTION

Presentation Amfipen Capsules (Ampicillin Capsules BP) are presented as grey and red capsules each containing 250 mg or 500 mg Ampicillin BP, imprinted 'Amfipen 250' or 'Amfipen 500'.

Amfipen Syrup (Ampicillin Mixture BPC) and Amfipen Syrup Forte (Strong Ampicillin Mixture BPC) are presented as bottles containing dry powder for the preparation of 100 ml of a pink-coloured suspension. On reconstitution each 5 ml dose contains 125 mg or 250 mg respectively Ampicillin BP.

Amfipen Injections (Ampicillin sodium for injection BP) are presented as vials containing 250 mg or 500 mg ampicillin as Ampicillin Sodium BP.

Uses Amfipen is a broad-spectrum penicillin for the treatment of a wide range of infections caused by ampicillin-sensitive organisms.

Dosage and administration *Usual adult oral dosage:* Ear, nose and throat infections: 250 mg four times a day.

Bronchitis: usually 250 mg four times a day in routine therapy; 1 g four times a day in high-dosage regimes.

Pneumonia: 500 mg four times a day.

Gastro-intestinal infection: 500–750 mg three or four times daily.

Urinary tract infections: 500 mg four times daily.

Enteric fevers: in acute cases 1–2 g four times a day for 14 days; carriers should be treated with this dosage for 4–12 weeks.

In the treatment of gonorrhoea 2 g should be given with 1 g probenecid as a single dose. In the treatment of females repeated doses are recommended.

Usual children's oral dosage: Half of the adult dosage.

The doses above are recommended dosages, only as a guide. In severe infections the dosages may be increased.

Amfipen should be given a half to one hour before meals.

Usual adult parenteral dosage: Septicaemia, endocarditis, osteomyelitis: 500 mg four to six times a day for one to six weeks by intramuscular or intravenous injection.

Meningitis: 2 g six-hourly for two days by intravenous injection, followed by 500 mg to 1 g six-hourly by intramuscular injection.

Usual children's parenteral dosage: Meningitis: 100 g per kg daily in divided doses by intravenous injections for two days, followed by 100 mg per kg daily.

The dosages above are recommended dosages only as a guide. In severe infections the dosages may be increased.

Administration: Amfipen may be administered orally as capsules or syrup or syrup forte. Parenteral dosage by means of Amfipen Injection should be administered as follows: For intramuscular injection dissolve 250 mg or

500 mg in 1.5 ml water for injections BP. For intravenous injection dissolve 500 mg in 10 ml water for injections BP and administer by injection over three to four minutes. For intraperitoneal injection and intrapleural injection dissolve 500–1,000 mg in 5–10 ml water for injections BP. For intra-articular injection 500 mg dissolved in up to 5 ml water for injections BP or 0.5% procaine hydrochloride.

Contra-indications, warnings, etc

Contra-indicated in patients with penicillin hypersensitivity and glandular fever.

Side-effects: Skin reactions may occur rarely, and be due to either penicillin hypersensitivity (urticarial rash) or specific ampicillin sensitivity (erythematous rash); treatment should be discontinued if a rash occurs. Occasionally, diarrhoea may occur. As with all ampicillins, Amfipen may reduce the efficacy of oral contraceptives, and patients should be warned accordingly.

Pharmaceutical precautions Amfipen preparations should be stored in a cool dry place. On reconstitution, Amfipen Syrup and Amfipen Syrup Forte should be used within seven days if stored in a cool place.

In order to obtain a homogeneous suspension it is recommended that the bottle be well shaken before reconstitution of the syrup.

Legal category POM.

Package quantities *Amfipen Capsules 250 mg:* Bottles of 250, and packs of 2,500.

Amfipen capsules 500 mg: Bottles of 250, and packs of 1,500.

Amfipen Syrup and Syrup Forte: Bottles for the preparation of 100 ml.

Amfipen Injections 250 mg and 500 mg: Boxes of 10 vials.

Further information Nil.

Product licence numbers

Amfipen Capsules 250 mg	0166/0065
Amfipen Capsules 500 mg	0166/0066
Amfipen Syrup	0166/0067
Amfipen Syrup Forte	0166/0068
Amfipen Injection 250 mg	0166/0069
Amfipen Injection 500 mg	0166/0070

ANTRADERM* MILD
ANTRADERM* ▼
ANTRADERM* FORTE ▼

Presentation *Antraderm Mild:* a pale yellow wax containing dithranol BP 0.5%. *Antraderm:* a pale yellow wax containing dithranol BP 1.0%. *Antraderm Forte:* a pale yellow wax containing dithranol BP 2.0%. Each presentation is packed as 8 g sticks in a plastic twist-up container.

Uses For the topical treatment of subacute and chronic psoriasis.

Dosage and administration Clinical experience has shown that, as with other methods of treatment, patient response is rather individualised and therefore it may be necessary to adjust treatment during the initial period. It is recommended that treatment be normally started with the 1.0% concentration. If irritation or stinging occurs and it persists the problem can often be overcome by changing to the lower 0.5% strength. If the effect of the 1.0% strength is insufficient or if tolerance develops after a period of treatment the 2.0% strength will often produce the required response.

Antraderm should be applied directly to the lesions, preferably at night before bedtime. The tip of the wax stick is softened by skin temperature enabling a thin layer of dithranol to be applied gently over the lesions. When treating very scaly lesions, the debris should be removed before applying Antraderm.

Treatment should continue until the skin is clear. Intermittent courses may be required to maintain therapeutic response.

Contra-indications, warnings, etc A small proportion of patients initially experience slight toxic reactions to dithranol. This reaction is often transient and is usually seen during the first 2-3 days of treatment. It is more likely to occur when potent topical steroids have recently been used. These effects can usually be overcome by:

- reducing the frequency of treatment for a few days e.g. applications very 2nd or 3rd night.
- using a lower concentration of Antraderm. If neither action overcomes the toxic response, it may be necessary to stop treatment.

Antraderm must not be used for psoriasis in the acute phase. Care should be taken to avoid application to surrounding areas of unaffected skin.

An excessive quantity should not be applied as this may cause unnecessary staining of clothing and bed linen. In the morning a bath will remove any surplus dithranol.

During treatment the edges of the lesions will gradually acquire a purplish-brown stain which will completely disappear after the treatment has finished.

Pharmaceutical precautions Keep in a cool place. Use within 6 months of breaking the foil outer pack.

Legal category

Antraderm Mild	P.
Antraderm	POM.
Antraderm Forte	POM.

Package quantities All strengths are supplied in 8 g sticks.

Further information Antraderm is suitable for home treatment as its advantages make it easier and more economic in use than other forms of dithranol. It is however equally suitable for use in dermatology wards and clinics as a standard dithranol treatment.

Product licence numbers

Antraderm Mild	0166/0103
Antraderm	0166/0104
Antraderm Forte	0166/0105

BICILLIN* INJECTION

Presentation Bicillin Injection is presented as vials of dry powder for the preparation of Fortified Procaine

Penicillin Injection BP. Each vial contains 3 mega units (3 g) procaine penicillin G and 1 mega unit (0.6 g) sodium penicillin G.

Uses Antibiotic for the treatment of infections due to penicillin-sensitive organisms, where prolonged release is desired.

Dosage and administration For intramuscular injection only.

Adults: 400,000 units (300 mg procaine penicillin G and 60 mg sodium penicillin G) 24-hourly or 12-hourly.

Children: Over 25 kg as for adults; under 25 kg proportionally.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to penicillin or procaine.

Special precautions: Appropriate treatment for systemic reactions should be readily available.

Side-effects: Skin reactions may occur but usually resolve on cessation of therapy; generalised systemic reactions are rare and usually associated with a history of allergy or penicillin intolerance.

The safety of Bicillin Injection during pregnancy has not been established.

Pharmaceutical precautions Store in a cool dry place. Use within five days after reconstitution if stored at room temperature or 14 days if stored at 4°C.

Legal category POM.

Package quantities Boxes of 10 vials and 100 vials each containing 4 mega units (3 g procaine penicillin G and 0.6 g sodium penicillin) per vial.

Further information Upon reconstitution with 7.5 ml Water for Injections BP, each ml of suspension contains 300,000 units (300 mg) procaine penicillin G and 100,000 units (60 mg) sodium penicillin G.

Product licence number 0166/0073.

BROCADOPA* CAPSULES BROCADOPA* TABLETS

Presentation Brocadopa is presented as clear colourless hard gelatine capsules each containing 125 mg, 250 mg or 500 mg Levodopa BP, imprinted 'Brocadopa 125', '250' or '500', and as white uncoated double-scored tablets each containing 500 mg Levodopa BP, imprinted 'Brocadopa 500'. Brocadopa Capsules and Brocadopa Tablets comply with the monographs for Levodopa Capsules BP and Levodopa Tablets BP respectively.

Uses Dopaminergic, for the treatment of all forms of Parkinsonism, except drug-induced (neuroleptic syndrome).

Dosage and administration By oral administration. **Adults:** Initially 250 mg daily in divided doses, increasing by 250 mg every three to four days until optimal response is obtained. This may occur at any level between 1 g and 8 g daily in divided doses after a period of four to six weeks.

Children: As for adults.

Contra-indications, warnings, etc

Contra-indicated in patients receiving monoamine oxidase inhibitors.

Special precautions: Use with caution in patients receiving pyridoxine, hypotensive agents, phenothiazines and butyrophenones, or tricyclic antidepressants, and in patients suffering from heart disease (heart block, myocardial infarct or insufficiency and cardiac arrhythmia), dementia and psychoses, liver disease or pregnancy.

Side-effects: Gastro-intestinal disturbances, such as nausea, vomiting and anorexia, are the commonest side-effects and occur early. They may be diminished by administration after food and by finer fractionation of the daily dose. A non-phenothiazine anti-emetic drug may be given half an hour before each dose.

Hypotension, generally postural in type, may occur, usually unaccompanied by symptoms or change in pulse rate. Smaller dosage increments will reduce the incidence.

Involuntary movements usually occur at higher dosage level, and may be alleviated by a small reduction in dosage of 0.5–1 g daily or by fractionation of dosage.

Psychic manifestations such as restlessness and nervousness may occur with some disturbance of sleep. More rarely, agitation or mania with hallucinations have been reported. Psychiatric side-effects are more likely to occur in patients with a pre-existing psychosis but may be diminished or abolished by reduction or cessation of dosage.

Cardiac disturbances, e.g. paroxysmal tachycardia and arrhythmias, have been reported. It may be advisable to stop dosage and recommence at a lower level.

Overdosage: No reports of overdosage have been received.

Pharmaceutical precautions Normal pharmaceutical storage and handling are indicated.

Legal category POM.

Package quantities Capsules: 250 × 125 mg, 100 × 250 mg, 250 × 250 mg, 100 × 500 mg and 250 × 500 mg.

Tablets: 100 × 500 mg.

Further information Nil.

Product licence numbers

Capsules 125 mg	016655013
Capsules 250 mg	0166/5014
Capsules 500 mg	0166/5015
Tablets 500 mg	0166/5023

BROCADOPA TEMTABS*

Presentation Brocadopa Temtabs are presented as white uncoated double-scored tablets each containing 500 mg Levodopa BP in a special formulation designed to effect a slow release of the active substance, and are imprinted 'Brocadopa Temtab'.

Uses Dopaminergic, for the treatment of all forms of Parkinsonism, except drug-induced (neuroleptic syndrome).

Dosage and administration By oral administration.

Adults: Initially 250 mg daily in divided doses, increasing by 250 mg every three to four days until optimal response is obtained. This may occur at any level between 1 g and 3 g daily in divided doses after a period of four to six weeks.

Children: As for adults.

Contra-indications, warnings, etc

Contra-indicated in patients receiving monoamine oxidase inhibitors.

Special precautions: Use with caution in patients receiving pyridoxine, hypotensive agents, phenothiazines and butyrophenones, or tricyclic antidepressants, and in patients suffering from heart disease (heart block, myocardial infarct or insufficiency and cardiac arrhythmia), dementia and psychoses, liver disease or pregnancy.

Side-effects: Gastro-intestinal disturbances, such as nausea, vomiting and anorexia, are the commonest side-effects and occur early. They may be diminished by administration after food and by finer fractionation of the daily dose. A non-phenothiazine antiemetic drug may be given half an hour before each dose.

Hypotension, generally postural in type, may occur, usually unaccompanied by symptoms or change in pulse rate. Smaller dosage increments will reduce the incidence.

Involuntary movements usually occur at higher dosage level, and may be alleviated by a small reduction in dosage of 0.5–1 g daily or by fractionation of dosage.

Psychic manifestations such as restlessness and nervousness may occur with some disturbance of sleep. More rarely, agitation or mania with hallucinations have been reported. Psychiatric side-effects are more likely to occur in patients with a pre-existing psychosis but may be diminished or abolished by reduction or cessation of dosage.

Cardiac disturbances, e.g. paroxysmal tachycardia and arrhythmias, have been reported. It may be advisable to stop dosage and recommence at a lower level.

Overdosage: No reports of overdosage have been received.

Pharmaceutical precautions Normal pharmaceutical storage and handling are indicated.

Legal category POM.

Package quantities 100 × 500 mg Temtabs.

Further information Nil.

Product licence number 0166/0050.

BRONTINA* TABLETS

Presentation Brontina Tablets are presented as white, square tablets, single-scored on one side, each containing 1 mg deproline citrate.

Uses In the treatment of asthma and chronic bronchitis, and for the prophylaxis and treatment of hay fever and perennial rhinitis.

Dosage and administration By oral administration. **Adults:** 1 mg twice daily.

Children: Not recommended.

Contra-indications, warnings, etc Contra-indicated in glaucoma and prostatic hypertrophy.

Special precautions: Use with caution in patients with micturition difficulties.

Side-effects: Occasionally dry mouth, blurred vision and micturition difficulties have been reported.

Overdosage: Could be expected to result in the symptoms of anticholinergic and antihistaminic overdosage.

Pharmaceutical precautions Normal pharmaceutical storage and handling are indicated.

Legal category POM.

Package quantities 100 × 1 mg tablets.

Further information Nil.

Product licence number 0166/5011.

BRONTISOL* AEROSOL

Presentation Brontisol Aerosol is presented as a pressurised aerosol, each 15 ml cartridge containing a suspension of 2 mg/ml depropine citrate and 3 mg/ml isoprenaline hydrochloride in a mixture of inert propellants. Each metered dose contains 0.1 mg depropine citrate and 0.15 mg isoprenaline hydrochloride.

Uses Bronchodilator for the treatment of asthma, asthmatic bronchitis, chronic bronchitis and other respiratory conditions where a combination of spasmolysis and control of secretions is advantageous.

Dosage and administration By inhalation.

Adults: 1–3 inhalations every four to five hours.

Children: 1–2 inhalations every four to five hours.

Not more than 8 inhalations should be taken in any 24-hour period. Brontisol Aerosol should only be given to children on the advice of a doctor and a responsible adult should supervise the administration of the prescribed dose.

Contra-indications, warnings, etc No contra-indications.

Special precautions: Use with caution in the presence of impaired cardiac function, diabetes, hyperthyroidism and hypertension.

Side-effects: These occur infrequently and are seldom severe, but when occurring are those normally associated with the use of sympathomimetic and anticholinergic drugs: dizziness, tachycardia, dry mouth and blurred vision. In practice these side-effects will usually diminish or disappear with continued usage. Dosage adjustments may occasionally be necessary.

Overdosage: Could be expected to result in the symptoms associated with sympathomimetic anticholinergic and antihistaminic overdosage.

Pharmaceutical precautions Normal pharmaceutical storage and handling are indicated.

Legal category POM.

Package quantities 1 × 15 ml cartridge and mouthpiece.

Further information As the aerosol is pressurised, it must not be punctured, or disposed of by burning.

Product licence number 0166/5000.

CYCLOSPASMOL* SUSPENSION

Presentation Cyclospasmol Suspension is presented as a dry powder, ready for reconstitution at the time of dispensing by the addition of 375 ml distilled water. The resulting suspension provides 90 doses each of 5 ml, each 5 ml dose containing 400 mg cyclandelate.

Uses For the treatment of organic vasospastic peripheral and cerebrovascular diseases associated with impaired circulation, especially in the long-term management of chronic insufficiency and in the sequelae of strokes, and in the improvement of mental function, dementia, confusion etc., and in intermittent claudication, Raynaud's phenomenon, chilblains, night cramps, acrocyanosis, cold hands and feet, etc.

Dosage and administration By oral administration.

Adults: 1,600 mg (20 ml) daily in 2 or 4 divided doses.

Children: A dosage for children has not been established

Contra-indications, warnings, etc Contra-indicated in the acute phase of a cerebrovascular accident.

Special precautions: None.

Side-effects: At very high dosage, nausea, gastro-intestinal distress or flushing may occur.

Overdosage: Gross overdosages have not been reported; theoretically circulatory collapse could occur and treatment would be gastric lavage and, if necessary, vasopressors.

Pharmaceutical precautions Normal pharmaceutical storage and handling are indicated. Upon reconstitution, Cyclospasmol suspension carries an expiry date of 3 months from the date of reconstitution.

Legal category P.

Package quantities Each bottle, after reconstitution, provides 90 doses each of 400 mg cyclandelate in 5 ml.

Further information Each 5 ml dose contains approximately 500 mg sucrose. For maximum therapeutic effect it is recommended that the daily dose of 1,600 mg be given; maximal therapeutic response may not be seen within the first one or two months of treatment.

Product licence number 0166/0062.

CYCLOSPASMOL* TABLETS CYCLOSPASMOL* CAPSULES

Presentation Cyclospasmol is presented as pink sugar-coated tablets each containing 400 mg cyclandelate, imprinted 'Cyclospasmol'; and as pink/grey hard gelatine capsules each containing 400 mg cyclandelate imprinted 'Cyclospasmol'.

Uses For the treatment of organic vasospastic peripheral and cerebrovascular diseases associated with impaired circulation, especially in the long-term management of chronic insufficiency and in the sequelae of strokes, and in the improvement of mental function, dementia, confusion, etc., and in intermittent claudication, Raynaud's phenomenon, chilblains, night cramps, acrocyanosis, cold hands and feet, etc.

Dosage and administration By oral administration.

Adults: 1,600 mg daily in 2 or 4 divided doses.

Children: A dosage for children has not been established

Contra-indications, warnings, etc Contra-indicated in the acute phase of a cerebrovascular accident.

Special precautions: None.

Side-effects: At very high dosages, nausea, gastro-intestinal distress or flushing may occur.

Overdosage: Gross overdoses have not been reported; theoretically circulatory collapse could occur and treatment would be gastric lavage and, if necessary, vasopressors.

Pharmaceutical precautions Normal pharmaceutical storage and handling are indicated.

Legal category P.

Package quantities Tablets 250 × 400 mg. Capsules 250 × 400 mg and treatment packs of 112 tablets.

Further information For maximum therapeutic effect, it is recommended that the daily dosage of 1,600 mg be given; maximal therapeutic response may not be seen within the first one or two months of treatment.

Product licence numbers

Cyclospasmol Capsules 0166/0021
Cyclospasmol Tablets 0166/0052

DE-NOL*

Presentation De-Nol is presented as a clear red liquid, in a 560 ml bottle, containing 120 mg tripotassium dicitrato bismuthate (as Bi_2O_3) in each 5 ml.

Uses Ulcer healing agent. For the treatment of gastric and duodenal ulcers.

Dosage and administration By oral administration.

Adults: 5 ml diluted with 15 ml water four times a day on an empty stomach, half an hour before each of the three main meals and two hours after the last meal of the day. In particularly resistant cases, especially duodenal ulcers, the dosage may be increased to 10 ml diluted with 15 ml water, six times a day, half an hour before and two hours after each of the three main meals. De-Nol should be taken for a minimum period of 28 days and it is important that patients do not miss a dose. In long-standing or resistant cases, a further course of De-Nol therapy may be necessary to achieve maximum therapeutic benefit.

Children: As for adults.

Contra-indications, warnings, etc

Contra-indicated on theoretical grounds in cases of severe renal insufficiency and in pregnancy.

Special precautions: De-Nol may inhibit the efficacy of orally administered tetracyclines.

Side-effects: Blackening of the stool usually occurs and darkening of the tongue has been reported. Electrolyte imbalance does not occur.

Overdosage: No reports of overdosage have been received; gastric lavage and if necessary supportive therapy would be indicated.

Pharmaceutical precautions Normal pharmaceutical storage and handling are indicated.

Legal category P.

Package quantities Treatment packs of 560 ml.

Further information Some patients with an associated gastritis may experience an initial discomfort.

Product licence numbers
0166/5024

DEPOCILLIN* INJECTION

Presentation Depocillin Injection is presented as vials of dry powder for the preparation of Procaine Penicillin Injection BP. Each vial contains 3 mega units (3 g) of procaine penicillin G.

Uses Antibiotic for the treatment of infections due to penicillin-sensitive organisms, where prolonged release is desired.

Dosage and administration For intramuscular injection only.

Adults: 300,000 units (300 mg) 24-hourly or 12-hourly.

Children: Over 25 kg as for adults; under 25 kg proportionally.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to penicillin or procaine.

Special precautions: Appropriate treatment for systemic reactions should be readily available.

Side-effects: Skin reactions may occur but usually resolve on cessation of therapy; generalised systemic reactions are rare and usually associated with a history of allergy or penicillin intolerance.

The safety of Depocillin Injection during pregnancy has not been established.

Pharmaceutical precautions Store in a cool dry place. Use within five days after reconstitution if stored at room temperature or 14 days if stored at 4°C.

Legal category POM.

Package quantities Boxes of 10 vials and 100 vials each containing 3 mega units (3 g) per vial.

Further information Upon reconstitution with 8 ml Water for Injections BP each ml of suspension contains 300,000 units (300 mg) of procaine Penicillin G.

Product licence number 0166/0072.

DEPOCILLIN* AQUEOUS INJECTION

Presentation Depocillin Aqueous Injection is presented as vials containing 10 ml Procaine Penicillin Injection BP, each ml containing 300,000 units (300 mg) procaine penicillin G.

Uses Antibiotic for the treatment of infections due to penicillin-sensitive organisms, where prolonged release is desired.

Dosage and administration For intramuscular injection only.

Adults: 300,000 units (300 mg) 24-hourly or 12-hourly.

Children: Over 25 kg as for adults; under 25 kg proportionally.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to penicillin or procaine.

Special precautions: Appropriate treatment for systemic reactions should be readily available.

Side-effects: Skin reactions may occur but usually resolve on cessation of therapy; generalised systemic reactions are rare and usually associated with a history of allergy or penicillin intolerance.

The safety of Depocillin Aqueous Injection during pregnancy has not been established.

Pharmaceutical precautions Store below 15°C.

Legal category POM.

Package quantities Boxes of 10 vials and 50 vials each containing 3 mega units (3 g) per vial.

Further information Nil.

Product licence number 0166/0074.

DIDRONEL* TABLETS ▼

Presentation White rectangular tablets, each tablet containing etidronate disodium 200 mg.

Uses Didronel is indicated for the treatment of Paget's disease of bone (osteitis deformans). Effectiveness has been demonstrated primarily in patients with polyostotic Paget's disease with symptoms of pain and with clinically significant elevations of urinary hydroxyproline and serum alkaline phosphatase. In other circumstances in which there is extensive involvement of the skull or the spine with the prospect of irreversible neurological damage, or when a weight-bearing bone may be involved, the use of Didronel may be considered.

Dosage and administration 5 mg/kg/day to 20 mg/kg/day as detailed below.

Adults: The recommended initial dose of Didronel for most patients is 5 mg/kg body weight/day, not to exceed a period of six months. Doses above 10 mg/kg should be reserved for use when there is an overriding requirement for suppression of increased bone turnover associated with Paget's disease or when the patient requires more prompt reduction of elevated cardiac output. Treatment with doses above 10 mg/kg/day should be approached cautiously and should not exceed three months duration. Doses in excess of 20 mg/kg/day are not recommended.

Retreatment should be undertaken only after a drug-free period of at least three months and after it is evident that reactivation of the disease has occurred and biochemical indices of the disease have become substantially re-elevated or approach pretreatment values (approximately twice the upper limit of normal or 75% of pretreatment value). In no case should duration of retreatment exceed the maximum duration of the initial treatment. Premature retreatment should be avoided. In clinical trials the biochemical improvements obtained during drug therapy have generally persisted for a period of three months to, in some cases, up to 2 years after drug withdrawal.

2. Children: Disorders of bone in children, referred to as juvenile Paget's disease, have been reported rarely. The relationship to adult Paget's disease has not been established. Didronel has not been studied in children for Paget's disease.

3. Heterotopic Ossification: In heterotopic ossification complicating hip replacement, the recommended adult dose is 20 mg/kg/day for one month pre-operatively followed by 20 mg/kg/day for three months post-operatively. The total treatment period is four months. There is no evidence that Didronel therapy will affect mature heterotopic bone.

In heterotopic ossification due to spinal cord injury the recommended adult dose of Didronel is 20 mg/kg/day for two weeks followed by 10 mg/kg/day for ten weeks. The total treatment period is twelve weeks. The recommended dosage should be instituted as soon as is medically feasible following the injury, preferably prior to any radiographic evidence of heterotopic ossification.

4. Directions for use: Didronel should be administered as a single, oral dose, two hours before meals. It may be given with fruit juice or water. Food in the stomach or upper portions of the small intestine, particularly materials high in calcium content such as milk, may reduce absorption. Therefore, eating should be avoided for two hours before and after drug administration.

5. Daily dosage guide:

Body Weight		Required Daily Regimen of 200 mg Tablets		
Kilograms	Stones	5 mg/kg*	10 mg/kg*	20 mg/kg†
50	8	1	3	5
60	9½	2	3	6
70	11	2	4	7
80	12½	2	4	8
90	14	2	5	9

* Course of therapy – 6 months. † Course of therapy – 3 months.

Contra-indications, warnings, etc *Contra-indications:* At present, clinical trials have demonstrated no absolute contra-indications to Didronel.

Precautions:

1. General: Didronel retards mineralisation of osteoid laid down during the bone accretion process. This effect is dose and time dependent. There may be an overlap of beneficial and mineralisation inhibition effects in some patients at higher doses. Extended periods of medication should be approached cautiously. When administered at doses of 20 mg/kg/day, Didronel suppresses bone turnover and essentially stops mineralisation of new bone in Pagetic lesions and, to a lesser extent, in the uninvolved skeleton. Mineralisation of Pagetic lesions has been demonstrated to occur normally after discontinuation of the drug.

Patients with Paget's disease of bone should maintain an adequate nutritional status, and particularly, an adequate intake of calcium and vitamin D. Patients with restricted vitamin D and calcium intake may be particularly sensitive to drugs that affect calcium homeostasis and should be closely followed while under treatment with Didronel.

In the treatment of heterotopic ossification, no problems relating to loosening of prosthetic devices have been encountered. The incidence of migration of the trochanter has not been observed to be increased with Didronel therapy.

Didronel is not metabolised but excreted intact via the kidney; therefore, treatment of patients with impaired renal function should be approached very cautiously, if at all.

Didronel therapy has been withheld from patients with enterocolitis because increased frequency of bowel movements and diarrhoea are seen in some patients when Didronel is administered at a dose of 20 mg/kg/day and may be increased occasionally at lower doses.

2. Pregnancy: Reproduction studies have been performed in rats and rabbits. In some of these studies there

was a decrease in the number of live born fetuses. There were no teratogenic effects. Because Didronel does not cross the placental barrier in these species, the decrease in number of live fetuses may have been due to a metabolic effect of Didronel in the mother. There is no experience in pregnant women given Didronel. Didronel should be used only when clearly needed in women who are or may become pregnant.

3. Nursing Mothers: It is not known whether this drug is excreted in human milk. As a general rule, nursing should not be undertaken while the patient is on a drug since many drugs are excreted in human milk.

Warnings: The physician should adhere to the recommended dose regimen in order to avoid overtreatment with Didronel. The response to therapy may be of slow onset and may continue even for months after treatment when the drug has been discontinued. Dosage should not be increased prematurely nor should treatment be resumed before there is clear evidence of reactivation of the disease process. Retreatment should not be initiated until the patient has had at least a three-month drug-free interval.

Increased or recurrent bone pain at existing Pagetic sites and/or the appearance of pain at sites previously asymptomatic has been reported. At the recommended dose (5 mg/kg/day) 1 out of 10 patients reported the phenomena; at higher doses the figure rose to 2 out of 10. In placebo-treated patients, the occurrence was 1 out of 15. In Didronel treated patients, the pain resolved while therapy was continued in some patients but persisted for several months in others.

Fractures are recognised as a common feature in patients with Paget's disease. There has been no evidence of increased risk at the recommended dose of 5 mg/kg/day for six months. The risk of fracture may be increased when Didronel is taken at a dose level of 20 mg/kg/day in excess of three months. This risk may be greater in patients with extensive and severe disease, a history of multiple fractures, and/or rapidly advancing osteolytic lesions. It is recommended that the drug be discontinued when fractures occur and that therapy not be reinstated until fracture healing is complete.

The incidence of osteogenic sarcoma is known to be increased in Paget's disease. Pagetic lesions, with or without therapy, may appear by x-ray to progress markedly, possibly with some loss of definition of periosteal margins. Such lesions should be evaluated carefully to differentiate these from osteogenic sarcoma.

Concomitant fractures are common in patients with spinal-cord injury. In controlled studies, no problems of fracture healing on stabilisation of the spine were encountered. In cases with multiple long bone fractures, it may be advisable to delay therapy for a short time until callus formation is evidenced.

Side-effects: Gastrointestinal complaints such as diarrhoea, loose bowel movement, and nausea are increased in some patients when Didronel is administered at doses greater than 5 mg/kg/day. The incidence is about 1 out of 15 in both placebo-treated patients and in patients on Didronel, 5 mg/kg/day. The incidence rises to approximately 2 out of 10 patients treated with Didronel at the dose of 20 mg/kg/day.

Overdosage: While there is no experience with acute overdosage, it is theoretically possible that enough Didronel could be taken to result in hypocalcaemia. Treatment should be by cessation of therapy, correction of hypocalcaemia with intravenous calcium gluconate

and maintenance of an adequate nutritional status, artificially supplemented if necessary.

Pharmaceutical precautions Normal pharmaceutical storage and handling are indicated.

Legal category POM.

Package quantities 60 × 200 mg tablets.

Further information Nil.

Product licence number 0166/0101.

DISIPAL* TABLETS DISIPAL* INJECTION

Presentation Disipal Tablets are presented as yellow sugar-coated tablets each containing 50 mg Orphenadrine Hydrochloride BP, imprinted 'Disipal'. Disipal Tablets comply with the monograph for Orphenadrine Hydrochloride Tablets BP.

Disipal Injection is presented as a sterile aqueous solution in clear glass 2 ml ampoules each containing 20 mg/ml Orphenadrine Hydrochloride BP.

Uses Anticholinergic, for the treatment of all forms of Parkinsonism, including drug-induced (neuroleptic syndrome).

Dosage and administration *By oral administration:*

Adults: Initially 150 mg daily in divided doses, increasing by 50 mg every two or three days until maximum benefit is obtained. Optimal dosage is usually 250–300 mg daily in divided doses in idiopathic and post-encephalitic Parkinsonism, 100–150 mg daily in divided doses in arteriosclerotic Parkinsonism, and 150–300 mg daily in divided doses in the neuroleptic syndrome. Maximal dosage, 400 mg daily in divided doses.

Children: As for adults.

By intramuscular injection: **Adults:** 20–40 mg (1–2 ml) as determined by the physician.

Children: As for adults.

Contra-indications, warnings, etc Contra-indicated in patients with glaucoma or prostatic hypertrophy.

Special precautions: Use with caution in patients with micturition difficulties or in pregnancy.

Side-effects: Occasionally dry mouth, disturbances of visual accommodation and micturition difficulties may occur; these usually disappear spontaneously or may be controlled by a slight reduction in dosage.

Overdosage: Toxic effects are anticholinergic in nature and the treatment is gastric lavage, cholinergics such as carbachol, anticholinesterases such as physostigmine and general non-specific treatment.

Pharmaceutical precautions Normal pharmaceutical storage and handling are indicated.

Legal category POM.

Package quantities *Tablets:* 100 × 50 mg, 250 × 50 mg, 1,000 × 50 mg, 10,000 × 50 mg.

Ampoules: 10 × 40 mg/2 ml.

Further information Although very rarely reported, there may be provocation of dextropropoxyphene side-effects when that drug is administered concurrently with orphenadrine.

Product licence numbers

Tablets 0166/5001

Injection 0166/5005

ELAMOL* CAPSULES

Presentation Elamol Capsules are presented as grey/orange hard gelatine capsules each containing 80 mg tofenacin hydrochloride, imprinted 'Elamol'.

Uses Antidepressant, for the treatment of mild to moderate depression in the older patient.

Dosage and administration By oral administration.

Adults: Up to 240 mg daily in divided doses as directed by the physician.

Children: Not recommended.

Contra-indications, warnings, etc Contra-indicated in patients with glaucoma or prostatic hypertrophy, or having suicidal tendencies or requiring ECT, or being pregnant; also in patients receiving monoamine oxidase inhibitors. Patients receiving MAOIs should discontinue therapy and allow a period of two weeks to elapse before instituting therapy with Elamol.

Special precautions: Use with caution in patients with micturition difficulties or patients who are receiving other antidepressant drugs or tranquillisers where concurrent administration of Elamol is considered desirable.

Side-effects: Occasionally dry mouth, disturbances of visual accommodation and tremor may occur; these usually disappear spontaneously or may be controlled by a slight reduction in dosage. Other side-effects which have been reported are gastro-intestinal disturbances, drowsiness, vertigo, agitation and skin rashes.

Overdosage: There have been no reports of overdosages; toxic effects would be anticholinergic in nature and the treatment would be gastric lavage, cholinergics such as carbachol, anticholinesterases such as physostigmine and general non-specific treatment.

Pharmaceutical precautions Normal pharmaceutical storage and handling are indicated.

Legal category POM.

Package quantities Capsules 100 x 80 mg.

Further information Nil.

Product licence number 0166/0001.

**LOCOID* CREAM
LOCOID* OINTMENT**

Presentation Locoid Cream, containing 0.1% hydrocortisone 17-butyrate in a cream base.

Locoid Ointment, containing 0.1% hydrocortisone 17-butyrate in an ointment base.

Uses The products are recommended for clinical use in the treatment of conditions responsive to topical corticosteroids, e.g. eczema, dermatitis and psoriasis.

The products are intended for topical application.

Dosage and administration For adults and children, to be applied to the affected part two to four times a day, or as directed by the physician.

Where necessary, application may be made under an occlusive dressing.

Contra-indications, warnings, etc These preparations are contra-indicated in the presence of viral or fungal infections, tubercular or syphilitic lesions, and in bacterial infections unless used in conjunction with appropriate chemotherapy. Contact with the eye should be avoided.

In pregnant animals, administration of corticosteroids can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

In infants, long-term continuous topical therapy should be avoided. Adrenal suppression can occur, even without occlusion.

Pharmaceutical precautions Store under normal pharmaceutical conditions of storage.

Legal category POM.

Package quantities *Locoid Cream:* Tubes of 30 g and 100 g.

Locoid Ointment: Tubes of 30 g and 100 g.

Further information Locoid is a non-fluorinated topical steroid. Whilst clinical trials have shown it to be as effective as the potent fluorinated steroids, in clinical practice there is a low incidence of reported clinical side-effects.

Product licence numbers

Locoid Cream 0166/0058

Locoid Ointment 0166/0059

**LOCROID* C CREAM
LOCROID* C OINTMENT**

Presentation Locoid C cream, containing 0.1% hydrocortisone 17-butyrate and 3% chlorquinaldol, in a cream base.

Locoid C ointment, containing 0.1% hydrocortisone 17-butyrate and 3% chlorquinaldol, in an ointment base.

Uses The products are recommended for clinical use in the treatment of conditions responsive to topical corticosteroids, e.g. eczema, dermatitis and psoriasis, where secondary bacterial or fungal infection is present or suspected, or may complicate the condition.

The products are intended for topical application.

Dosage and administration For adults and children, to be applied to the affected part two to four times a day, or as directed by the physician, until the infection has resolved. If the underlying dermatological condition still persists, treatment may be continued with Locoid cream or ointment.

Contra-indications, warnings, etc *Contra-indications:* These preparations are contra-indicated in the presence of viral, tubercular or syphilitic lesions. Contact with the eye should be avoided.

Warnings: In pregnant animals, administration of corticosteroids can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

In infants, long-term continuous topical therapy should be avoided. Adrenal suppression can occur, even without occlusion.

Occlusive dressings are not recommended in the presence of infections.

Locoid C preparations should not be used for longer than 14 days at a time, nor should more than 60 g be applied during this period.

Pharmaceutical precautions Store under normal pharmaceutical conditions of storage.

Legal category POM.

Package quantities *Locoid C cream*: Tubes of 30 g.

Locoid C ointment: Tubes of 30 g.

Further information Locoid is a non-fluorinated topical steroid. Whilst clinical trials have shown it to be as effective as the potent fluorinated steroids, in clinical practice there is a low incidence of reported side-effects.

Chlorquinaldol is an effective topical antibacterial and antimycotic.

Product licence numbers

Locoid C cream 0166/0056

Locoid C ointment 0166/0057

LOCOID* SCALP LOTION

Presentation Locoid Scalp Lotion contains 0.1% hydrocortisone 17-butyrate in an iso-propyl alcohol/water base, specially formulated for the treatment of skin disorders of the scalp.

Uses In the treatment of steroid-responsive dermatoses of the scalp, including seborrhoea capitis with or without an associated severe dandruff.

Dosage and administration Apply twice daily to the scalp, or as directed.

Contra-indications, warnings, etc These preparations are contra-indicated in the presence of viral or fungal infections, tubercular or syphilitic lesions, and in bacterial infections unless used in conjunction with appropriate chemotherapy. Contact with the eye should be avoided.

In pregnant animals, administration of corticosteroids can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

In infants, long-term continuous topical therapy should be avoided. Adrenal suppression can occur, even without occlusion.

Pharmaceutical precautions Store under normal pharmaceutical conditions of storage.

Legal category POM.

Package quantities Plastic squeeze bottles of 20 ml and 100 ml.

Further information Locoid lotion should be kept away from the eyes, and not used near a fire or naked flame.

Product licence number 0166/0060.

MEDITAR* STICK

Presentation Meditar Stick is presented as a 20 g greenish-brown stick in a twist-up plastic container. The stick consists of a wax base containing 5% coal tar.

Uses Topical treatment of psoriasis and eczema mainly in chronic phases.

Dosage and administration Apply to the affected area once or twice daily or as directed by the physician. When used in conjunction with U.V.B. light, the tar should be removed before exposure to U.V.B. The Meditar Stick softens on contact with skin enabling a thin layer to be applied lightly and accurately to the affected area.

Contra-indications, warnings, etc The use of Meditar is not recommended in generalised pustular psoriasis, infections of the skin or in patients allergic to coal tar.

Coal tar can sensitise the skin to U.V. light which can lead to sunburn. Coal tar should, therefore, be used cautiously in sunlight.

Pharmaceutical precautions Keep in a cool place.

Legal category P.

Package quantities 20 g containers.

Further information Nil.

Product licence number 0166/0106.

PIMAFUCIN* CREAM

Presentation Pimafucin Cream is presented as a white cream in 25 g tubes containing 20 mg/g natamycin (2%).

Uses Antifungal antibiotic for the treatment of candidal infections of the anus, genitalia, skin, nails and oral mucosa, and acute fungal skin infections.

Dosage and administration By topical application.

Adults: Apply two to three times a day. (In cases of chronic paronychia and onychia treatment must continue for several months to prevent relapses.)

Children: As for adults.

Contra-indications, warnings, etc

Contra-indications: None.

Special precautions: None.

Side-effects: None have been reported.

Overdosage: Has not been reported.

Pharmaceutical precautions Normal pharmaceutical storage and handling are indicated.

Legal category POM.

Package quantities Tubes 25 g.

Further information Nil.

Product licence number 0166/5009.

PIMAFUCIN* 1% SUSPENSION

Presentation Pimafucin 1% Suspension is presented as a cream-white sterile suspension in ready-to-use 5 ml dropper bottles containing 10 mg/ml natamycin.

Uses Antifungal antibiotic for the treatment of oral thrush (due to *Candida albicans*) and also for mouth ulcers secondarily infected with *Candida albicans*.

Dosage and administration By local oral administration.

Infants: 4 drops under the tongue after every feed.

Children and adults: 10 drops after each meal, preferably directly on to the lesions.

Contra-indications, warnings, etc

Contra-indications: None.

Special precautions: None.

Side-effects: None have been reported.

Overdosage: Has not been reported.

Pharmaceutical precautions Normal pharmaceutical storage and handling are indicated. Store away from light.

Legal category POM.

Package quantities 5 ml dropper/dispenser.

Further information Nil.

Product licence number 0166/0047.

PIMAFUCIN* 2½% SUSPENSION

Presentation Pimafucin 2½% Suspension is presented as a cream-white sterile suspension in a clear glass 20 ml vial, containing 25 mg/ml natamycin (2½%).

Uses Antifungal antibiotic for the treatment of infections of the lungs and respiratory tract caused by fungi and yeasts, particularly *Aspergillus* spp. and *Candida albicans*.

Dosage and administration By inhalation.

Adults: 2.5 mg natamycin three times a day for four weeks and 2.5 mg twice a day thereafter until a consistently negative sputum culture for the causative organism is obtained. A minimum total treatment period of six weeks is usually necessary. Administration must be made by a power nebuliser. The suspension should be diluted with sterile physiological saline or a sterile mucolytic preparation, and used within 48 hours of preparation.

Children: As for adults.

Contra-indications, warnings, etc

Contra-indications: None.

Special precautions: None.

Side-effects: None have been reported.

Overdosage: Has not been reported.

Pharmaceutical precautions Normal pharmaceutical storage and handling are indicated.

Legal category POM.

Package quantities Vials 20 ml.

Further information Nil.

Product licence number 0166/5010.

PIMAFUCIN* VAGINAL TABLETS

Presentation Pimafucin Vaginal Tablets are presented as creamy-white ovoid vaginal tablets, each containing 25 mg natamycin, imprinted 'Pimafucin'.

Uses Antifungal antibiotic with antitrichomonal activity, for the treatment of vaginal irritation and discharge whether due to candidal, trichomonal or mixed infections.

Dosage and administration By intravaginal administration.

Candida Albicans: One Tablet should be inserted at night, and one in the morning for a total of ten days. Alternatively, one tablet to be inserted nightly for a total of 21 nights.

Trichomonas Vaginalis: One tablet to be inserted nightly for a total of 21 nights.

Children: Not recommended.

Contra-indications, warnings, etc

Contra-indications: None.

Special precautions: Insert with care during pregnancy.

Side-effects: Occasionally local irritation may occur.

Overdosage: Has not been reported.

Pharmaceutical precautions Normal pharmaceutical storage and handling are indicated.

Legal category POM.

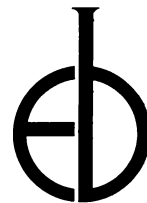
Package quantities Vaginal tablets 20 × 25 mg with applicator.

Further information Nil.

Product licence number 0166/5008.

*Trade Mark

Edwin Burgess Limited
Longwick Road
Princes Risborough
Aylesbury
Buckinghamshire
HP17 9RR



BETIM*

Presentation White, flat circular tablets engraved with '102' on the scored face and with an Assyrian lion on the reverse. Each tablet contains timolol maleate 10 mg.

Uses *Mode of Action:* Betim is a beta-adrenergic receptor blocking agent. It competitively antagonises the action of adrenergic transmitters on beta receptors and thus blocks beta-sympathomimetic activity in the heart, the bronchi and blood vessels.

Betim is considered to be a highly specific beta-adrenergic blocking drug since it does not block the chronotropic or inotropic effects of calcium, glucagon, theophylline or digitalis. It does not have significant local anaesthetic or direct myocardial depressant activity nor any significant beta-adrenergic stimulant effect.

Betim reduces heart rate, force of myocardial contractions and myocardial oxygen consumption. The modification of the cardiac response to stress or exercise is therapeutically useful in angina pectoris.

Betim is also of therapeutic value in hypertension although the mechanism of action is unclear.

Betim is rapidly absorbed from the gut. Its beta blocking activity is apparent within thirty minutes of administration and has been shown to last for up to 24 hours.

Indications: Betim is indicated in angina pectoris due to ischaemic heart disease and for the treatment of hypertension and to reduce mortality and reinfarction in patients surviving acute myocardial infarction. Betim is also indicated in the prophylactic treatment of patients with common and classic migraine in which it effectively reduces the incidence of attacks.

Dosage and administration *For angina and hypertension:* The recommended dose range is 10–60 mg per day. Therapy should begin with a dose of 10 mg daily increasing, if necessary, in steps of 10 mg at intervals of 3–4 days.

Most hypertensive patients will be controlled by 10–30 mg timolol which can be administered once daily or in divided doses if preferred. The dose of Betim may need adjustment when used in conjunction with other antihypertensive drugs.

In angina, Betim should be administered in divided doses.

After myocardial infarction: Start with 5 mg ($\frac{1}{2}$ tablet) twice daily for two days. If there are no adverse reactions, increase dosage to 10 mg twice daily and maintain at this dose.

For the prophylactic treatment of common and classic migraine: 10 to 20 mg once daily or in two divided doses.

Contra-indications, warnings, etc *Contra-indications:* Heart failure, unless adequately controlled. Sinus bradycardia or heart block. Cardiogenic shock. Bronchial asthma, chronic obstructive pulmonary disease. Anaesthesia with agents that produce myocardial depression, such as chloroform and ether. Pregnancy.

Precautions: Although Betim has no direct myocardial depressant activity, the continued depression of sympathetic drive through beta-blockade may lead to cardiac failure. All patients should be observed for evidence of cardiac failure, and, if it occurs, digitalisation and diuretic therapy should be considered.

Betim should be administered with caution to patients subject to spontaneous hypoglycaemia or diabetic patients who are on insulin or oral hypoglycaemic agents.

Beta-adrenergic blockers may mask the premonitory signs and symptoms of acute hypoglycaemia.

Caution is recommended when Betim is administered to patients on catecholamine depleting drugs such as reserpine or guanethidine.

Betim should be administered with caution to patients with impaired renal function or impaired hepatic function. Parasthesiae and coldness of the limb extremities have also been reported.

Side-effects: Gastro-intestinal symptoms (e.g. epigastric distress, nausea, vomiting, diarrhoea), dizziness, insomnia, sedation, depression, weakness, dyspnoea, bradycardia, heart block, bronchospasm and heart failure.

Warning: There have been reports of skin rashes, and/or dry eyes associated with the use of beta-adrenergic blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuation of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with the beta-blocker should be gradual.

Overdosage: The most common signs of overdosage are bradycardia, hypotension, bronchospasm, and acute cardiac failure.

Suggested treatments are as follows:

Severe bradycardia: I.V. atropine sulphate 0.25–2 mg. If bradycardia persists, I.V. isoprenaline 25 mcg may be given.

Severe hypotension: I.V. noradrenaline or adrenaline.

Bronchospasm: Isoprenaline hydrochloride, orciprenaline or salbutamol.

Acute cardiac failure: Digitalis, diuretics and oxygen. In refractory cases I.V. aminophylline and I.V. glucagon 0.5–1 mg have been reported useful.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Packs of 100 tablets.

Further information Timolol maleate crosses the placenta and appears in breast milk.

Product licence number 0748/0015

CENTYL* TABLETS

Presentation *Tablets 2.5 mg:* Each contains 2.5 mg Bendrofluazide BP, white uncoated tablets, no coding marks.

Tablets 5 mg: Each contains 5 mg Bendrofluazide BP, white uncoated tablets, circular groove embossed on one face and score line on other.

Uses *Mode of Action:* Centyl contains the diuretic bendrofluazide, which is as effective as chlorothiazide at 100th the dose and produces a more prolonged diuresis. The diuresis is usually complete in 12–18 hours. In common with other thiazides, it increases the renal excretion of sodium, chloride and to a lesser extent potassium ions, together with an accompanying volume of water.

Indications: *Hypertension:* Control of blood pressure in mild and in some cases of moderate hypertension.

Oedema: Oedema of cardiac, hepatic or renal origin. Pre-menstrual oedema. Toxaemia of pregnancy. Oedema induced by use of steroids.

Dosage and administration *Adults:* Initially, 5–10 mg bendrofluazide once daily. Maintain with 2.5–10 mg daily. Centyl should be taken in the morning to avoid nocturia.

Children: Pro rata, according to age and body weight.

Contra-indications, warnings, etc *Contra-indications:* Anuria. Centyl should not be used in patients with renal failure or with a history of hypersensitivity to thiazides. As with other diuretics, Centyl should not be administered concurrently with lithium salts. Diuretics can reduce lithium clearance resulting in high serum levels of lithium.

Precautions: Thiazide diuretics should be used with caution in patients with renal or hepatic dysfunction. Fluid and electrolyte levels should be measured in patients undergoing prolonged or intense diuresis as potassium depletion may occur and potassium supplements may be needed. Potassium depletion is a particular danger to digitalised patients or those with hepatic cirrhosis with ascites. Periodic testing for urine glucose is advisable in patients with latent or overt diabetes. The dose of hypoglycaemic agents in diabetic patients may require adjustment.

Adverse Reactions: Thiazide diuretics may cause excessive depletion of fluid and electrolytes during prolonged or intense use. Symptoms are muscle pain or fatigue, thirst, gastro-intestinal upset and oliguria. Hypokalaemia is most severe in patients already depleted of potassium, as in renal or hepatic insufficiency.

Coma may be precipitated in hepatic cirrhosis.

The thiazide diuretics may induce hyperglycaemia and glycosuria in diabetic and other susceptible patients. This is usually reversible if the treatment is stopped. Hyperuricaemia sometimes occurs but an attack of gout is rare. The thiazide diuretics increase blood urea which

is most pronounced in patients with renal disease and pre-existing retention of nitrogen.

Reports of other adverse reactions include skin rashes with associated photosensitivity, necrotising vasculitis, acute pancreatitis, blood dyscrasias and aggravation of pre-existing myopia.

Pregnancy: Thiazide diuretics cross the placenta and are secreted in breast milk.

Overdosage: General measures to restore blood volume, maintain blood pressure and correct electrolyte imbalance.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Bottles of 100 tablets.

Further information Nil.

Product licence numbers

Tablets 2.5 mg 0748/5901

Tablets 5 mg 0748/5902

CENTYL* K

Presentation Each tablet contains Bendrofluazide BP (Centyl) 2.5 mg and Potassium Chloride BP 573 mg (7.7 mmol potassium in a slow-release wax core). Green ovoid tablets. No identification marks.

Uses *Mode of Action:* Centyl K is a combination of the diuretic bendrofluazide with a potassium supplement.

Bendrofluazide is as effective as chlorothiazide at 100th the dose and produces a more prolonged diuresis, which is usually complete in 12–18 hours. In common with other thiazides, it increases the renal excretion of sodium, chloride and, to a lesser extent, potassium ions together with an accompanying volume of water. Potassium depletion is frequently associated with prolonged diuretic therapy; a potassium supplement is therefore included in Centyl K. This should minimise potassium depletion.

Because of the risk of localised high concentrations of potassium salts in the small bowel, potassium is included in an inert wax core, from which it is released slowly over several hours. Bendrofluazide is contained in a shell which surrounds the central core.

Indications: *Oedema:* Oedema of cardiac, hepatic or renal origin. Toxaemia of pregnancy.

Hypertension: Control of blood pressure in mild and in some cases of moderate hypertension.

Renal calcium stones: Prophylaxis against recurrent renal calcium stones.

Dosage and administration *Oedema and Hypertension:* Initially 2–4 tablets daily. Maintain with 1–4 tablets daily or on alternate days. Centyl K should be taken in the morning to avoid nocturia.

For renal calcium stones: 2–3 tablets daily.

Contra-indications, warnings, etc *Contra-indications:* Anuria. As with other diuretics, Centyl K should not be administered concurrently with lithium salts. Diuretics can reduce lithium clearance resulting in high serum levels of lithium.

Precautions: Thiazide diuretics should be used with caution in patients with renal or hepatic dysfunction. Fluid and electrolyte levels should be measured in patients undergoing prolonged or intense diuresis. Even

though Centyl K contains a potassium supplement, depletion may occur, which is of particular danger to digitalised patients or those with hepatic cirrhosis with ascites.

Periodic testing for urine glucose is advisable in patients with latent or overt diabetes. The dose of hypoglycaemic agents in diabetic patients may require adjustment. Thiazide diuretics are used to treat hypertension. Therefore it may be necessary to reduce the dose of other hypotensive agents, e.g. reserpine, hydralazine, β -blocking agents and ganglion blocking agents, when used with Centyl K.

Non-specific small bowel lesions characterised by stenosis and possibly accompanied by ulceration have been associated with the oral administration of tablets and capsules containing potassium salts. Symptoms and signs which might indicate ulceration or obstruction of the small bowel in patients taking tablets or capsules containing potassium salts are indications for stopping treatment with such a preparation immediately.

Adverse Reactions: Thiazide diuretics may cause excessive depletion of fluid and electrolytes during prolonged or intense diuresis. Symptoms are muscle pain or fatigue, thirst and dry mouth, gastro-intestinal upset and oliguria. Hypokalaemia is most severe in patients already depleted of potassium, as in renal or hepatic insufficiency. Coma may be precipitated in hepatic cirrhosis. The thiazide diuretics may induce hyperglycaemia and glycosuria in diabetic and other susceptible patients. This is usually reversible if treatment is stopped.

Hyperuricaemia sometimes occurs, but an attack of gout is rare. The thiazide diuretics may increase blood urea, which is most pronounced in patients with renal disease and pre-existing retention of nitrogen.

Reports of other adverse reactions include skin rashes with associated photosensitivity, necrotising vasculitis, acute pancreatitis, blood dyscrasias and aggravation of pre-existent myopia.

Pregnancy: Thiazide diuretics cross the placenta and are secreted in breast milk.

Overdosage: General measures to restore blood volume, maintain blood pressure and correct electrolyte imbalance.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Packs of 100, 500 and 1,000 tablets.

Further information Nil.

Product licence number 0748/5903.

HEPARIN (MUCOUS) INJECTION BP

Presentation Heparin (Mucous) Injection BP 1,000 units per ml: each ml contains 1,000 units sodium heparin. (Presented in 5 ml ampoules without preservative, and 5 ml vials with preservative.)

Heparin (Mucous) Injection BP 5,000 units per ml: each ml contains 5,000 units sodium heparin.

Heparin (Mucous) Injection BP 25,000 units per ml: each ml contains 25,000 units sodium heparin.

Uses *Mode of Action:* Heparin is a naturally occurring anticoagulant which prevents the coagulation of blood in-vivo and in-vitro. It potentiates the inhibition of several activated coagulation factors, including thrombin and factor X.

The anticoagulant properties of heparin are valuable for the prophylaxis and management of intravascular clotting and embolism. It is also used in extra-corporeal circulation i.e. heart-lung and renal dialysis machines and blood transfusions.

In addition to the anticoagulant properties heparin also has some lipaemia-clearing effect which may be utilised in the treatment of fat embolism.

Indications: Treatment of thromboembolic disorders such as: deep vein thrombosis, thrombophlebitis, pulmonary embolism, fat embolism.

Dosage and administration Heparin is usually administered by intravenous injection or subcutaneously. Although the intramuscular route can be used, it is not recommended because of the high incidence of haematomata.

The increase in clotting time provided by heparin becomes apparent immediately after administration and lasts for 4 to 6 hours after intravenous injection and for about eight hours after subcutaneous injection.

Dosage: Intravenous administration: 5,000–10,000 units every 4 hours either by bolus injection or continuous infusion in Sodium Chloride Injection or Dextrose Injection. However, the dose should be monitored with coagulation tests, and varied according to individual response.

Subcutaneous administration: 5,000 units every eight hours.

The treatment period varies from 7–10 days in peri-operative prophylaxis to as much as 6 weeks in the treatment of established thrombosis.

Contra-indications, warnings, etc *Contra-indications:* Haemorrhagic disorders and patients with an actual or potential bleeding site, e.g. peptic ulcer.

Precautions: Heparin therapy should be given with caution to patients about to undergo surgery, and those with impaired renal or hepatic function.

Overdosage: The effect of heparin can be reversed immediately by intravenous administration of a 1% protamine sulphate solution. The quantity of protamine required for neutralisation falls rapidly with the lapse of time after the administration of heparin and can be accurately determined by titration of the patient's plasma, containing heparin, with protamine. If given within 15 minutes of the heparin injection 10 mg of protamine will neutralise 1,000 units of heparin, while 30 minutes after the heparin injection, only 5 mg of protamine per 1,000 units of heparin is needed.

It is important to avoid overdosage of protamine sulphate because protamine itself has anticoagulant properties. A single dose of protamine sulphate should never exceed 50 mg. Intravenous injection of protamine may cause a sudden fall in blood pressure, bradycardia, dyspnoea and transitory flushing, but these may be avoided or diminished by slow and careful administration.

Pharmaceutical precautions Store below 25°C. Admixture of heparin with solutions of other medicinal products may result in precipitation or loss of potency.

Legal category POM.

Package quantities Heparin 1,000 units per ml: 5 ml ampoules (without preservative), 5 ml vials (with preservative). Packs of 5.

Heparin 5,000 units per ml: 5 ml. Packs of 5 vials.

Heparin 25,000 units per ml: 5 ml: 1 vial.

Further information Preservative used: 1,000 units (with preservative) and 5,000 units: 0.5% Chlorbutol. 25,000 units: 0.4% Chlorbutol.

Menstruation and pregnancy are not contra-indications to heparin therapy. Heparin does not cross the placenta or appear in breast milk.

Available for low dose prophylactic use: single dose ampoules containing 5,000 units sodium heparin in 0.2 ml.

Product licence numbers

1,000 units (with preservative)	0748/0007
1,000 units (without preservative)	0748/0040
5,000 units	0748/0008
25,000 units	0748/0009

HEPARIN (MUCOUS) INJECTION BP

5,000 units in 0.2 ml (25,000 units per ml).

Presentation Single dose ampoules containing sodium heparin 5,000 units in 0.2 ml (Preservative: 0.4% Chlorbutol).

Uses *Mode of Action:* Heparin is an anticoagulant which, even in low doses, prevents the formation of thrombin by accelerating the neutralisation of activated factor X by naturally occurring inhibitors.

Indications: Prophylaxis against deep vein thrombosis and thromboembolic events in susceptible patients.

Dosage and administration Administration is by subcutaneous injection. Patients undergoing surgery: 5,000 units in 0.2 ml should be given 2 to 6 hours preoperatively and every 8 hours postoperatively for 10–14 days, or until ambulation, whichever is the longer.

Other patients: 5,000 units in 0.2 ml should be given every 8–12 hours.

Contra-indications, warnings, etc Low doses of heparin, administered as recommended above, do not cause alterations in clotting times in most patients, but occasionally local haematomata may occur at injection sites.

Patients with haemorrhagic disorders may experience bleeding, especially from surgical wounds. The relative risks and benefits of heparin administration in these patients should be assessed carefully. Oral anticoagulants or drugs which interfere with platelet function, e.g. aspirin and dextran solutions, should be administered with caution.

Overdosage: If bleeding should occur, the effect of heparin can be reversed immediately by intravenous administration of a 1% protamine sulphate solution. The dose of protamine sulphate required for neutralisation should be determined accurately by titrating with the patient's plasma.

Pharmaceutical precautions Store below 25°C. Admixture of heparin with solutions of other medicinal products may result in precipitation or loss of potency.

Legal category POM.

Package quantities 15 ampoules of 0.2 ml.

Further information Menstruation and pregnancy are not contraindications to heparin therapy. Heparin does not cross the placenta or appear in breast milk.

Heparin (Mucous) Injection BP is also available in

strengths of 1,000 units per ml (with and without preservative), 5,000 units per ml and 25,000 units per ml.

Product licence number 0748/0011

NATUDERM*

Presentation Natuderm is a white cream. The cream is a stable ambiphilic emulsion system.

Composition: The lipid component (about 35% of total product) contains approximately:

Free fatty acids	14.26%
Squalene	9.4%
Squalane	1.41%
Waxes	19.97%
Sterol Esters	3.81%
Free Sterols	2.37%
Glycerides	44.27%
Phospholipids	0.48%
dl- α -tocopherol	0.0085%
Butylated Hydroxyanisole	0.0085%
Span 60 Sorbitan Monostearate	2.71%
Phenonip	1.27%

The aqueous component (about 65% of total product) contains approximately:

Glycerol	5.63%
Polyoxyethylene Sorbitan Monostearate	1.64%
De-ionised water	92.2%
Phenonip	0.46%

Uses Natuderm is an emollient and protective cream. It has a lipid component similar in composition to human sebum.

Its uses include conditions where skin film emulsion deficiency is a factor.

Indications: As a moisturising emollient and protective for general dermatological use where the secretion of skin film emulsion is deficient.

Dosage and administration A thin application of the cream should be made to the affected area three times daily or as required. It should be rubbed gently into the skin. When used as a protective cream, Natuderm should be applied sparingly to areas of skin at risk, just before or immediately after exposure to potentially harmful factors.

Contra-indications, warnings, etc For external use only. Natuderm is entirely compatible with skin physiology and does not contain unmodified lanolin.

Contra-indications: Nil.

Side-effects: Hypersensitivity is a rare possibility.

Overdosage: Not applicable.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Jars of 40 g and 450 g and tubes of 100 g.

Further information Nil.

Product licence number 0748/0001.

PONDOCILLIN* TABLETS ▼

PONDOCILLIN* SUSPENSION ▼

Presentation *Tablets:* Each tablet contains 500mg pivampicillin – a white film-coated ovoid tablet with the number 128 printed on one side and an Assyrian Lion on the other.

Suspension: Bottles containing powder for the preparation of 50 ml and 100ml suspension. When reconstituted each 5 ml contains 162 mg pivampicillin.

Uses Pondocillin (pivampicillin) is the pivaloyloxy-methyl ester of ampicillin, and is rapidly hydrolysed in the body to ampicillin by non-specific enzymes present in serum, gastro-intestinal mucosa and other tissues.

After oral administration of Pondocillin, the plasma levels of ampicillin are 2–3 times higher than those obtained with equimolar doses of oral ampicillin. The tablets are formulated to disintegrate readily and produce rapid therapeutic plasma levels. A peak level generally occurs after 1 hour compared to approximately 2 hours with oral ampicillin. These levels are comparable to those obtained with an equimolar dose of intramuscular ampicillin.

Concentrations achieved in the urine are similarly raised. Generally, twice the amount of antibiotic can be recovered after treatment with Pondocillin when compared with equimolar doses of oral ampicillin. Whereas between 30–40% of the administered dose appears in the urine in the first 6 hours after oral administration of ampicillin, 70% can be recovered after an equimolar dose of Pondocillin.

Pondocillin is stable in the presence of gastric acid, and, unlike oral ampicillin, absorption is not affected by the presence of food. Plasma concentrations achieved in the post-prandial state do not differ significantly when compared with the fasting state. Like ampicillin, Pondocillin is destroyed by penicillinase-producing bacteria.

Indications: Like ampicillin, Pondocillin has a broad spectrum of activity against both gram-negative and gram-positive organisms. It is particularly indicated for the treatment of infections caused by susceptible strains of *Shigella*, *Salmonella*, *N. gonorrhoea*, *Esch. coli*, *H. influenzae*, *Pr. mirabilis* and is also indicated for pneumococcal, streptococcal and non-penicillinase-producing staphylococcal infections.

Specific infections include:

- (a) Acute and chronic bronchitis
- (b) Pneumonia
- (c) Ear, nose and throat infections
- (d) Gynaecological infections
- (e) Urinary tract infections
- (f) Skin and soft tissue infections
- (g) Gonorrhoea

Dosage and administration *Tablets:* Usual dosage for adults: 500 mg pivampicillin to be administered twice daily. Dosage may be doubled in cases of severe infection. Gonorrhoea: 1.5–2 g pivampicillin as a single dose. 1 g probenecid can be given concurrently as desired. The medication may be taken with food or fluids.

Suspension: Infants under 1 yr: 40–60 mg/Kg body-weight per day.

Children aged 1–5 yrs: 10–15 ml per day

Children aged 6–10 yrs: 15–20 ml per day

Adults and children over 10 yrs: 30ml per day.

The daily dosage may be given either as 2 or 3 equal divided doses.

Dosage may be doubled where appropriate.

Contra-indications, warnings, etc *Contra-indications:* Pondocillin is contra-indicated in any patient with a history of hypersensitivity to any of the penicillins or cephalosporins. Because of the high frequency of exanthemata associated with ampicillin therapy in infectious mononucleosis, treatment with Pondocillin is contra-indicated in this disease.

Pondocillin is also contra-indicated in infections caused by penicillinase producing bacteria.

Precautions: Care should be exercised when treating patients with a history of sensitivity to a variety of allergens, since serious hypersensitivity (anaphylactic) reactions are more likely to occur. If lymphatic leukaemia is treated with Pondocillin then caution is urged because of the frequency of exanthemata associated with ampicillin therapy.

The use of concurrent antacid therapy with Pondocillin is not recommended, since it reduces absorption of the antibiotic, and may cause underdosing.

During long-term therapy it is advisable to carry out routine liver and kidney function tests.

Pregnancy: In keeping with current practice use during the first trimester of pregnancy should be avoided. Ampicillin crosses the placenta and small amounts have been detected in breast milk.

Adverse Reactions: Pondocillin is a compound of low toxicity. Like ampicillin, skin rashes of two types have been noted: a non-specific erythema which usually disappears during treatment, and urticaria which may cause withdrawal of the drug. Anaphylactic reactions have occurred as with other penicillins.

Upper gastro-intestinal disturbances, such as nausea, vomiting, retrosternal pain and flatulence have occurred more frequently when a dose has been given on an empty stomach. Diarrhoea has been reported, but less frequently than with ampicillin. This observation underlines the importance of giving Pondocillin with or just after a meal. None of these effects appear to be dose-related. Other side effects reported are dizziness and pruritis.

Warning: Pondocillin suspension is not recommended for the treatment of severe infections in infancy.

Overdosage: There is no experience of overdosage with Pondocillin. However, excessive doses of Pondocillin are likely to induce nausea, vomiting and gastritis. Treatment should be restricted to symptomatic and supportive measures.

Pharmaceutical precautions *Tablets:* Nil.

Suspension: Pondocillin suspension when reconstituted, is stable for 14 days at room temperature or for 4 weeks when kept in a refrigerator.

Legal category POM.

Package quantities *Tablets:* Bottles of 100 and 20 tablets.

Suspension: Available in amber bottles making 50 ml and 100 ml suspension when dispensed.

Further information Nil.

Product licence numbers

Tablets 0748/0019

Suspension 0748/0020

TENAVOID* TABLETS

Presentation Each tablet contains Bendrofluazide BP 3 mg, Meprobamate BP 200 mg. Orange, ovoid coated tablets. No identification marks.

Uses *Mode of Action:* Bendrofluazide is an effective diuretic which alleviates the mastalgia and abdominal and pelvic discomfort often associated with the premenstrual tension syndrome.

Meprobamate is included to minimise the psychological component of the syndrome.

Indications: Pre-menstrual tension.

Dosage and administration *Adults:* 1 tablet three times daily beginning five to seven days before the expected onset of the period.

Contra-indications, warnings, etc *Contra-indications:* Because of the meprobamate content, Tenavoid should not be used in epileptic patients or in patients in whom habituation to meprobamate has occurred.

As with other diuretics, Tenavoid should not be administered concurrently with lithium salts. Diuretics can reduce lithium clearance resulting in high serum levels of lithium.

Pregnancy:

Tenavoid should not be used in patients with a history of hypersensitivity to the active ingredients.

Precautions: Because Tenavoid is used intermittently electrolyte disturbance is uncommon. However, it may be desirable to monitor serum electrolytes, particularly serum potassium, in patients undergoing regular Tenavoid therapy. Potassium supplements may be particularly necessary in digitalised patients.

Periodic testing for urine glucose is advisable in patients with latent or overt diabetes. The dose of hypoglycaemic agents in diabetic patients may need adjustment.

Adverse Reactions: Prolonged courses of thiazides may cause depletion of fluid and electrolytes, but these

symptoms should normally not occur during the intermittent treatment of premenstrual tension.

Coma may be precipitated in hepatic cirrhosis. The thiazide diuretics may induce hyperglycaemia and glycosuria in diabetic and other susceptible patients. This is usually reversible if treatment is stopped. Hyperuricaemia sometimes occurs, but an attack of gout is rare.

Skin rashes with associated photosensitivity, necrotising vasculitis, acute pancreatitis, blood dyscrasias and aggravation of pre-existent myopia have been reported.

Drowsiness is the most common adverse effect of meprobamate use. Other effects include skin rashes, headache, nausea, vomiting, blood disorders and hypotension. Habituation to meprobamate and precipitation of epileptic convulsions on withdrawal of the drug have been reported.

Overdosage: For bendrofluazide general measures should be taken to restore blood volume, maintain blood pressure and correct electrolyte disturbance.

With reference to the meprobamate content, raise the urine flow rate by increasing diuresis or by using haemodialysis in severe cases of overdosage.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Pack of 24 tablets.

Further information Both bendrofluazide and meprobamate cross the placenta and are detected in cord blood and breast milk.

Product licence number 0748/5900

**Trade Mark*

Calmic Medical Division The Wellcome Foundation Limited Crewe Hall Crewe, Cheshire CW1 1UB



AEROSPORIN*

Presentation Each rubber-capped vial contains 500,000 i.u. of sterile freeze-dried Polymyxin B Sulphate BP.

Uses Bactericidal antibiotic.

In systemic, urinary tract, meningeal, and local infections caused by a wide range of susceptible Gram-negative organisms, particularly *Pseudomonas aeruginosa*.

Dosage and administration *Intrathecal administration* (for meningitis).

Adults and children over 2 years: 50,000 to a maximum of 100,000 units once daily.

Children under 2 years: 20,000 to a maximum of 40,000 units once daily. Administer the appropriate dosage in 1–2 mls of 0.9% sterile sodium chloride solution.

Treatment should continue daily until the cerebrospinal fluid is sterile and then on alternate days for 1–3 weeks.

If systemic infection is present, concurrent parenteral therapy is required.

Intravenous administration – Adults and children: 15,000–25,000 units per kg. bodyweight per day. Total daily dosage must not exceed 2,000,000 units.

No dosage information is available for intravenous administration in neonates.

The total daily dose may be given as a continuous infusion or as 2 infusions per day each for 1–2 hours and given 12 hours apart. 5% Dextrose in water is recommended as the diluent.

Intramuscular administration – Adults and children: 15,000 to 25,000 units per kg bodyweight per day. Total daily dosage must not exceed 2,000,000 units.

Neonates: 15,000–45,000 units per kg bodyweight per day.

The total daily dose should be given in 4 equally divided doses at 6-hourly intervals. 1–2 mls of water for injection, 0.9% sterile sodium chloride or 1% sterile procaine hydrochloride solution should be used as diluent.

Dosage in renal failure:

<i>Creatinine clearance</i>	<i>Dosage (units/kg/day)</i>
Normal or 80% of normal	25,000
80% to 30% of normal	1st day: 25,000 Daily thereafter 10,000–15,000
25% of normal	1st day: 25,000 Every 2–3 days thereafter 10,000–15,000
Anuria	1st day: 25,000 Every 5–7 days thereafter 10,000

Patients with impaired renal function excrete the drug more slowly and an appropriate adjustment in the intravenous or intramuscular dosage should be made. The table above gives guidelines based on creatinine clearance. Additional guidance should be obtained by regular monitoring of serum levels of polymyxin B and renal function. The serum level of polymyxin B should be kept below 10 µg/ml.

Local administration: A solution of 0.1–1% (approximately 10,000–100,000 units/ml) in sterile saline or an ointment or cream of similar strength is recommended. When used as a solution it may be applied either as drops, as a wet dressing, as a spray, by irrigation or as an aerosol.

Inhalation of an aerosol containing Aerosporin is particularly valuable in treating pulmonary infections due to *Ps. aeruginosa*, *E. coli* and *H. influenzae*. Inhalation of 1–2 ml of solution of 1,000–10,000 i.u. per ml in sterile saline or 5% dextrose in water four to eight times daily is recommended. The total amount given per day should not be more than that used parenterally.

For the treatment of superficial eye infections Aerosporin may be applied in the form of eye drops or by subconjunctival injection:

Eye drops: 3 drops of a 0.1% solution in sterile water or 0.9% sodium chloride solution should be instilled hourly, then less frequently depending on the response.

Subconjunctival injection: Up to 100,000 units per day is recommended, administered in water for injection or sterile 0.9% sodium chloride solution. A concentration of 500,000 units per ml is suggested and not more than 1 ml of diluent should be administered per injection.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to polymyxins.

Precautions: Nephropathy and neuropathy may result from the use of this drug. It may therefore be advisable to monitor renal function before and during parenteral therapy.

The concomitant use of other potentially nephrotoxic drugs should be avoided if possible.

Due to the possibility of neuromuscular blockade leading to respiratory paralysis and apnoea, caution is advised in the administration of other agents with a similar action (eg muscle relaxants, general anaesthetics, antibiotics with muscle relaxant properties).

Side- and adverse effects: Occasionally mild drug fever and a variety of skin eruptions, including urticaria, have been reported after parenteral therapy. Allergic reactions after topical application are rare.

Local pain at the injection site may occur when the drug is given intramuscularly. Subconjunctival injection may also be painful. Intrathecal injection may cause meningeal irritation, particularly in daily doses above 50,000 units and the patient should be observed for reactions.

Polymyxin B may cause nephrotoxicity. This effect is

dose-related and rarely a serious clinical problem in patients with adequate renal function receiving recommended doses; it is usually reversible on discontinuation of the drug.

Neurological symptoms of varying intensity may occur. There may be circumoral and peripheral paraesthesia, some dizziness and a feeling of weakness without, however, any objective signs. These effects are transient and disappear within 48 hours of stopping treatment.

Use in pregnancy and lactation: The safety of Aerosporin in pregnancy has not been established. No information is available on its excretion in breast milk.

Toxicity and treatment of overdose: Antihistamines may relieve some of the subjective symptoms. If respiratory paralysis occurs, artificial respiration should be instituted. There is some evidence that haemodialysis lowers serum levels of the drug. However, the value of this procedure is open to doubt due to tissue localisation of the antibiotic.

Pharmaceutical precautions Store in a dry place, below 25°C. Protect from light. Use immediately after reconstitution.

Legal category POM.

Package quantities Rubber-capped vial of 500,000 i.u.

Further information It is desirable to continue therapy until the lesions are healed; otherwise infecting organisms may reappear if the antibiotic is withdrawn too soon.

In the strengths recommended, Aerosporin is not irritating to delicate tissues such as the eye, mucous membranes or granulating surfaces.

Product licence number 0003/5006.

ANECTINE* INJECTION

Presentation Solution of Suxamethonium Chloride BP 100 mg in 2 ml.

Uses Short-acting depolarising neuromuscular blocking agent for producing muscular relaxation during anaesthesia.

Dosage and administration *Adults:* In most cases an intravenous dose of 60–100 mg will paralyse for about three to five minutes. For continuous drip administration, solutions of 0.1–0.2% of suxamethonium chloride have been employed. Tachyphylaxis may occur after approximately one hour. After a full relaxing dose for intubation the effects have been maintained by infusions of 2.5–4 mg per minute.

Children: Proportionate reduction according to weight. Neonates and premature infants may be relatively resistant to Anectine and develop phase II block more readily.

Contra-indications, warnings, etc

Contra-indications: Since Anectine may cause a rise in intra-ocular pressure it is contra-indicated in patients with glaucoma, detached retina or open eye injury.

Anectine injection is followed by a rise in serum potassium concentration, which may be important in patients with pre-existing hyperkalaemia, for instance, due to renal impairment. The hyperkalaemic response may be excessive, and possibly lead to cardiac arrest in patients with a history of severe burns or trauma several

weeks previously and in patients with an upper or lower motor neurone lesion of a nerve supplying a large muscle mass, spinal cord injuries, tetanus, congenital cerebral palsy and pseudo-hypertrophic muscular dystrophy. Anectine is generally contra-indicated in these patients.

Precautions: Since Anectine causes paralysis of the respiratory muscles it should only be used in the presence of an experienced anaesthetist and when resuscitative equipment is immediately available.

In normal patients Anectine is rapidly hydrolysed by serum cholinesterase. Its action may therefore be prolonged in patients with conditions leading to a reduction in this enzyme, and in individuals with a congenital absence or deficiency of cholinesterase. In such cases respiration must be artificially supported or maintained until it has returned spontaneously and fully.

Anectine should be used with caution, if at all, in the presence of certain major neurological and muscular disorders such as myotonia dystrophica, muscular dystrophy and the myasthenic syndrome. Its action is prolonged by neostigmine, procaine, lignocaine, procainamide, propanidid, quinidine, promazine, diethyl ether, tacrine and hexafluorenum. Its action is opposed by d-tubocurarine, gallamine, cyclopropane, halothane and trifluoperazine.

Side- and adverse effects: Anaphylaxis and bronchospasm have been reported following Anectine.

Anectine may cause bradycardia and, more rarely, tachycardia and increased blood pressure. It is recommended that atropine is given as a premedication prior to the administration of Anectine.

Post-operative muscular pains may occur, particularly in ambulant patients. Some anaesthetists employ small doses of a non-depolarising relaxant prior to administering Anectine as it is believed this will reduce the possibility of muscular pain.

Malignant hyperthermia has followed the use of Anectine in susceptible patients.

Use in pregnancy and lactation: Anectine is generally considered safe in obstetrics although some infants may show decreased respiration and tonus. Anectine is poorly absorbed orally and is unlikely to present a problem in breast-fed infants.

Toxicity and treatment of overdose: The main problem is likely to be prolonged apnoea. Institute general support of respiration until spontaneous recovery.

Pharmaceutical precautions Anectine is rapidly destroyed by alkalis. Although it can be mixed with thiopentone sodium solutions immediately before injections, this is inadvisable because suxamethonium may act before thiopentone. Store below 4°C. Protect from light. Do not freeze.

Legal category POM.

Package quantities Box of 5 × 2 ml ampoules.

Further information Nil.

Product licence number 0003/5203.

CALPOL* SUSPENSION

Presentation Each 5 ml dose contains 120 mg Paracetamol BP in a pleasantly-flavoured pink suspension.

Uses For the relief of pain (including teething pain) and feverishness.

Dosage and administration *Children 3–12 months:* 5 ml four times daily.

1 year to under 6 years: 10 ml four times daily.

6 years to under 12 years: 20 ml four times daily.

Not more than 4 doses should be administered in any 24-hour period; do not repeat doses more frequently than 4-hourly. Dosage for children under 3 months is at physician's discretion.

Contra-indications, warnings, etc

Contra-indications: None known.

Precautions: To be used with caution in the presence of renal or hepatic dysfunction.

Side- and adverse effects: Side-effects with Calpol are rare in therapeutic doses. Paracetamol has been widely used and reports of adverse reactions are rare and are generally associated with overdosage. Isolated cases of thrombocytopenic purpura, methaemoglobinaemia and agranulocytosis have been recorded. Nephrotoxic effects are uncommon and have not been reported in association with therapeutic doses except after prolonged administration. Overdosage may cause hepatic necrosis.

Use in pregnancy and lactation: There is epidemiological evidence of safety with paracetamol in human pregnancy. Paracetamol is excreted in breast milk but not in clinically significant quantities.

Toxicity and treatment of overdosage: Even in severe cases, initial symptoms are likely to be mild and may comprise pallor, nausea and vomiting. Liver damage may not become apparent until 24 hours to 6 days after ingestion.

Overdosage should therefore be treated promptly by gastric lavage followed by i.v., N-acetylcysteine or oral methionine. Additional therapy (further methionine, i.v. N-acetylcysteine or i.v. cysteamine) is normally considered in the light of blood paracetamol content and the time elapsed since ingestion. Such therapy is probably best undertaken in a specialised unit.

Pharmaceutical precautions Store below 25°C. Protect from light.

Legal category P.

Package quantities Bottles of 70 ml, 140 ml and 1 litre.

Further information Nil.

Product licence number 0003/5067.

CICATRIN* AEROSOL

Presentation Each gram contains:

Neomycin Sulphate BP	16,500 units
Zinc Bacitracin BP	1,250 units
L-Cysteine	12 mg
Glycine	60 mg

Uses Topical broad-spectrum antibacterial.

Superficial bacterial infections of skin.

Dosage and administration *Adults:* A thin, uniform spray should be applied to affected areas, as required. This can be obtained from a spray of about one second's duration to the wound surface at a distance of not less than 20 cm. The application of one can of spray daily for a maximum period of 10–12 weeks should not be exceeded in adults. After such a course, treatment should not be repeated for at least three months.

Children: The maximum dosage should be reduced in proportion to body weight.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to bacitracin or the neomycin group of antibiotics.

Precautions: The following statements take into account the possibility that the constituent drugs of Cicatrin Aerosol, particularly neomycin, may be absorbed to a significant degree after topical application.

Ototoxicity and nephrotoxicity have been reported in association with large or prolonged doses of neomycin and nephrotoxicity has also been reported with inappropriate dosing with bacitracin. While these effects are normally reversible on cessation of therapy, the ototoxic effect of neomycin is not.

In cases where there is established partial nerve deafness and where a significant degree of neomycin absorption could occur it might be inappropriate to use any neomycin-containing product and treatment with an antibacterial without an aminoglycoside constituent should be used if possible. In renal impairment the plasma clearance of neomycin is reduced, therefore a reduction in dose should be made that relates to the degree of renal impairment.

The inappropriate use of topical antibiotics has been associated with the emergence of resistant strains of bacteria.

The spray should not be used on large denuded areas (e.g. burns or ulcers) because of the risk of systemic absorption.

Concurrent administration of other aminoglycoside antibiotics is not recommended.

As neomycin has a neuromuscular blocking effect, patients concurrently receiving other agents with a similar action should be observed for signs of possible respiratory insufficiency.

Side- and adverse effects: Allergic reactions following the topical application of neomycin have been reported in the literature, but such reactions following the application of zinc bacitracin are rare events.

Use in pregnancy: Due to a lack of detailed information, the use of Cicatrin during pregnancy cannot be recommended in circumstances where significant systemic absorption of the active ingredients may occur.

Toxicity and treatment of overdosage: In the event of signs of toxicity developing following significant systemic absorption of the active ingredients of Cicatrin aerosol the patient's general status, hearing acuity and renal function should be monitored and blood levels of neomycin and zinc bacitracin determined. Serum levels of neomycin can be reduced by haemodialysis.

Pharmaceutical precautions Store below 25°C. Keep away from heat. Do not puncture or incinerate.

Legal category POM.

Package quantities Aerosol pack. Net content of powder 3 g approx.

Further information Nil.

Product licence number 0003/5083

**CICATRIN* POWDER
CICATRIN* CREAM**

Presentation Each gram of powder/cream contains:

Neomycin Sulphate BP 3,300 units

Zinc Bacitracin BP	250 units
L-Cysteine	2 mg
Glycine	10 mg
dl-Threonine	1 mg

Uses Topical broad-spectrum antibacterial.

Superficial bacterial infection of skin, such as impetigo, varicose ulcers, pressure sores, trophic ulcers and burns.

Dosage and administration *Adults:* A light dusting of the powder or thin layer of the cream should be applied to the affected skin area up to three times daily. See Contra-indications, warnings, etc.

Children: As for adults.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to bacitracin or the neomycin group of antibiotics.

Precautions: The following statements take into account the possibility that the constituent drugs of Cicatrin Powder/Cream, particularly neomycin, may be absorbed to a significant degree after topical application.

Ototoxicity and nephrotoxicity have been reported in association with large or prolonged doses of neomycin and nephrotoxicity has also been reported with inappropriate dosing with bacitracin. While these effects are normally reversible on cessation of therapy the ototoxic effect of neomycin is not. In consequence, the application of two 30 g tubes of the cream daily for three weeks, or one 50 g puffer pack of the powder daily for four weeks should not be exceeded in adults. After such a course, treatment should not be repeated for at least three months. In children this maximum dosage should be reduced in proportion to body weight.

In renal impairment the plasma clearance of neomycin is reduced, therefore a reduction in dose should be made that relates to the degree of renal impairment.

In cases where there is established partial nerve deafness and where a significant degree of neomycin absorption could occur it might be inappropriate to use any neomycin-containing product and treatment with an antibacterial without an aminoglycoside constituent should be used if possible.

Concurrent administration of other aminoglycoside antibiotics is not recommended.

As neomycin has a neuromuscular blocking effect, patients concurrently receiving other agents with a similar action should be observed for signs of possible respiratory insufficiency.

Side- and adverse effects: Allergic reactions following the topical application of neomycin have been reported in the literature, but such reactions following the application of zinc bacitracin are rare events.

Use in pregnancy: Due to a lack of detailed information, the use of Cicatrin during pregnancy cannot be recommended in circumstances where significant systemic absorption of the active ingredients may occur.

Toxicity and treatment of overdose: In the event of signs of toxicity developing following significant systemic absorption of the active ingredients of Cicatrin Powder/Cream the patient's general status, hearing acuity and renal function should be monitored and blood levels of neomycin and zinc bacitracin determined. Serum levels of neomycin can be reduced by haemodialysis.

Pharmaceutical precautions Store below 25°C. Keep dry.

Legal category POM.

Package quantities *Cicatrin Powder:* Puffer packs of 15 g and 50 g.

Cicatrin Cream: Tubes of 15 g and 30 g.

Further information Nil.

Product licence numbers

Powder 0003/5081.

Cream 0003/5082.

COPARVAX* ▼

Presentation Each vial contains 7 mg (dry weight on the *Corynebacterium parvum* organisms (inactivated) WFL strain CH 6134) in a freeze-dried form. Thiomersal and glycine are added to concentrations of 0.01% and 2.3% prior to freeze-drying.

Uses Coparvax is indicated for the alleviation of malignant pleural effusions and malignant ascites.

Dosage and administration The recommended dose is 7–14 mg, although some patients have responded to lower doses.

Freeze-dried Coparvax should be reconstituted with 1 ml of physiological saline for injection and diluted in a further volume of 10–20 ml prior to injection into the pleural or peritoneal cavity.

Coparvax is injected into the pleural or peritoneal cavity via the paracentesis needle immediately after the effusion has been aspirated. Instillation of Coparvax may be repeated, if necessary, at intervals of one to four weeks.

The suspension should be administered within 24 hours of reconstitution.

Contra-indications, warnings, etc

Contra-indications: There are no specific contra-indications.

Precautions: The incidence and severity of side-effects attributable to Coparvax administered intrapleurally appears to be intensified if given within 10 days of thoracotomy and lung resection probably due to enhanced systemic absorption of Coparvax. It should not be given during the immediate post-operative period.

Following intrapleural or intra-abdominal administration, leakage of Coparvax into subcutaneous tissues may result in local tenderness. Intense fibrinous reaction in the pleural and peritoneal cavities has been observed following local administration of Coparvax. Intestinal obstruction due to the formation of adhesions is a theoretical possibility, although it has not been reported as a complication of Coparvax administration.

Side- and adverse effects: Fever occurs in 10 to 40% of patients following intracavitary injection of Coparvax.

Abdominal pain or mild abdominal discomfort has been reported in some 20% of patients following intraperitoneal injection of Coparvax. Nausea and vomiting may occur in a minority of patients following intracavitary administration of Coparvax.

Use in pregnancy: Since there is no laboratory or clinical data on mutagenicity of teratogenicity, Coparvax should not be administered during pregnancy.

Pharmaceutical precautions Store between 2 and 8°C. Do not freeze.

Legal category POM.

Package quantities Single vials of 7 mg.

Further information Nil.

Product licence number 0003/0097.

CYCLIMORPH* 10 INJECTION CYCLIMORPH* 15 INJECTION

Presentation Cyclimorph 10 Injection contains morphine tartrate 10 mg, cyclizine tartrate 50 mg, in 1 ml.

Cyclimorph 15 Injection contains morphine tartrate 15 mg, cyclizine tartrate 50 mg, in 1 ml.

Uses Cyclimorph Injection is indicated in all medical and surgical conditions where cyclizine is needed in addition to morphine. Cyclimorph contains cyclizine, a non-phenothiazine anti-emetic, which minimises the nausea and vomiting which may be caused by the narcotic. It is particularly useful in the management of myocardial infarction where control of nausea and vomiting is also clearly desirable. Cyclimorph can also be used for the relief of severe pain; left ventricular failure, pulmonary oedema, shock, and post-operative sedation.

Dosage and administration *Adults and children over 12 years:* Usual adult dose – 10–20 mg morphine tartrate subcutaneously, intramuscularly or intravenously.

Children 6–12 years: 5–10 mg morphine tartrate as a maximum single dose.

1–5 years: 2.5–5 mg morphine tartrate as a maximum single dose.

If required, repeat not more often than 4-hourly with not more than 3 doses (representing 150 mg cyclizine tartrate) in any 24-hour period.

Contra-indications, warnings, etc

Contra-indications: Respiratory depression; obstructive airways disease. Concurrent administration with monoamine oxidase inhibitors or within 2 weeks of their discontinuation.

Precautions: Use reduced dosage in the elderly, in hypothyroidism and chronic hepatic disease. Administration during labour may cause respiratory depression in the new-born infant.

Side- and adverse effects: Tolerance and dependence may occur. Drowsiness, dry mouth and blurred vision may occur in a small number of patients, due to the cyclizine component.

Use in pregnancy and lactation:

Morphine: There is inadequate evidence of safety in human pregnancy but the drug has been widely used for many years without apparent ill consequence and animal studies have not shown any hazard. No data available on its excretion in breast milk.

Cyclizine: There is some clinical evidence of safety in human pregnancy. No data available on its excretion in breast milk.

Toxicity and treatment of overdose: These are likely to consist of respiratory depression, hypotension, with circulatory failure and deepening coma.

Naloxone, given intravenously, intramuscularly or subcutaneously, effectively antagonises the toxic effects of morphine. The circulation should be maintained with infusions of dextrose and suitable electrolyte solutions. Assisted respiration may be required.

Note: The use of the specific antidote in addicts tolerant to morphine may produce withdrawal symptoms.

Pharmaceutical precautions Store below 25°C, protect from light.

Legal category POM, MDA.

Package quantities *Cyclimorph 10 Injection;* 1 ml ampoules: Box of 5.

Cyclimorph 15 Injection; 1 ml ampoules: Box of 5.

Further information Nil.

Product licence numbers

Cyclimorph 10 0003/5022.

Cyclimorph 15 0003/5023.

DICONAL* TABLETS

Presentation Each tablet contains 10 mg of Dipiprone Hydrochloride BP and 30 mg of Cyclizine Hydrochloride BP, coloured deep pink, scored and coded 'Wellcome F3A'.

Uses Analgesic with anti-emetic action.

Indicated in those medical and surgical conditions where morphine would normally be used. It also contains cyclizine, an anti-emetic which effectively overcomes the nausea and vomiting which may be caused by the narcotic. Often effective in patients who have ceased to respond to morphine or pethidine.

Dosage and administration *Adults:* In all cases an initial dose of 1 tablet should not be exceeded. The onset of action is within an hour and adequate relief from a single dose will last about six hours. The dose can be repeated every six hours if necessary. Should the initial dose prove inadequate, as in cases of severe intractable pain or where other potent analgesics have been used previously, the dose may be increased subsequently by $\frac{1}{2}$ tablet increments. It will seldom be necessary to exceed a dose of 3 tablets.

Children: Not applicable.

Contra-indications, warnings, etc

Contra-indications: Respiratory depression, obstructive airways disease. Concurrent administration with monoamine oxidase inhibitors or within 2 weeks of their discontinuation.

Precautions: Use with caution in patients with severe liver or kidney diseases.

As with all potent analgesics the possibility of addiction cannot be excluded and the usual precautions should be observed.

As with morphine-type drugs respiratory depression is a hazard. Particular care should therefore be taken when increasing the dosage and when treating patients with impaired respiration. Concurrent administration with other CNS depressants including alcohol may enhance the central effects of Diconal.

Side- and adverse effects: Cyclizine may cause drowsiness, dryness of the mouth and blurred vision in a small number of patients.

Use in pregnancy and lactation: No data are available on the use of Diconal in human pregnancy nor of the excretion of it or its metabolites in human milk. Its administration to pregnant or lactating mothers is best avoided unless there are compelling reasons for its use.

Toxicity and treatment of overdose: The main problem with overdose is likely to be respiratory depression. Depressed respiration can be counteracted by the administration of naloxone. Gastric lavage. Oxygen and respiratory support if necessary.

Pharmaceutical precautions Store below 25°C. Protect from light. Keep dry.

Legal category POM, MDA.

Package quantities Bottle of 100 tablets.

Further information Nil.

Product licence number 0003/5027.

DRAPOLENE* CREAM

Presentation Benzalkonium chloride 0.01%, cetrimide 0.2%, in a pink, water-miscible, cream base.

Uses Prevention and treatment of urinary ammonia dermatitis, particularly nappy rash, treatment of minor burns and wounds.

Dosage and administration *Adults:* To be applied twice daily.

Children: To be applied evenly at each nappy change, particular attention being paid to the folds of the skin.

Before applying Drapolene, the affected area should be dry and free from all traces of soap.

Contra-indications, warnings, etc

Contra-indications: Patients with a hypersensitivity to either of the constituents.

Side- and adverse effects: Allergic reactions to Drapolene are rare.

Toxicity and treatment of overdosage: Not applicable.

Pharmaceutical precautions Store below 25°C.

Legal category GSL.

Package quantities Tubes of 55 g and 100 g. Jar of 500 g.

Further information Nil.

Product licence number 0003/5069.

ESBATAL* TABLETS

Presentation

1. Esbatal Tablets containing 10 mg Bethanidine Sulphate BP in each tablet. Peach coloured, scored and coded 'Wellcome P3A'.

2. Esbatal Tablets containing 50 mg Bethanidine Sulphate BP in each tablet. Peach coloured, scored and coded 'Wellcome T3A'.

Uses Antihypertensive agent.

Esbatal is an adrenergic neurone blocking agent which acts selectively on peripheral sympathetic nerves.

It is indicated for all grades of hypertension. Because of its speed of action, it is of special value in malignant hypertension, hypertensive crises and hypertensive heart disease.

Adrenergic neurone blockade is apparent within two hours, with peak effect two to four hours later, and usually disappears within 10–12 hours. There may be some cumulative effect where renal function is impaired.

Esbatal has been used successfully in combination with other established antihypertensive agents.

Dosage and administration *Adults:* Blood pressure should be recorded when the patient is standing.

Starting dose – one 10 mg tablet three times daily, after meals. Where necessary the dosage should be

increased by half a tablet three times daily, at intervals, until effective control is obtained. It is seldom necessary to exceed a dosage of 200 mg daily. Diuretics may be given concurrently. For the elderly and patients with a history of a cerebrovascular accident, half the starting dose is recommended.

Where rapid lowering of blood pressure is urgently needed, an initial dose of 20 mg should be increased by 10–20 mg every four to six hours until control is achieved.

Children: Consult manufacturer.

Contra-indications, warnings, etc

Contra-indications: Patients become very sensitive to any circulating sympathomimetic agent after adrenergic neurone blockade. Hence Esbatal is contra-indicated for patients with phaeochromocytoma. Adrenaline, amphetamine or any other sympathomimetic such as, for example, appetite suppressants, should not be used in patients on Esbatal except on the very rare occasion that its action requires antagonising.

Precautions: Special care should be taken when treating hypertension in patients with disease of cerebral or coronary vasculature or with severe renal damage. As Esbatal is excreted mainly by the kidneys, reduced doses may suffice in renal impairment.

Tricyclic antidepressants antagonise the activity of Esbatal thus necessitating larger doses. If simultaneously prescribed tricyclic antidepressants are discontinued, a substantial reduction in Esbatal requirements must be anticipated.

Side- and adverse effects: The beneficial effects of Esbatal derive from reduced peripheral vascular resistance and are most marked in the erect posture. Transient symptoms of a further reduction in resistance such as faintness, sweating, muscle fatigue and headache may occur with sudden changes in posture, excessive exercise and extremes of temperature, all of which should be avoided. Regularly repeated symptoms can be managed by reducing the size of the dose preceding their onset or by taking the dose after a meal. Sometimes Esbatal disturbs the normal ejaculation of semen. After omission of one or two doses normal sexual function returns. Nasal stuffiness and disturbed micturition may occur. It rarely causes diarrhoea.

Use in pregnancy and lactation: Esbatal has been used to treat hypertension during pregnancy with no apparent untoward effect. There are no data on its use in lactating mothers.

Toxicity and treatment of overdosage: The main problem with overdosage would be severe hypotension. Treatment of overdosage is by means of general supportive measures with intravenous injection of plasma. *Slow* intravenous injection of noradrenaline or phenylephrine may be given under expert supervision.

Pharmaceutical precautions Store below 25°C in a dry place.

Legal category POM.

Package quantities *Tablets 10 mg:* Bottles of 100 and 500 tablets.

Tablets 50 mg: Bottle of 100 tablets.

Further information Nil.

Product licence numbers

Tablets 10 mg 0003/5037.

Tablets 50 mg 0003/5038.

FERROMYN* TABLETS FERROMYN* ELIXIR

Presentation Ferromyn Tablets each contain 100 mg of Ferrous Succinate BP (equivalent to 35 mg elemental iron). Orange coloured.

Ferromyn Elixir: each 5 ml contains 106 mg Ferrous succinate BP (equivalent to 37 mg elemental iron). Brown coloured.

Uses For the prevention and treatment of iron-deficiency anaemias.

Dosage and administration *Adults:* 1 tablet three times a day or 5 ml elixir three times a day.

Children: Ferromyn Elixir.

Up to 2 years: Up to 1 ml twice daily.

2-5 years: 2.5 ml three times daily.

5-10 years: 5 ml twice daily.

Over 10 years: As for adults.

Ferromyn Elixir may be diluted with Syrup BP.

Contra-indications, warnings, etc

Contra-indications: No special comments.

Precautions: May be less well absorbed if taken with food. Iron absorption may be impaired by magnesium trisilicate and carbonates.

If Ferromyn and oral tetracycline are given concomitantly, absorption and therefore serum levels of the antibiotic will be reduced. As with other conventional iron preparations, Ferromyn should not be given within 2 to 3 hours of an oral dose of tetracycline.

Side- and adverse effects: Rarely, gastrointestinal upset may occur.

Use in pregnancy and lactation: As pregnancy is frequently an indication for iron therapy there is no reason to expect problems with Ferromyn therapy. Iron is excreted in breast milk but not in clinically significant amounts (about 0.5 mg/day).

Toxicity and treatment of overdose: The initial symptoms of acute overdose with iron are acute gastric disturbance with epigastric pain, nausea, vomiting and diarrhoea. Haematemesis may occur. These features may be followed by profound cardiovascular collapse and acute encephalopathy.

If serum iron levels exceed 5 mg/l within six hours of dosing, then treatment is a matter of urgency.

Lavage should be carried out using a solution of desferrioxamine (2 g/l of warm water) and 5 g of lesferrioxamine (in 50 to 100 ml water) should be left in the stomach. In addition, 1 g should be given twice daily by intramuscular injection. The antidote may be administered by continuous infusion (15 mg/kg/hr) but blood pressure should be monitored to avoid desferrioxamine hypotension.

It is important to maintain an adequate urine flow.

Pharmaceutical precautions *Tablets:* Store below 15°C.

Elixir: Store below 25°C. Protect from light.

Legal category P.

Package quantities *Ferromyn Tablets:* Plastic container of 100 tablets.

Ferromyn Elixir: Bottle of 100 ml.

Further information Nil.

Product licence numbers

Tablets 0003/5086.

Elixir 0003/5088.

FERROMYN* 'B' TABLETS FERROMYN* 'B' ELIXIR

Presentation Ferromyn 'B' Tablets each contain 106 mg Ferrous Succinate BP (equivalent to 37 mg elemental iron), Thiamine Hydrochloride BP 1 mg, Riboflavin BP 1 mg, Nicotinamide BP 10 mg. Chocolate brown coloured.

Ferromyn 'B' Elixir. Each 5 ml contains 106 mg Ferrous Succinate BP (equivalent to 37 mg elemental iron), Thiamine Hydrochloride BP 1 mg, Riboflavin BP 1 mg, Nicotinamide BP 10 mg. Dark brown coloured.

Uses For the prevention and treatment of iron-deficiency anaemias accompanied by vitamin B deficiency.

Dosage and administration *Adults:* 1 tablet or 5 ml elixir three times a day, between meals.

Children: Ferromyn 'B' Elixir.

Up to 2 years: Up to 1 ml twice daily.

2-5 years: 2.5 ml three times daily.

5-10 years: 5 ml twice daily.

Over 10 years: As for adults.

Ferromyn 'B' Elixir may be diluted with Syrup BP.

Contra-indications, warnings, etc

Contra-indications: No special comments.

Precautions: May be less well absorbed if taken with food. Iron absorption may be impaired by magnesium trisilicate and carbonates.

If Ferromyn 'B' and oral tetracycline are given concomitantly, absorption and therefore serum levels of the antibiotic will be reduced. As with other conventional iron preparations, Ferromyn 'B' should not be given within 2 to 3 hours of an oral dose of tetracycline.

Side- and adverse effects: Rarely gastrointestinal upset may occur.

Use in pregnancy and lactation: As pregnancy is frequently an indication for iron therapy there is no reason to expect problems with Ferromyn 'B' therapy. Iron is excreted in breast milk but not in clinically significant amounts (about 0.5 mg/day).

Toxicity and treatment of overdose: The initial symptoms of acute overdose with iron are acute gastric disturbance with epigastric pain, nausea, vomiting and diarrhoea. Haematemesis may occur. These features may be followed by profound cardiovascular collapse and acute encephalopathy.

If the serum iron levels exceed 5 mg/l within six hours of dosing, then treatment is a matter of urgency.

Lavage should be carried out using a solution of desferrioxamine (2 g/l of warm water) and 5 g of desferrioxamine (in 50 to 100 ml water) should be left in the stomach. In addition, 1 g should be given twice daily by intramuscular injection. The antidote may be administered by continuous infusion (15 mg/kg/hr) but blood pressure should be monitored to avoid desferrioxamine hypotension.

It is important to maintain an adequate urine flow.

Pharmaceutical precautions *Tablets:* Store below 25°C.

Elixir: Store below 25°C. Protect from light.

Legal category P.

Package quantities *Ferromyn 'B' Tablets:* Container of 100 tablets.

Ferromyn 'B' Elixir: Bottle of 100 ml.

Further information Nil.

Product licence numbers

Tablets 0003/5091.

Elixir 0003/5090.

FERROMYN* 'S' TABLETS

Presentation Ferromyn 'S' Tablets each contain 106 mg Ferrous Succinate BP (equivalent to 37 mg elemental iron) and succinic acid 110 mg. Orange coloured.

Uses For the prevention and treatment of iron-deficiency anaemias.

Dosage and administration *Adults:* 1 tablet three times a day.

Children: Not applicable.

Contra-indications, warnings, etc

Contra-indications: No special comments.

Precautions: May be less well absorbed if taken with food. Iron absorption may be impaired by magnesium trisilicate and carbonates.

If Ferromyn 'S' and oral tetracycline are given concomitantly, absorption and therefore serum levels of the antibiotic may be reduced. As with other conventional iron preparations, Ferromyn 'S' should not be given within 2 to 3 hours of an oral dose of tetracycline.

Side- and adverse effects: Rarely, gastrointestinal upset may occur.

Use in pregnancy and lactation: As pregnancy is frequently an indication for iron therapy there is no reason to expect any problems with Ferromyn 'S' therapy. Iron is excreted in breast milk, but not in clinically significant amounts (about 0.5 mg/day).

Toxicity and treatment of overdosage: The initial symptoms of acute overdosage with iron are acute gastric disturbance with epigastric pain, nausea, vomiting and diarrhoea. Haematemesis may occur. These features may be followed by profound cardiovascular collapse and acute encephalopathy.

If the serum iron levels exceed 5 mg/l within six hours of dosing, then treatment is a matter of urgency.

Lavage should be carried out using a solution of desferrioxamine (2 g/l of warm water) and 5 g of desferrioxamine (in 50 to 100 ml water) should be left in the stomach. In addition, 1 g should be given twice daily by intramuscular injection. The antidote may be administered by continuous infusion (15 mg/kg/hr) but blood pressure should be monitored to avoid desferrioxamine hypotension.

It is important to maintain an adequate urine flow.

Pharmaceutical precautions Store below 25°C.

Legal category P.

Package quantities Container of 100 tablets.

Further information Succinic acid is an iron absorption promoter.

Product licence number 0003/5084.

FERROMYN* 'S' FOLIC TABLETS

Presentation Ferromyn 'S' Folic Tablets each contain 106 mg Ferrous Succinate BP (equivalent to 37 mg elemental iron), succinic acid 110 mg and Folic Acid BP 100 mcg. Cerise coloured.

Uses For the prevention and treatment of combined iron and folic acid deficiency states, such as occur in pregnancy.

Dosage and administration *Adults:* 1 tablet three times a day.

Children: Not applicable.

Contra-indications, warnings, etc

Contra-indications: No special comments.

Precautions: May be less well absorbed if taken with food. Iron absorption may be impaired by magnesium trisilicate and carbonates.

If Ferromyn 'S' Folic and oral tetracycline are given concomitantly, absorption and therefore serum levels of the antibiotic will be reduced. As with other conventional iron preparations, Ferromyn 'S' Folic should not be given within 2 to 3 hours of an oral dose of tetracycline.

Side- and adverse effects: Rarely, gastrointestinal upset may occur.

Use in pregnancy and lactation: Since pregnancy is frequently an indication for iron and folic acid therapy there is no reason to expect any problems with Ferromyn 'S' Folic therapy. Iron is excreted in breast milk but not in clinically significant amounts (about 0.5 mg/day).

Toxicity and treatment of overdosage: The initial symptoms of acute overdosage with iron are acute gastric disturbance with epigastric pain, nausea, vomiting and diarrhoea. Haematemesis may occur. These features may be followed by profound cardiovascular collapse and acute encephalopathy.

If the serum iron levels exceed 5 mg/l within six hours of dosing, then treatment is a matter of urgency.

Lavage should be carried out using a solution of desferrioxamine (2 g/l of warm water) and 5 g of desferrioxamine (in 50 to 100 ml of water) should be left in the stomach. In addition, 1 g should be given twice daily by intramuscular injection. The antidote may be administered by continuous infusion (15 mg/kg/hr) but blood pressure should be monitored to avoid desferrioxamine hypotension.

It is important to maintain an adequate urine flow.

Pharmaceutical precautions Store below 25°C.

Legal category POM.

Package quantities Plastic container of 100 tablets.

Further information Succinic acid is an iron absorption promoter.

Product licence number 0003/5085.

HYPON* TABLETS

Presentation Each tablet contains:

Acetylsalicylic Acid BP	325 mg
Caffeine BP	10 mg
Codeine Phosphate BP	5 mg

The tablets are yellow and impressed with the word 'HYPON' on one side.

Uses Analgesic and antipyretic.

For symptomatic relief of pain and fever associated with acute and chronic rheumatism, dysmenorrhoea, neuralgia, tonsillitis, influenza, coryza, headaches, and all conditions where an analgesic is indicated.

Dosage and administration *Adults:* 2 tablets every four hours.

Children 6–12 years: 1 tablet every four hours.

A maximum of 12 tablets to be taken in 24 hours.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to any of the constituents. Contra-indicated in haemophiliacs and in those with active peptic ulcers.

Precautions: Aspirin may prolong labour and contribute to maternal and neonatal bleeding, and is best avoided at term. Aspirin may enhance the effects of oral hypoglycaemics and anticoagulants and inhibit the action of uricosurics. It may precipitate bronchospasm or asthma in susceptible patients. Caution is necessary in renal impairment.

Side- and adverse effects: Occasionally, aspirin may induce hypersensitivity or asthmatic reactions. Gastrointestinal haemorrhages, (occasionally major) have been reported with aspirin. Codeine may sometimes cause constipation.

Use in pregnancy and lactation: No data are available on the use of Hypon in human pregnancy nor on the excretion of it or its metabolites in human milk.

Toxicity and treatment of overdosage: Acute aspirin toxicity would be characterised mainly by vomiting, abdominal pain, tinnitus and hyperventilation. In severe cases, there may be pyrexia and convulsions. Hypoglycaemia and convulsions occur most commonly in children. Respiratory depression from the codeine content may occur.

Treatment comprises gastric aspiration with thorough lavage. Replace fluids and electrolytes as necessary. Forced alkaline diuresis is the treatment of choice for accelerating elimination of absorbed salicylate.

Pharmaceutical precautions Store below 25°C in a dry place.

Legal category P.

Package quantities Strip pack of 12. Drum of 300.

Further information Nil.

Product licence number 0003/0119.

IEOSPORIN* EYE DROPS

Presentation Each ml of the sterile faintly opalescent solution contains:

Polymyxin B Sulphate BP	5,000 units
Neomycin Sulphate BP	1,700 units
Gramicidin USNF	25 units

Also contains Thiomersal BP (0.001%) as preservative.

Uses Topical antibacterial agent.

For the prophylaxis and treatment of external bacterial infections of the eye. Prophylactically, it is useful following removal of foreign bodies, and before and after phthalmic surgery, to help provide and maintain a sterile field.

Dosage and administration *Adults:* 1 or 2 drops in the affected eye, two to four times daily or more frequently as required. In severe infections, therapy

should be started with 1 or 2 drops every 15 to 30 minutes, reducing the frequency of instillation gradually as the infection is controlled.

Children: As for adults.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to polymyxins, gramicidin or the neomycin group of antibiotics.

Precautions: Neomycin is ototoxic and nephrotoxic if absorbed from open surfaces. Polymyxin B and gramicidin are also nephrotoxic. However, these effects are unlikely with ocular administration.

Side- and adverse effects: Allergic reactions following the topical application of neomycin have been reported in the literature, but such reactions following the application of polymyxin B and gramicidin are rare events.

Toxicity and treatment of overdosage: Not applicable.

Pharmaceutical precautions Store below 15°C. Keep dry. Protect from light.

Not suitable for injection. Discard four weeks after opening.

Legal category POM.

Package quantities Special dropper tube of 5 ml.

Further information Neosporin is a non-irritating isotonic solution and is well tolerated by the sensitive structures of the eye.

Product licence number 0003/5108.

OTOSPORIN* DROPS

Presentation Each ml of aqueous vehicle contains:

Polymyxin B Sulphate BP	10,000 units
Neomycin Sulphate BP	3,400 units
Hydrocortisone BP	10 mg

White in colour.

Uses Topical antibacterial and anti-inflammatory.

In the treatment of bacterial infection and inflammation of the external auditory meatus.

Dosage and administration *Adults:* 3 drops should be instilled into the affected ear three or four times daily. Alternatively, a gauze wick may be introduced into the external auditory canal and kept saturated with the solution; the wick may be left in place for 24 to 48 hours.

Children: As for adults.

The external auditory meatus and canal should be thoroughly cleansed and carefully dried before each application, but soap should not be used as the antibiotics may be inactivated by it.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to polymyxins or the neomycin group of antibiotics.

Precautions: Delayed progressive ototoxicity has been reported in animals following administration of neomycin and polymyxin B to the middle ear. In patients who may have a perforation of the ear drum, it is recommended that the dosage should be restricted to a maximum of three drops three times daily for 10 days.

Prolonged use may result in overgrowth of non-susceptible organisms, including fungi.

In infants long-term continuous topical steroid therapy should be avoided. Adrenal suppression can occur, even without occlusion.

Side- and adverse effects: Allergic reactions following the topical application of neomycin have been reported in the literature, but such reactions following the application of polymyxin B are rare events.

Toxicity and treatment of overdosage: Not applicable.

Pharmaceutical precautions Store below 15°C. Protect from light.

Legal category POM.

Package quantities Bottles of 5 ml and 10 ml.

Further information Nil.

Product licence number 0003/5106.

PARAHYPON* TABLETS

Presentation Each tablet contains:

Paracetamol BP	500 mg
Codeine Phosphate BP	5 mg
Caffeine BP	10 mg

The tablets are pink, scored on one side and impressed with the name 'PARA-HYPON' on the other.

Uses Analgesic.

For the relief of pain associated with arthritis, rheumatism and other diseases of the skeletal system, headache, toothache, colds and influenza and other conditions where simple analgesia is required.

Dosage and administration *Adults and children over 12 years:* 2 tablets up to four times daily.

Children 6–12 years: 1 tablet up to four times daily.

Not more than 4 doses should be administered in any 24-hour period; do not repeat dose more frequently than 4-hourly.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to any of the constituents.

Precautions: Use with caution in the presence of renal or hepatic dysfunction.

Side- and adverse effects: Side-effects with Parahypion are rare in therapeutic doses. Paracetamol has been widely used and reports of adverse reactions are rare, and are generally associated with overdosage. Isolated cases of thrombocytopenic purpura, methaemoglobinemia, and agranulocytosis have been recorded. Nephrotoxic effects are uncommon and have not been reported in association with therapeutic doses, except after prolonged administration.

Codeine may sometimes cause constipation.

Use in pregnancy and lactation: No data are available on the use of Parahypion in human pregnancy nor on the excretion of it or its metabolites in human milk.

Toxicity and treatment of overdosage: Even in severe cases, initial symptoms are likely to be mild and may comprise pallor, nausea and vomiting. Liver damage may not become apparent for 24 hours to 6 days after ingestion.

Overdosage should therefore be treated promptly by gastric lavage followed by i.v. N-Acetylcysteine or oral methionine. Additional therapy (further methionine, i.v. N-Acetylcysteine or i.v. cysteamine) is normally considered in the light of blood paracetamol content and the time elapsed since ingestion. Such therapy is probably best undertaken in a specialised unit.

Pharmaceutical precautions Store below 25°C. Keep dry. Protect from light.

Legal category P.

Package quantities Strip-pack of 12. Container of 100 tablets.

Further information Nil.

Product licence number 0003/0118.

POLYBACTRIN* SOLUBLE GU

Presentation One vial contains, in sterile dry powder

Polymyxin B Sulphate BP	75,000 units
Neomycin Sulphate BP	20,000 units
Bacitracin BP 1968	1,000 units

Uses Antibacterial for bladder irrigation only.

To treat and prevent bacteriuria and prevent Gram-negative rod bacteraemia associated with the use of indwelling catheters. For temporary retention in the bladder following intermittent catheterisation and following cystoscopy.

Dosage and administration Reconstitute in 10 ml of isotonic saline then transfer to the appropriate volume of isotonic saline and mix. *Adults:* For continuous irrigation of the bladder for periods up to 10 days, a three-way catheter should be used. Two vials of powder dissolved in 500 ml of isotonic saline provide for a slow drip to be delivered over 24 hours. For patients with a urine output exceeding 2 litres per day, it is recommended that the drip rate be doubled.

Following intermittent catheterisation or cystoscopy 1 vial of powder dissolved in 10–40 ml of isotonic saline may be introduced into the bladder and retained for an hour. This treatment may be used twice daily. See Contra-indications, warnings, etc.

Children: Proportionate reduction in dose according to weight.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to polymyxins, bacitracin or the neomycin group of antibiotics.

Precautions: The following statements take into account the possibility that the constituent drugs of Polybactrin Soluble GU, particularly neomycin, may be absorbed to a significant degree after topical application. There is some evidence that neomycin diffuses across, particularly the denuded, bladder mucosa, hence such factor should be taken into consideration in the use of Polybactrin Soluble GU.

Ototoxicity and nephrotoxicity have been reported in association with large or prolonged doses of neomycin nephrotoxicity and neurotoxicity with polymyxin B nephrotoxicity with inappropriate dosing of bacitracin. While these effects are normally reversible on cessation of therapy, the ototoxic effect of neomycin is not.

Due to the fact that if neomycin-related ototoxicity occurs there is a delay in onset of its appearance, it would be unwise to give a further course of Polybactrin Soluble GU before three months have elapsed from the prior course, by which time any such effects would be evident on examination.

In renal impairment the plasma clearance of neomycin is reduced, therefore a reduction in dose should be made that relates to the degree of renal impairment.

In cases where there is established partial nerve deafness and where a significant degree of neomycin

bsorption could occur it might be inappropriate to use any neomycin-containing product and treatment with an antibacterial without an aminoglycoside constituent should be used if possible.

Concurrent administration of other aminoglycoside antibiotics is not recommended.

As neomycin has a neuromuscular blocking effect, patients concurrently receiving other agents with a similar action should be observed for signs of possible respiratory insufficiency.

Side- and adverse effects: Allergic reactions following the topical application of neomycin have been reported in the literature, but such reactions following the application of polymyxin B and bacitracin are rare events.

Use in pregnancy: Due to a lack of detailed information the use of Polybactrin Soluble GU during pregnancy cannot be recommended in circumstances where significant systemic absorption of the active ingredients may occur.

Toxicity and treatment of overdosage: In the event of signs of toxicity developing following significant systemic absorption of the active ingredients of Polybactrin Soluble GU, the patient's general status, hearing acuity, renal function and neuromuscular function should be monitored and blood levels of polymyxin B, neomycin, and bacitracin determined. Serum levels of neomycin can be reduced by haemodialysis.

Pharmaceutical precautions Store below 15°C. Keep dry. Protect from light.

Solutions should be used within 24 hours of their preparation.

Legal category POM.

Package quantities Pack of 5 sterile vials.

Further information Nil.

Product licence number 0003/5055.

'POLYBACTRIN' SPRAY

Presentation A sterile powder. Each 115 ml pressurised canister contains:

Polymyxin B Sulphate BP	150,000 units
Neomycin Sulphate BP	495,000 units
Zinc Bacitracin BP	37,500 units

an aerosol propellant.

Uses Topical antibacterial powder.

Prevention of wound infection in surgery. Treatment of infected skin.

Dosage and administration *Adults:* A thin, uniform spray should be applied to affected areas, as required. This can be obtained from a spray of about one second's duration to the wound surface at a distance of not less than 20 cm. The application of one can of spray daily for even days should not be exceeded. After such a course, treatment should not be repeated for at least three months.

Children: The maximum dosage should be reduced in proportion to body weight.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to polymyxins, bacitracin or the neomycin group of antibiotics.

Precautions: The following statements take into account the possibility that the constituent drugs of Polybactrin

Spray, particularly neomycin, may be absorbed to a significant degree after topical application.

Ototoxicity and nephrotoxicity have been reported in association with large or prolonged doses of neomycin; nephrotoxicity and neurotoxicity with polymyxin B; nephrotoxicity with inappropriate dosing of bacitracin. While these effects are normally reversible on cessation of therapy, the ototoxic effect of neomycin is not.

In cases where there is established partial nerve deafness and where a significant degree of neomycin absorption could occur it might be inappropriate to use any neomycin-containing product and treatment with an antibacterial without an aminoglycoside constituent should be used if possible.

In renal impairment the plasma clearance of neomycin is reduced, therefore a reduction in dose should be made that relates to the degree of renal impairment.

The inappropriate use of topical antibiotics has been associated with the emergence of resistant strains of bacteria.

The spray should not be used on large denuded areas (e.g. burns or ulcers) because of the risk of systemic absorption.

Concurrent administration of other aminoglycoside antibiotics is not recommended.

As neomycin has a neuromuscular blocking effect, patients concurrently receiving other agents with a similar action should be observed for signs of possible respiratory insufficiency.

Side- and adverse effects: Allergic reactions following the topical application of neomycin have been reported in the literature, but such reactions following the application of polymyxin B and bacitracin are rare events.

Use in pregnancy: Due to a lack of detailed information the use of Polybactrin Spray during pregnancy cannot be recommended in circumstances where significant systemic absorption of the active ingredients may occur.

Toxicity and treatment of overdosage: In the event of signs of toxicity developing following significant systemic absorption of the active ingredients of Polybactrin Spray, the patient's general status, hearing acuity, renal function and neuromuscular function should be monitored and blood levels of polymyxin B, neomycin, and bacitracin determined. Serum levels of neomycin can be reduced by haemodialysis.

Pharmaceutical precautions Do not expose to temperatures over 50°C. Do not puncture or incinerate even after use. Do not autoclave.

Legal category POM.

Package quantities Pressurised aerosol powder spray, volume 115 ml.

Further information Nil.

Product licence number 0003/5056.

POLYFAX' OINTMENT

Presentation Polyfax Ointment contains 10,000 units of Polymyxin B Sulphate BP and 500 units of Zinc Bacitracin BP per gram, in a stable petrolatum base. The ointment is pale yellow in colour.

Uses Topical antibacterial agent.

Polyfax Ointment is indicated for the treatment of infected wounds, burns, skin grafts, ulcers, pyoderma, sycosis barbae, impetigo, and in secondarily infected

skin lesions of scabies, pediculosis, tinea pedis and contact and allergic dermatitis.

Dosage and administration *Adults:* Polyfax Ointment should be applied thinly over the affected area, which is best left exposed. Two or more applications a day may be necessary, depending on the severity of the condition.

Children: As for adults.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to bacitracin and polymyxins.

Precautions: The following statements take into account the possibility that the constituent drugs of Polyfax Ointment may be absorbed to a significant degree after topical application.

Nephrotoxicity may result from the absorption of bacitracin, and nephrotoxicity and neurotoxicity from polymyxin B. These effects are normally reversible after cessation of therapy.

In patients with renal impairment the dosage of polymyxin B should be restricted to 10,000 to 15,000 units/kg/day, which is equivalent to about three tubes of Polyfax Ointment each day for an average adult.

Side- and adverse effects: Allergic reactions following topical application of polymyxin B and zinc bacitracin have rarely been reported.

Use in pregnancy: Due to a lack of detailed information, the use of Polyfax Ointment during pregnancy cannot be recommended in circumstances where significant systemic absorption of the active ingredients may occur.

Toxicity and treatment of overdosage: In the unlikely event of significant systemic absorption of the active ingredients of Polyfax Ointment occurring, signs of neurotoxicity and nephrotoxicity may be noted. In such an event, the patient's general status and renal function should be monitored and blood levels of polymyxin B and zinc bacitracin determined.

Pharmaceutical precautions Store below 25°C.

Legal category POM.

Package quantities Tube of 20 g.

Further information Nil.

Product licence number 0003/5230.

POLYFAX* OPHTHALMIC OINTMENT

Presentation Polyfax Ophthalmic Ointment contains 10,000 units of Polymyxin B Sulphate BP and 500 units of Zinc Bacitracin BP per gram, in a stable petrolatum base. The ointment is pale yellow in colour.

Uses Topical antibacterial agent.

Polyfax Ophthalmic Ointment is indicated for the treatment of styes, conjunctivitis, keratitis, corneal ulcers and blepharitis. It may also be used prophylactically after the removal of foreign bodies from the eye, and in pre- and post-operative management.

Dosage and administration *Adults:* Polyfax Ophthalmic Ointment should be applied thinly to the affected area or inside the lower eyelid. Two or more applications a day depending on the severity of the condition.

Children: As for adults.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to bacitracin or polymyxins.

Precautions: Polymyxin B and bacitracin are nephrotoxic if absorbed from open surfaces. However, these effects are unlikely with ocular administration.

Side- and adverse effects: Allergic reactions following topical application of polymyxin B and zinc bacitracin have rarely been reported.

Toxicity and treatment of overdosage: Not applicable.

Pharmaceutical precautions Store below 25°C.

Legal category POM.

Package quantities Tube of 4 g.

Further information Polyfax Ophthalmic Ointment is bland and non-irritating and is well tolerated by the sensitive structures of the eye.

Product licence number 0003/5229.

SUDAFED* TABLETS SUDAFED* ELIXIR

Presentation Each tablet contains 60 mg Pseudoephedrine Hydrochloride BP, and is white in colour and coded 'Wellcome S7A'.

Each 5 ml of deep pink elixir contains 30 mg Pseudoephedrine Hydrochloride BP.

Uses Nasal and sinus decongestant.

Dosage and administration *Adults and children over 12 years:* 1 tablet or 10 ml three times a day.

Children: 6-12 years: 7.5 ml elixir three times a day.

1-6 years: 5 ml elixir three times a day.

3-12 months: 2.5 ml elixir three times a day
Sudafed elixir may be diluted with Syrup BP.

Pharmacology: Pseudoephedrine has direct and indirect sympathomimetic activity and is an orally effective upper respiratory tract decongestant. Pseudoephedrine is substantially less potent than ephedrine in producing both tachycardia and elevation in systolic blood pressure and considerably less potent in causing stimulation of the central nervous system.

Contra-indications, warnings, etc

Contra-indications: Contra-indicated in patients who have previously shown intolerance to pseudoephedrine. It is contra-indicated in persons under treatment with monoamine oxidase inhibitors and within two weeks of stopping such treatment.

Precautions: Although pseudoephedrine has virtually no pressor effect in patients with normal blood pressure, Sudafed should be used with caution in patients with cardiovascular disorders, including hypertension. The effect of antihypertensive agents which modify sympathetic activity may be partially reversed by Sudafed.

Caution should also be exercised in patients taking other sympathomimetic agents, such as decongestants, appetite suppressants and amphetamine-like psychostimulants. The effects of a single dose on the blood pressure of these patients should be observed before recommending repeated or unsupervised treatment.

As with other sympathomimetic agents, caution should be exercised in patients with prostatic enlargement or bladder dysfunction.

In severe hepatic or renal dysfunction a single dose of

Sudafed should be given and the patient's response used as a guide to the dosage requirement for further administration.

The antibacterial agent furazolidone is known to cause a progressive inhibition of monoamine oxidase and although there are no reports of hypertensive crises having occurred, it should not be administered concurrently with Sudafed.

Side- and adverse effects: Side-effects are uncommon. In some patients pseudoephedrine may occasionally cause insomnia.

A fixed drug eruption to pseudoephedrine, taking the form of erythematous nummular patches has been reported, but is a rare occurrence.

Use in pregnancy and lactation: No data are available on the use of Sudafed in human pregnancy nor on the excretion of it or its metabolites in human milk.

Toxicity and treatment of overdose: As with other sympathomimetic agents, symptoms of overdose include irritability, convulsions, palpitations, hypertension and difficulty in micturition. Gastric lavage and supportive measures for respiration and circulation should be performed if indicated. Convulsions should be controlled with an anticonvulsant. Catheterisation of the bladder may be necessary. Alpha-adrenergic blockade may be required to treat hypertensive crises and beta-adrenergic blockade for the control of supraventricular dysrhythmias.

Pseudoephedrine has a renal excretion half-life of approximately seven hours and if desired the elimination can be accelerated by acid diuresis or by dialysis.

Pharmaceutical precautions Store below 25°C in a dry place. Elixir should be protected from light.

Legal category P.

Package quantities *Sudafed tablets:* Container of 100 tablets. 12 tablets in blister strips of 6.
Sudafed elixir: Bottles of 100 ml and 1 litre.

Further information Nil.

Product licence numbers

Tablets 0003/5061.

Elixir 0003/5062.

UDAFED[®]-CO TABLETS

Description White scored tablets coded 'Wellcome 7C' containing 500 mg Paracetamol BP and 60 mg pseudoephedrine Hydrochloride BP.

Uses For the relief of conditions where upper respiratory congestion is associated with pyrexia or pain. These conditions include the common cold, influenza, sinusitis and nasopharyngitis.

Dosage and administration *Adults and children over 2 years:* One tablet three times a day.

Children 6–12 years: Half a tablet three times a day.

Pharmacology: Pseudoephedrine has direct and indirect sympathomimetic activity and is an orally effective upper respiratory tract decongestant. Pseudoephedrine is substantially less potent than ephedrine in producing both tachycardia and elevation in systolic blood pressure and is considerably less potent in causing stimulation of the central nervous system. Paracetamol provides analgesic and antipyretic activity, probably by antagonising cerebral prostaglandin synthetase.

Contra-indications, warnings, etc

Contra-indications: Contra-indicated in patients with a known hypersensitivity to paracetamol or pseudoephedrine. It is contra-indicated in persons under treatment with monoamine oxidase inhibitors and within two weeks of stopping such treatment.

Precautions: Although pseudoephedrine has virtually no pressor effect in patients with normal blood pressure, Sudafed-Co should be used with caution in patients with cardiovascular disorders including hypertension. The effect of antihypertensive agents which modify sympathetic activity may be partially reversed by Sudafed-Co.

Also caution should be exercised in patients taking other sympathomimetic agents, such as decongestants, appetite suppressants and amphetamine-like psychostimulants. The effects of a single dose on the blood pressure of these patients should be observed before recommending repeated or unsupervised treatment.

As with other sympathomimetic agents, caution should be exercised in patients with prostatic enlargement or bladder dysfunction.

In severe hepatic or renal dysfunction a single dose of Sudafed-Co should be given and the patient's response used as a guide to the dosage requirement for further administration.

The antibacterial agent furazolidone is known to cause a progressive inhibition of monoamine oxidase and, although there are no reports of a hypertensive crisis having occurred, it should not be administered concurrently with Sudafed-Co.

Side- and adverse effects: Side-effects are uncommon. In some patients pseudoephedrine may occasionally cause insomnia. A fixed drug eruption to pseudoephedrine taking the form of erythematous nummular patches has been reported but is a rare occurrence. Paracetamol has been widely used and reports of adverse reactions are rare, and are generally associated with overdose. Isolated cases of thrombocytopenic purpura, methaemoglobinemia and agranulocytosis have been recorded. Nephrotoxic effects are uncommon and have not been reported in association with therapeutic doses, except after prolonged administration.

Use in pregnancy and lactation: No data are available on the use of Sudafed-Co in human pregnancy or the excretion of it or its metabolites in human milk.

Toxicity and treatment of overdose: Pallor, nausea and vomiting may occur due to the paracetamol component. With pseudoephedrine, symptoms of overdose may include irritability, convulsions, palpitations, hypertension, and difficulty in micturition. Hepatotoxicity may be a complication from the paracetamol content but may not be apparent from 24 hours–6 days after ingestion.

Overdose should, therefore, be treated promptly by gastric lavage followed by i.v. N-acetylcysteine, or oral methionine. Additional therapy (further methionine or i.v. cysteamine or i.v. N-acetylcysteine) is normally considered in the light of blood paracetamol content and the time elapsed since ingestion. Such therapy is probably best undertaken in a specialised unit. Supportive measures for respiration and circulation should be performed if indicated. Convulsions should be controlled with an anticonvulsant. Catheterisation of the bladder may be necessary. Alpha-adrenergic blockade may be required to treat hypertensive crises and beta-adrenergic blockade for the control of supraventricular dysrhythmias. Pseudoephedrine has a renal excretion half-life of approximately seven hours and if desired the elimination can be accelerated by acid diuresis or by dialysis.

Pharmaceutical precautions Store below 25°C in a dry place. Protect from light.

Legal category P.

Package quantities 12 tablets in blister strips of 6.

Further information Nil.

Product licence number 0003/0157.

SUDAFED* EXPECTORANT

Presentation Each 5 ml of orange red syrup contains 100 mg Guaiphenesin BP and 30 mg Pseudoephedrine Hydrochloride BP.

Uses Conditions where an expectorant and upper respiratory tract decongestant are required.

Dosage and administration *Adults and children over 12 years:* 10 ml three times a day.

Children 6–12 years: 5 ml three times a day.

1–6 years: 2.5 ml three times a day.

May be diluted with Syrup BP.

Pharmacology: Pseudoephedrine has direct and indirect sympathomimetic activity and is an orally effective upper respiratory tract decongestant. Pseudoephedrine is substantially less potent than ephedrine in producing both tachycardia and elevation in systolic blood pressure and considerably less potent in causing stimulation of the central nervous system. On the basis of widespread and long established clinical use, guaiphenesin is recognised as an expectorant in bronchitis.

Contra-indications, warnings, etc

Contra-indications: Contra-indicated in patients who have previously shown intolerance to pseudoephedrine or guaiphenesin. Sudafed Expectorant is contra-indicated in persons under treatment with monoamine oxidase inhibitors and within two weeks of stopping such treatment.

Precautions: Although pseudoephedrine has virtually no pressor effect in patients with normal blood pressure, Sudafed Expectorant should be used with caution in patients with cardiovascular disorders, including hypertension. The effect of antihypertensive agents, which modify sympathetic activity may be partially reversed by Sudafed Expectorant.

Also caution should be exercised in patients taking other sympathomimetic agents, such as decongestants, appetite suppressants and amphetamine-like psychostimulants. The effects of a single dose of Sudafed Expectorant on the blood pressure of these patients should be observed before recommending repeated or unsupervised treatment.

As with other sympathomimetic agents, caution should be exercised in patients with prostatic enlargement or bladder dysfunction.

In severe hepatic or renal dysfunction a single dose of Sudafed Expectorant should be given and the patient's response used as a guide to the dosage requirement for further administration.

The antibacterial agent furazolidone is known to cause a progressive inhibition of monoamine oxidase and, although there are no reports of hypertensive crises having occurred, it should not be administered concurrently with Sudafed Expectorant.

Side- and adverse effects: Side-effects are uncommon.

In some patients pseudoephedrine may occasionally cause insomnia.

A fixed drug eruption to pseudoephedrine, taking the form of erythematous nummular patches has been reported, but is a rare occurrence.

Use in pregnancy and lactation: No data are available or the use of Sudafed Expectorant in human pregnancy or the excretion of it or its metabolites in human milk.

Toxicity and treatment of overdosage: As with other sympathomimetic agents, symptoms of overdosage include irritability, convulsions, palpitations, hypertensor and difficulty in micturition. Gastric lavage and supportive measures for respiration and circulation should be performed if indicated. Convulsions should be controlled with an anticonvulsant. Catheterisation of the bladder may be necessary.

Alpha-adrenergic blockade may be required to treat hypertensive crises and beta-adrenergic blockade for the control of supraventricular dysrhythmias. Pseudoephedrine has a renal excretion half-life of approximately seven hours and if desired the elimination can be accelerated by acid diuresis or by dialysis.

Pharmaceutical precautions Store below 25°C. Protect from light. Do not refrigerate.

Legal category P.

Package quantities Bottle of 1 litre.

Further information Nil.

Product licence number 0003/0145.

TUBARINE* INJECTION

Presentation Each ampoule contains 15 mg of Tubocurarine Chloride BP in 1.5 ml (Tubocurarine Injection BP).

Uses d-Tubocurarine is a non-depolarising agent used to relax the muscles for surgical, anaesthetic and investigatory procedures, and to facilitate control of respiration.

Dosage and administration *Adults:* Intravenous administration of d-tubocurarine induces a paralysis of skeletal muscles within minutes. The level of consciousness is not affected.

Because there is a wide variation in the response to d-tubocurarine the dosage should be adjusted individually for each patient, and the following doses are intended only as a guide.

A 20 mg dose could be taken as an average for a 70 kg man. The mean recovery time from this dose (to 25% twitch suppression) has been shown to be 26 minutes.

Increments of 5 mg d-tubocurarine have been used to maintain relaxation during surgery in adults.

Children: 1 mg per 3 kg bodyweight is suggested as a guide. Neonates are more sensitive than adults to the neuromuscular blocking effect of d-tubocurarine when given on a mg/kg basis. 250 mcg/kg at birth, increased to 500 mcg/kg at 28 days of age has been recommended as an initial dose, but this should be reduced in cases of prematurity, acidosis and hypothermia. Incremental doses of one-fifth to one-sixth the original dose have been used.

Contra-indications, warnings, etc

Contra-indications: Tubarine is contra-indicated in patients who have a history of allergic or hypersensitive reactions to d-tubocurarine.

Precautions: Like other neuromuscular blocking agents, d-tubocurarine causes paralysis of the respiratory muscles. It should only be used in the presence of an experienced anaesthetist, and when resuscitative equipment is immediately available.

Diminished renal function may prolong the duration of action of d-tubocurarine at high doses.

d-Tubocurarine requirements may be increased in patients with liver damage.

Respiratory acidemia has been found to prolong, and respiratory alkalemia to reduce, the time taken to recover from d-tubocurarine-induced neuromuscular blockade.

Prolonged curarisation following 20 mg d-tubocurarine has been reported in a patient with hypocalcaemia.

Patients with myasthenia gravis have been shown to be, on average, $5\frac{1}{2}$ times more sensitive to d-tubocurarine than non-myasthenic subjects. Increased sensitivity to d-tubocurarine has also been shown in patients with myasthenic syndrome complicating bronchial carcinoma, in carcinomatous neuropathy, amyotrophic lateral sclerosis, von Recklinghausen's disease and Duchenne muscular dystrophy.

Cooling decreases the magnitude of the neuromuscular blockade produced by d-tubocurarine. Thus, in patients after operations under hypothermia, prolonged curarisation could occur on rewarming.

Two cases have been reported in which malignant hyperpyrexia may have been triggered by d-tubocurarine.

The neuromuscular blocking action of d-tubocurarine is reported to be potentiated by:

1. Anaesthetic agents such as halothane, isoflurane, enflurane and methoxyflurane. The interaction is particularly marked in the case of diethyl ether. Generally, the degree of potentiation is related to the alveolar concentrations of these agents.

2. Antibiotics such as neomycin, streptomycin, kanamycin, colistin, polymyxin B, certain tetracyclines, possibly bacitracin, clindamycin, lincomycin and entamicin.

3. Other non-depolarising neuromuscular blocking agents, such as gallamine and pancuronium. d-Tubocurarine and suxamethonium are basically antagonistic, though synergism has occurred.

4. Magnesium sulphate.

5. Propranolol, lignocaine, procainamide, diphenylhydantoin and quinidine.

6. Frusemide and possibly mannitol.

Patients receiving treatment with azathioprine or lymphocyte globulin may require twice the usual dose of d-tubocurarine. The effect of azathioprine is further increased by concomitant administration of methylnalazine.

Side- and adverse effects: Bronchospasm and cardiac arrest following d-tubocurarine administration have been reported in a patient with a minor history of allergic asthma.

d-Tubocurarine frequently causes a fall in mean arterial pressure, peripheral vascular resistance and central venous pressure; and a rise in heart rate. Normally, these changes are slight and transient. The hypotensive effect of d-tubocurarine may be enhanced by halothane.

Use in pregnancy and lactation: A single case has been reported in which arthrogryposis multiplex congenita allowed the use of d-tubocurarine for a 10-day period the 10th–12th week of pregnancy. After administration during obstetric operations, d-tubocurarine can be

detected in the cord serum in very low concentrations, which are unlikely to be of any clinical significance to the foetus.

Tubarine is poorly absorbed orally and is unlikely to present a problem to the breast-fed infant.

Toxicity and treatment of overdosage: The neuromuscular blockade due to d-tubocurarine may be reversed by an anticholinesterase such as neostigmine 2.5–5 mg given intravenously. Atropine (1.2–2.4 mg) should be injected intravenously at the same time or immediately before the neostigmine.

In neonates, one hour after the recommended initial dose, reversal may be obtained with atropine 0.018 mg/kg and neostigmine 0.08 mg/kg given intravenously.

If neuromuscular blockade cannot be adequately reversed by the use of an anticholinesterase, then measures should be taken to maintain respiration and, if necessary, the circulation, until neuromuscular function returns. Sedation may also be required.

Pharmaceutical precautions Store below 25°C. Protect from light.

Legal category POM.

Package quantities Box of 5 × 1.5 ml ampoules.

Further information Nil.

Product licence number 0003/5065.

VALOID* TABLETS VALOID* INJECTION

Presentation Valoid Tablets each contain 50 mg Cyclizine Hydrochloride BP, scored, coded 'Wellcome T4A', white in colour.

Valoid Injection contains 50 mg cyclizine lactate in each 1 ml ampoule.

Uses Anti-emetic. In the prevention and treatment of nausea and vomiting and drug-induced vomiting, especially that associated with the administration of narcotic drugs. It has been widely and effectively used in the prophylaxis and treatment of motion sickness, in the symptomatic management of vertigo and labyrinthine disorders (Meniere's syndrome), in postoperative vomiting and in radiation sickness, particularly when this is associated with the treatment of breast cancer.

Dosage and administration *Valoid Tablets: Adults and children over 10 years:* 1 tablet three times daily.

Children 1–10 years: $\frac{1}{2}$ tablet three times daily.

Valoid Injection: Adults and children over 10 years: 50 mg intramuscularly or intravenously three times daily.

For the prevention of postoperative nausea and vomiting, administer the first dose 15–20 minutes before the anticipated end of surgery.

Contra-indications, warnings, etc

Contra-indications: In the light of present knowledge and uncertainties about possible teratogenic agents, current authoritative opinion is that no drug should be taken by a pregnant woman, especially during the first four months of pregnancy, except under medical supervision.

Precautions: Drowsiness, dryness of the mouth and blurred vision may occur in a small number of patients. It is, therefore, advisable that patients should determine their responses before driving or operating machinery. In

some patients the action of Valoid may be potentiated by alcohol and other central sedatives.

Side- and adverse effects: Intravenous cyclizine may increase the incidence of tremors and muscle movements if given before methohexitone anaesthesia.

Although very rare, anaphylaxis of a severe degree has been reported with the co-administration of intravenous cyclizine and propanidol.

Use in pregnancy and lactation: See contra-indications above. No information is available on the use of cyclizine in lactating mothers.

Toxicity and treatment of overdosage: Toxicity may comprise drowsiness, dizziness, convulsions, hyperpyrexia and respiratory depression. Rarely, agitation, ataxia and hallucinations may occur. Gastric lavage and general supportive measures are indicated. Control any convulsions with diazepam injections.

Pharmaceutical precautions *Injection:* Store below 25°C. Protect from light.

Tablets: Store below 25°C.

Legal category Tablets P.
Injection POM.

Package quantities *Valoid Tablets:* Bottle of 100.
Tablet Injection: Box of 5 ampoules.

Further information Nil.

Product licence numbers
Tablets 0003/5213.
Injection 0003/5212.

VASOXINE* INJECTION

Presentation Each 1 ml ampoule contains 20 mg Methoxamine Hydrochloride BP (Methoxamine Injection BP).

Uses Methoxamine is indicated for counteraction of hypotension. The most common clinical application for methoxamine is the correction or prevention of hypotension associated with the use of antihypertensive drugs and spinal anaesthetics.

Methoxamine is indicated when pressor therapy is deemed appropriate during, and as a result of, the administration of cyclopropane or halogenated anaesthetics.

Methoxamine is also indicated for the arrest of supraventricular tachycardia.

Dosage and administration *Adults:* 5–10 mg (0.25–0.5 ml) Vasoxine intravenously at a rate of 1 mg/min.
5–20 mg (0.25–1.0 ml) Vasoxine by intramuscular injection.

Children: 80 mcg Vasoxine per kg bodyweight intravenously.
250 mcg Vasoxine per kg bodyweight by intramuscular injection.

A second dose should not be injected until the first dose has ceased to act.

Contra-indications, warnings, etc

Contra-indications: Vasoxine is contra-indicated in cases of pre-existent severe hypertension.

Precautions: The effect of increased arterial pressure on a patient with pre-existing vascular disease or myocardial impairment should be considered before administering Vasoxine.

An exaggerated response to methoxamine may be

expected in patients with hyperthyroidism: in patients who have received treatment with monoamine oxidase inhibitors within the previous two weeks, and in hypertensive patients with temporarily lowered arterial pressure due to spinal anaesthesia. The initial dosages should be decided accordingly.

Methoxamine should not be administered unless facilities are available to make repeated arterial pressure measurements.

The use of Vasoxine in combination with local anaesthetics to prolong their action at local sites is not recommended.

Methoxamine has been reported as curtailing ventricular dysrhythmias usually in conditions associated with hypotension such as after myocardial infarction. The mode of action is almost certainly only indirect and related to improved perfusion resulting from a higher perfusion pressure. This is not a recommended indication for methoxamine and its use in such situations depends entirely on the discretion of the attending physician.

Concomitant use of Vasoxine with sympathomimetic agents, such as decongestants, some appetite suppressants and amphetamine-like psychostimulants or with monoamine oxidase inhibitors, which interfere with the catabolism of sympathomimetic amines, may cause an exaggerated response to methoxamine. Appropriate care should be taken therefore when administering methoxamine to patients who have received such drugs.

Side- and adverse effects: Subjective effects reported by patients receiving methoxamine include dull headaches, feelings of cold and other skin sensations resulting from piloerection, sensation of fullness in neck and chest and a desire to micturate.

Adrenergic receptor stimulation is inevitable but the unsought objective effects have little clinical importance.

Bradycardia may be excessive during the use of methoxamine. This can be abolished by 0.8 mg atropine given intravenously. This dosage may be reduced as appropriate for children.

Projectile vomiting may occur particularly after high dosage.

Topical methoxamine decongests mucous membrane but the effect is not usually apparent with the dose given systemically.

Use in pregnancy and lactation: When considering administering Vasoxine during pregnancy, any potential risk to which the foetus may be exposed must be weighed against the risk of the maternal disease process. (No record of use in human pregnancy is available. Vasoxine is poorly absorbed orally and is unlikely to present a problem to the breast-fed infant.)

Toxicity and treatment of overdosage: In cases of overdosage with methoxamine, when after waiting a appropriate time blood pressure has not returned to normal, management of associated hypertension can be achieved by phentolamine (5 mg) being administered intravenously and repeated as necessary.

Pharmaceutical precautions Store below 25°C. Do not freeze.

Legal category POM.

Package quantities Box of 5 ampoules.

Further information Because methoxamine is active only on alpha-adrenergic receptors it has little direct effect on cardiac adrenoceptors which are predominantly beta. Hence it is appropriate for use with

halogenated anaesthetics which cause beta receptor sensitisation.

Methoxamine has no central nervous system activity.

Product licence number 0003/5066.

ZYLORIC® TABLETS

ZYLORIC-300® TABLETS

Presentation Zyloric Tablets each contain 100 mg allopurinol BP imprinted Zyloric 100 and coded U4A. Creamy white in colour. Zyloric-300 Tablets each contain 300 mg Allopurinol BP imprinted Zyloric 300 and coded C9B. Creamy white in colour.

Uses

Conditions of excess body urate including gout: Zyloric is used to reduce urate levels in the body when these levels are excessive (serum is theoretically saturated with urate at a concentration between 0.38–0.42 mmol/l (6.4–7.0 mg%)). The higher levels seen in practice may be accounted for by (a) the formation of supersaturated solutions; (b) protein binding of urate. Excess body urate may be indicated by hyperuricaemia and/or hyperuricosuria. It may lead to deposition of urate in the tissues or it may be present with no obvious signs or symptoms.

Its main clinical manifestations of urate deposition are: gouty arthritis, skin tophi and/or renal involvement. Excess body urate is frequently of idiopathic origin but may also be found in association with other conditions including the following: neoplastic disease and its treatment; certain enzyme disorders (in particular Lesch-Nyhan syndrome); renal failure; renal calculus formation; uretic therapy and psoriasis.

Calcium renal lithiasis: Zyloric is of benefit in the prophylaxis and treatment of calcium renal lithiasis in patients with raised serum or urinary uric acid.

Allopurinol and its major metabolite, oxipurinol, act by inhibiting the enzyme xanthine oxidase which catalyses the end stage of the metabolism of purines to uric acid. Allopurinol and its metabolites are excreted by the kidney at the renal handling is such that allopurinol has a plasma half-life of about one hour whereas that of oxipurinol exceeds 18 hours. Thus therapeutic effect may be achieved by once-a-day dosage.

Dosage and administration **Adults:** The initial dosage should be in the range 100–300 mg per day which may be taken as a single dose. Doses in excess of 300 mg could be administered in divided doses. It has rarely been found necessary to exceed 900 mg per day. The dose should be adjusted by monitoring serum uric acid and/or urinary uric acid levels at appropriate intervals until the desired effect is attained, which may take one to three weeks. The maintenance dose is normally 200–300 mg per day.

Children: 10–20 mg/kg bodyweight/day.

Use in children is mainly indicated in malignant conditions especially leukaemia, and certain enzyme disorders (e.g. Lesch-Nyhan syndrome).

Initiation of therapy: In early stages of treatment with Zyloric, as with the uricosuric agents, an acute attack of gouty arthritis may be precipitated. Therefore it is advisable to give a prophylactic dose of a suitable anti-inflammatory agent or colchicine for at least one month.

Use with uricosurics: As Zyloric does not interfere with the action of uricosuric agents, they may be given

concurrently. When changing from uricosuric therapy to Zyloric, one to three weeks overlap of treatments is recommended to ensure a continuous hypouricaemic effect.

To prevent acute uric acid nephropathy in neoplastic conditions, treatment with Zyloric should precede treatment with cytotoxic drugs (see also sections under *Contra-indications, warnings, etc.*).

Dose recommendations in impaired renal function: Since allopurinol and its metabolites are excreted via the kidney, impairment of renal function may lead to retention of the drug and its metabolites with consequent prolongation of action. Thus the amount and frequency of the dosage may require reduction as indicated by monitoring serum uric acid levels. The following schedule is provided for guidance in adults.

If creatinine clearance exceeds 20 ml/minute – give standard dose.

If creatinine clearance is between 20 and 10 ml/minute – give 100–200 mg/day.

If creatinine clearance is less than 10 ml/minute – give 100 mg/day or at longer intervals.

Dose recommendations in renal dialysis: Allopurinol and its metabolites are removed by renal dialysis. If frequent dialysis is required, an alternative schedule of 300–400 mg Zyloric after each dialysis, with none in the interim, should be considered.

Contra-indications, warnings, etc

Contra-indications: Known intolerance of allopurinol. Zyloric is contra-indicated as a treatment for the acute attack of gout. Prophylactic therapy may be started when the acute attack has completely subsided, provided anti-inflammatory agents are also taken.

Precautions: Treatment with Zyloric should not be started during an attack of gout. When Puri-Nethol® (6-mercaptopurine) or Imuran® (azathioprine) is given concurrently with Zyloric, only one quarter of the usual dose of Puri-Nethol or Imuran should be given because inhibition of xanthine oxidase will prolong their activity. There is no unequivocal evidence that Zyloric potentiates the activity of other cytotoxic drugs. A reduction of dosage should be considered in the presence of severe renal or hepatic disorders.

Side- and adverse effects: Adverse reactions in association with Zyloric are usually rare and mostly of a minor nature. The incidence is higher in the presence of renal and/or hepatic disorders.

In the early stages of treatment with Zyloric, as with the uricosuric agents, an acute attack of gouty arthritis may be precipitated. Therefore it is advisable to give a prophylactic dose of a suitable anti-inflammatory agent or colchicine for at least one month.

Although there is no evidence that the interaction between allopurinol and the coumarins seen under experimental conditions has any clinical significance, this possibility should be borne in mind when a patient on anticoagulants is given Zyloric. If Zyloric is given concomitantly with chlorpropamide when renal function is poor, there may be an increased risk of prolonged hypoglycaemic activity.

Skin reactions: These are the most common reactions and may occur at any time during treatment. They may be pruritic, maculopapular, sometimes scaly or purpuric and rarely exfoliative. Zyloric should be withdrawn immediately should such reactions occur. After recovery from mild reactions Zyloric may, if desired, be reintroduced at a low dose (e.g. 50 mg/day) which may be

gradually increased. If the rash recurs, Zyloric should be permanently withdrawn.

Generalised hypersensitivity: Exfoliative skin reactions associated with other signs of hypersensitivity including fever, lymphadenopathy, arthralgia and eosinophilia occur rarely. If they do occur, it may be at any time during treatment, Zyloric should then be withdrawn immediately and permanently. Corticosteroids may be beneficial in overcoming such reactions. Patients manifesting generalised hypersensitivity reactions usually have pre-existing renal and/or hepatic disorders.

Gastro-intestinal disorder: Nausea and vomiting have been reported. This reaction is not a significant problem and can be avoided by taking Zyloric after meals.

Blood and lymphatic system: There have been occasional reports of transient reduction in the numbers of circulating formed elements of the blood, usually in association with pre-existing renal and/or hepatic disorders. The clinical significance has yet to be demonstrated.

Miscellaneous: Exacerbation of acute gouty attacks may occur in the early stages of hypouricaemic therapy (see section under *Dosage and administration*). In those conditions where the body's miscible urate pool is greatly increased (e.g. malignant disease and its treatment; Lesch-Nyhan syndrome), the rise in the xanthine concentration resulting from the action of Zyloric may lead to tissue deposition of xanthine. Fluid intake should ensure adequate urinary output. Xanthine crystals have been seen in muscle tissue of patients receiving allopurinol, but this appears to have no clinical significance.

The following complaints have been reported occasionally, but do not appear to have a clear cause and effect relationship with allopurinol; fever, general malaise, headache, vertigo, somnolence, taste perversion, hepatic necrosis, granulomatous hepatitis, abnormal liver function tests, hyperlipaemia, visual disorder, cataracts, macular changes, neuropathy, impotence, diabetes mellitus, furunculosis, alopecia, hypertension, haematuria, oedema.

Use in pregnancy and lactation: High dose intraperito-

neal allopurinol in mice has been associated with foetal abnormalities but extensive animal studies with oral allopurinol have shown none. In human pregnancy there is no evidence that Zyloric taken orally causes foetal abnormalities; however, as with all drugs, due caution should be exercised in the use of Zyloric in pregnancy. No data are available on the excretion of allopurinol and its metabolites in human breast milk.

Toxicity and treatment of overdosage: No reports of overdosage or acute intoxication are available. The most likely reaction would be gastro-intestinal intolerance. Massive absorption of Zyloric may lead to considerable inhibition of xanthine oxidase activity which should have no untoward effects unless 6-mercaptopurine and/or azathioprine is being taken concomitantly. In this case the risk of increased activity of these drugs must be recognised. Adequate hydration to maintain optimum diuresis facilitates excretion of allopurinol and its metabolites. Dialysis may be resorted to if considered necessary.

Pharmaceutical precautions Store below 25°C. Keep dry.

Legal category POM.

Package quantities *Zyloric Tablets:* bottle of 10 tablets.

Zyloric-300 Tablets: Calendar pack of 2 x 14 tablets.

Further information Zyloric presents definite advantages over uricosuric agents or simple anti-inflammatory drugs, especially in patients with gouty nephropathy, in those who form renal urate stones and those with unusually severe disease. In most patients with extensive tophaceous deposits, progressive formation of tophi has been halted and draining urate sinuses have healed.

Product licence numbers

Zyloric Tablets	0003/5207.
Zyloric-300 Tablets	0003/0092.

***Trade Mark**



CUPAN*

Presentation *Acupan Tablets*: White, film-coated, circular, biconvex tablets, 7 mm in diameter, marked PN on one side. Each tablet contains nefopam hydrochloride 30 mg.

Acupan Injection: Each 2 ml ampoule contains 1 ml of solution of nefopam hydrochloride 20 mg/ml.

Uses *Acupan* is indicated for the relief of acute and chronic pain, including: post-operative pain; dental pain; musculo-skeletal pain; acute traumatic pain and cancer pain.

Acupan is a potent and rapidly-acting analgesic. It is totally distinct from other centrally-acting analgesics such as morphine, codeine, pentazocine and propoxyphene.

Unlike the narcotic agents, *Acupan* has been shown not to cause respiratory depression. There is no evidence from pre-clinical research of habituation occurring with *Acupan*.

Dosage and administration *Adults: Acupan Tablets*: Dosage may range from 1 to 3 tablets three times daily depending on response. The recommended starting dosage is 2 tablets three times daily.

Acupan Injection: 20 mg (1 ml) intramuscularly or intravenously repeated if necessary every six hours (see instructions for administration). Onset of effect after intramuscular injection is within 15–20 minutes and peak effect is reached at one to one-and-a-half hours after administration.

Treatment started with *Acupan* injection may be continued with *Acupan* Tablets. 60 mg *Acupan* (2 tablets) is approximately bioequivalent to 20 mg (1 ampoule) given by injection.

Instructions for administration of *Acupan* Injection: *Acupan* Injection should always be given with the patient lying down. When given intramuscularly, aspiration should be performed before injection to ensure that the needle is not in a blood vessel. When given intravenously, the injection should be given *slowly* through a 26 gauge needle at a rate not exceeding 5 mg per minute (four minutes for 20 mg). After injection by either the intramuscular or intravenous route the patient should remain lying down for 15–20 minutes. The patient could then get up slowly. Too rapid administration of the injection can give rise to syncope.

Children: Since *Acupan* has not been evaluated in children no dosage recommendation can be given for children under 12 years.

Contra-indications, warnings, etc *Side-effects*: Drowsiness, nervousness, dry mouth and lightheadedness may occur. Less frequently, vomiting, blurred vision, dizziness, sweating, insomnia, headache and tachycardia have been reported.

Interaction: The side-effects of *Acupan* may be additive to

those of other agents with anticholinergic or sympathomimetic activity. It should not be used in the treatment of myocardial infarction since there is no clinical experience in this indication. Hepatic and renal insufficiency may interfere with the metabolism and excretion of nefopam. Caution should be exercised when nefopam is administered concurrently with tricyclic antidepressants.

Contra-indications: *Acupan* is contra-indicated in patients with a history of convulsive disorders and should not be given to patients taking mono-amine-oxidase (MAO) inhibitors.

Overdosage: A few cases of overdosage with *Acupan* have been reported and successfully treated. Treatment should consist of general supportive measures. Diazepam should be given, preferably by mouth, if CNS excitement occurs.

In dogs given abnormally high doses of paracetamol, correspondingly excessive doses of nefopam potentiated the known hepatotoxicity of paracetamol. These studies indicated that repeated oral doses of 236 mg/kg/day of paracetamol with 24 mg/kg/day of nefopam showed potentiation of paracetamol hepatotoxicity. These doses are about six to eight times higher than the average human doses. Lower doses equivalent to three to four times the human dose produced no evidence of hepatotoxicity potentiation.

Pharmaceutical precautions No special storage precautions are required.

Package quantities *Acupan Tablets*: Bottles of 30 and 100 tablets.

Acupan Injection: Boxes containing 5 x 2 ml ampoules filled with 1 ml of solution.

Legal category POM.

Further information Nil.

Product licence numbers

Acupan Tablets 0068/0061

Acupan Injection 0068/0069

DIFFLAM* CREAM ▼

Presentation *Difflam* is a white, pleasant-smelling cream, containing benzydamine hydrochloride 3% w/w.

Uses *Difflam* cream is a topical analgesic and anti-inflammatory treatment for the relief of symptoms associated with painful inflammatory conditions of the musculo-skeletal system, including:

Acute inflammatory disorders such as myalgia and bursitis.

Traumatic conditions such as sprains, strains, contusions and the after-effects of fractures.

Difflam cream is well absorbed through the skin. It

concentrates in inflamed tissue where it has been shown to have anti-inflammatory and local anaesthetic actions.

Dosage and administration Difflam cream should be massaged lightly into the affected area three times daily and at the discretion of the doctor, up to six times daily in more severe conditions.

Contra-indications, warnings, etc *Side-effects:* Benzydamine is very well tolerated; the only adverse effect that occurred in clinical studies was a local skin reaction which varied from erythema to a papular eruption; the incidence was low (less than two per cent of patients) and the skin returned to normal on stopping treatment.

Caution: To avoid possible irritation, Difflam cream should be kept away from eyes and mucosal surfaces.

Overdosage: Difflam is unlikely to cause adverse systemic effects, even if accidental ingestion should occur. No special measures are required.

Pharmaceutical precautions Avoid extremes of temperature.

Legal category P.

Package quantities Tube containing 30 g.

Further information Nil.

Product licence number 0068/0088.

DIFFLAM* ORAL RINSE ▼

Presentation Difflam Oral Rinse is a pleasant tasting, clear, green solution, containing benzydamine hydrochloride 0.15% w/v.

Uses Difflam Oral Rinse is a locally acting analgesic and anti-inflammatory treatment for the relief of painful inflammatory conditions of the mouth and throat including:

Traumatic conditions: Pharyngitis following tonsillectomy or the use of a naso-gastric tube; dental surgery;

Inflammatory conditions: Pharyngitis, aphthous ulcers and oral ulceration due to radiation therapy.

Benzydamine is absorbed into inflamed tissue. It is a unique preparation which concentrates in inflamed tissue, where it exerts an anti-inflammatory and analgesic action by stabilising the cellular membrane and inhibiting prostaglandin synthesis.

Dosage and administration Rinse or gargle with 15 ml (approximately 1 tablespoonful) every 1½ to 3 hours as required for pain relief. Not suitable for children aged 12 years or under. The solution should be expelled from the mouth after use. Difflam Oral Rinse should generally be used undiluted, but if 'stinging' occurs the rinse may be diluted with water. Uninterrupted treatment should not exceed seven days, unless under medical supervision.

Contra-indications, warnings, etc *Side-effects:* Benzydamine is well tolerated; side-effects are minor. Occasionally, oral tissue numbness or 'stinging' sensations may occur.

Overdosage: Difflam is unlikely to cause adverse systemic effects, even if accidental ingestion should occur. No special measures are required.

Pharmaceutical precautions Do not leave the uncartoned bottle in direct sunlight.

Legal category P.

Package quantities Bottle containing 200 ml

Further information Nil.

Product licence number 0068/0096.

DUROMINE*

Presentation Duromine is available in two strengths. Each capsule contains phentermine 15 mg or 30 mg as an ion-exchange resin complex.

Duromine 15 mg: Opaque green-grey size No. 3 capsules printed Duromine 15.

Duromine 30 mg: Opaque maroon-grey size No. 1 capsules printed Duromine 30.

Uses Duromine is an appetite-depressant and is indicated in all types of simple obesity.

Phentermine is a sympathomimetic amine with marked anorectic activity. In efficacy it compares favourably with amphetamine, but it produces much less CNS excitation.

After ingestion, the medicament is gradually released from the ion-exchange resin complex over a period of 10–14 hours. Therapeutic blood levels are reached within one hour of administration and are maintained by the continuous and smooth release of phentermine from the resinate. This smooth and prolonged activity avoids peaking of blood level concentrations and minimises the chance of adverse CNS reactions.

Dosage and administration *Adults:* One 15 mg or 30 mg capsule daily at breakfast time.

Children: 6–12 years: One 15 mg capsule daily at breakfast time.

Duromine is not recommended for children under the age of six.

Contra-indications, warnings, etc *Side-effects:* Slight dryness of the mouth or a tendency to early waking may be experienced at higher dosage.

Caution: Duromine should be used with caution in patients under treatment with antihypertensive agent since it may cause some loss of blood pressure control.

Contra-indications: Duromine is contra-indicated in patients under treatment with monoamine-oxidase (MAO) inhibitors.

Overdosage: Symptoms: Initially irritability, agitation, disorientation and tremor may occur, followed by cardiac arrhythmias, convulsions, hallucinations and coma.

Treatment: The stomach should be emptied by emesis or stomach tube and washed out with water if the preparation has been ingested within the last three or four hours. Diazepam, preferably by mouth (cautiously by intravenous injection) should be used to control marked excitement and convulsions. Provided renal function is adequate, elimination of phentermine may be assisted by acidification of the urine by agents such as lysine hydrochloride or arginine hydrochloride.

Pharmaceutical precautions No special storage precautions are required.

Legal category POM.

Package quantities Duromine 15 mg: Bottles of 3 capsules.

Duromine 30 mg: Bottles of 30 capsules.

Further information Nil.

Product licence numbers

5 mg 0068/5055

0 mg 0068/5056

HIPREX*

Representation White, oblong tablet with breakline, marked HX on one side. Each Hiprex tablet contains methenamine hippurate 1 g.

Uses

Hiprex is indicated in the prophylaxis and treatment of urinary tract infections:

1. As maintenance therapy after successful initial treatment of acute infections with antibiotics.
2. As long-term therapy in the prevention of recurrent cystitis.
3. To suppress urinary infection in patients with indwelling catheters and to reduce the incidence of catheter blockage.
4. To provide prophylaxis against the introduction of infection into the urinary tract during instrumental procedures.
5. Asymptomatic bacteriuria, including bacteriuria of pregnancy.

Methenamine hippurate is readily absorbed from the gastro-intestinal tract and excreted via the kidney.

With Hiprex, as with other specific urinary antibacterial agents of this type, antibacterial activity is confined to the urinary tract. The chemical structure of methenamine hippurate is such that a two-fold antibacterial action is obtained:

1. The slow release of the bactericidal formaldehyde, from the methenamine part, in the urine; acid pH is necessary for this reaction to occur. It is obtained and maintained there by the presence of hippuric acid.
2. The bacteriostatic effect of hippuric acid itself on urinary tract pathogens.

Hiprex has a wide antibacterial spectrum covering both gram-positive and gram-negative organisms. It is active against the bacteria which most commonly cause urinary tract infection – *Escherichia coli*, *Aerobacter*

aerogenes, *Pseudomonas* and some strains of *Proteus*. Urinary antibacterial activity can be shown within 30 minutes of administration.

Hiprex is particularly useful for long-term treatment because neither tolerance to its effect nor bacterial resistance occurs. The incidence of side-effects is extremely low.

Dosage and administration *Adults*: 1 g twice daily.

In patients with catheters the dosage may be increased to 1 g three times daily.

Children: 6–12 years: 500 mg twice daily.

The tablets may be halved, or they can be crushed and taken with a drink of milk or fruit juice if the patient prefers.

Contra-indications, warnings, etc *Side-effects*: Occasionally rashes, gastric irritation or irritation of the bladder may occur.

All side-effects are reversible on withdrawal of the drug.

Contra-indications: Hepatic insufficiency, severe dehydration, metabolic acidosis, or severe renal failure (serum creatinine > 5 mg%). Hiprex may be used where mild to moderate renal insufficiency is present.

Hiprex should not be administered concurrently with sulphonamides because of the possibility of crystalluria, or with alkalinising agents, such as mixture of potassium citrate.

Overdosage: Vomiting and haematuria may occur. Bladder symptoms can be treated by the consumption of copious quantities of water and 2–3 teaspoonfuls of bicarbonate of soda.

Pharmaceutical precautions The container should be kept tightly closed.

Legal category P.

Package quantities Bottles of 100 tablets.

Further information Nil.

Product licence number 0068/5003

**Trade Mark*

G. W. Carrick Co Ltd.
Victoria House
Bloomsbury Square
London WC1B 4EB



HORMONIN*

Presentation Each pink tablet contains:

Oestriol	0.27 mg
Oestradiol	0.6 mg
Oestrone	1.40 mg

Uses Hormonin has been designed for replacement therapy in oestrogen-deficiency states, particularly those associated with the menopause such as nocturnal sweating, vasomotor disturbances, psychological upsets, atrophic vaginitis and pruritus vulvae. By maintaining the physiological levels of the three naturally occurring human oestrogens, Hormonin helps to prevent these symptoms that are associated with the menopause.

Dosage and administration Hormonin is given by mouth. The dosage for the relief of menopausal symptoms range from 2 tablets per day to $\frac{1}{2}$ tablet per day or 1 tablet on alternate days, depending upon the severity of the symptoms. In general, the maximum dosage is required for not more than two weeks to initiate therapy. Where it is necessary to control irregular cycles in women approaching the menopause, a dosage of 1 tablet daily is usually adequate.

For prophylactic use in post-menopausal women, a dosage of 1 tablet is recommended daily or on alternate days, according to the needs of the individual patient. Cyclic therapy may be used.

Contra-indications, warnings, etc Hormonin is contra-indicated in patients with pre-existing genital cancer or primary cancer of the breast. A very small proportion of women may complain of a sense of fullness or slight pain in the breasts. This is usually controlled by stopping therapy on alternate days, or, in post-menopausal women, for one week each month. Oestrogens should not be administered to women with recurrent mastitis or abnormal mammograms except in instances where the physician feels that treatment is warranted despite the possibility of aggravation of the mastitis or stimulation of undiagnosed oestrogen neoplasia. A complete pre-treatment physical examination should be followed with special reference to the pelvis and breast. Oestrogen-withdrawal bleeding during cyclic therapy of women patients is a natural occurrence. However, irregular uterine bleeding or spotting should always be thoroughly investigated. The physician should be alert to the earliest manifestation of thrombotic disorders. Should this problem occur, discontinue oestrogen therapy immediately. Pre-existing fibromyomata may increase in size while using oestrogen. For this reason, patients should be examined at regular intervals. Prolonged use might increase the risk of the development of endometrial carcinoma.

Pharmaceutical precautions The product should be stored where there is not excessive heat, moisture or light.

Legal category POM.

Package quantities Securitainers of 100 tablets.

Further information Nil.

Product licence number 0271/5000.

MIDRID*

Presentation Each scarlet Midrid capsule contains:

Isometheptene mucate	65 mg
Dichloralphenazone	100 mg
Paracetamol	325 mg

Uses In the treatment of vascular headaches, including migraine and tension headaches. Midrid contains iso metheptene, a cerebral vasoconstrictor, which provide prompt relief of vascular head-pain by reducing the underlying cerebrovascular disturbances. Midrid also contains dichloralphenazone, which is a sedative/tranquilliser.

The addition of paracetamol in Midrid is designed to bring relief to the throbbing head-pain of migraine; this is the first consideration of the patient. Acting centrally it raises the pain threshold between the thalamus and the cortex, in doses that produce few, if any, other central or peripheral effects.

Dosage and administration *Treatment of migraine headache:* 2 capsules at once, followed by 1 capsule every hour until relief is obtained. Up to 5 capsules with a 12-hour period.

Treatment of tension headache: 2 capsules at once followed by 1 or 2 capsules every four hours. Up to 6 capsules a day. Administration is by the oral route.

Contra-indications, warnings, etc

Contra-indications: Midrid is contra-indicated in severe renal, hepatic or organic heart disease, severe hypertension, glaucoma, and in those patients who are on monoamine-oxidase inhibitor therapy.

Side-effects; Transient dizziness may appear in hypersensitive patients. This can usually be eliminated by reducing the dose.

Overdosage; No specific antidote. Gastric lavage plus appropriate supportive treatment.

Pharmaceutical precautions Store in a close container away from excessive moisture, heat or light.

Legal category POM.

Package quantities Securitainers of 50 capsules.

Further information Nil.

Product licence number 0271/5001.

*Trade Mark

EUGLUCON®

Presentation Euglucon is available as:

1. White, circular, biconvex tablets, 6 mm in diameter, marked EU on one side and 2.5 on the reverse. Each tablet contains 2.5 mg Glibenclamide BP.

2. White, oblong 10 mm x 5 mm tablets containing 5 mg Glibenclamide BP. Each side has a breakline and is inscribed BM/EU, such that when a tablet is broken into half, one side is marked BM, and the other EU.

Uses Euglucon is an oral hypoglycaemic agent of the sulphonylurea type.

Euglucon is indicated for the treatment of maturity-onset diabetes which is not adequately controlled by dietary measures alone.

Dosage and administration Euglucon should be taken with or immediately after food. The total daily dosage is preferably given as a single dose at breakfast with the first main meal, but due consideration should be given to the patient's meal habits and daily activity when apportioning dosage.

New Diabetics. In maturity-onset diabetes of mild to moderate severity, treatment should be started with 5 mg daily or 2.5 mg in debilitated or elderly patients. If this dosage is not sufficient for proper control it should be increased by 2.5 mg at intervals of one week, or as directed by the clinician. The total daily dose of Euglucon rarely exceeds 15 mg. Increasing dosage beyond this level is unlikely to produce further response.

Transfer from other sulphonylureas: Transfer to Euglucon can usually be carried out without any break in therapy.

Euglucon treatment should be started with 5 mg daily and, if necessary, adjusted in steps of 2.5 or 5 mg. A dose of 5 mg Euglucon is approximately equivalent to 1,000 mg tolbutamide, 250 mg chlorpropamide, 25 mg libornuride or 5 mg glipizide.

Changeover from biguanides: Euglucon treatment should be started with 2.5 mg of Euglucon and the biguanide withdrawn. Dosage should then be adjusted by increments of 2.5 mg to achieve control.

Combination with biguanides: If adequate control is not possible with diet and 15 mg of Euglucon, control can often be re-established by a combination of Euglucon and a biguanide derivative.

Euglucon and insulin: While it is appreciated that most patients who are on insulin therapy will continue to need it, there may be a few patients, particularly those on low daily dosages, who will remain stabilised if transferred to Euglucon.

No dosage recommendations can be made for the administration of Euglucon to children.

Contra-indications, warnings, etc Euglucon is contra-indicated in:

1. The treatment of juvenile or unstable diabetes.

2. Patients who have had serious metabolic decompensation with ketosis and, in particular, diabetic pre-coma and coma.

3. Serious impairment of renal, hepatic, thyroid or adrenocortical function.

4. Pregnancy. After delivery. Euglucon therapy can be started or resumed.

Precautions: The hypoglycaemic action of oral anti-diabetic agents including Euglucon may be enhanced by sulphonamides, salicylates, phenylbutazone, coumarin derivatives, beta-blocking agents, monoamine-oxidase inhibitors, cyclophosphamide, chloramphenicol and tuberculostatics. Conversely, thiazide diuretics, frusemide, ethacrynic acid, oral contraceptives containing oestrogens, and corticosteroids may diminish hypoglycaemic activity.

In patients suffering from intercurrent infections or trauma, the dosage of Euglucon may need to be increased. If such complications are severe, diabetic control may be lost necessitating withdrawal of Euglucon and maintenance of diabetic control with insulin. Euglucon should be re-introduced when the patient has recovered from the infection or trauma.

Side-effects: Euglucon is well tolerated and side-effects serious enough to necessitate withdrawal are uncommon. Gastro-intestinal symptoms (nausea, anorexia and diarrhoea) are uncommon and allergic skin reactions are seldom encountered.

Reversible leucopenia and thrombocytopenia have been reported but are rare. Transient changes in liver enzyme concentrations and liver function tests during treatment with glibenclamide have been reported, but these are not known to be directly attributable to the product. As with other agents, hypoglycaemia can occur with Euglucon, but is not usually prolonged and responds to appropriate therapeutic measures.

Effects of overdosage and their treatment: If a hypoglycaemic reaction should occur, the conscious patient may be treated with dextrose or 3–4 lumps of table sugar with water. This may be repeated, if necessary, in 15 minutes.

If the patient is comatose, sucrose or dextrose may be given by stomach tube or dextrose given intravenously. Glucagon may be administered in a dose of 1 mg subcutaneously or intramuscularly to produce consciousness.

Pharmaceutical precautions No special storage requirements.

Legal category POM.

Package quantities 5 mg tablets: Blister packs of 100.

2.5 mg tablets: Blister packs of 100.

Further information Absorption studies in healthy human volunteers using labelled glibenclamide formu-

lated as Euglucon tablets showed a mean absorption of $84 \pm 9\%$.

Excretion was approximately 50% in the urine and 50% in the faeces. Absorbed glibenclamide was completely metabolised and the three isolated metabolites in the concentrations found had no significant hypoglycaemic activity.

Product licence numbers

Euglucon 2.5 mg Tablets 0109/0073
Euglucon 5 mg Tablets 0109/5023

PROCTOFIBE* ▼

Presentation Proctofibe is available as beige biconvex film-coated tablets, 12 mm in diameter, each containing 375 mg of a fibrous extract of grain and 94 mg of a fibrous extract of citrus.

Uses Colonic and gastro-intestinal disorders where a high-fibre regimen is indicated including uncomplicated diverticular disease, irritable colon, simple constipation, haemorrhoidal disorders, anal fissure, pregnancy, myocardial infarction and other conditions where straining at stool should be avoided.

Dosage and administration *Adults:* 4–12 tablets daily in divided doses, or as directed by the physician.

Children: Over three years of age, as adults.

The tablets should be swallowed with ample water. (Alternatively, they may be crushed and dispersed in water.)

Contra-indications, warnings, etc Intestinal obstruction, gluten enteropathies, coeliac disease. As with other fibre presentations, transient bloating and flatulence may occasionally be reported in the first two weeks of treatment.

Pharmaceutical precautions Store in a cool, dry place.

Legal category P.

Package quantities Bottles of 125 tablets.

Further information Nil.

Product licence number 0109/0081.

PROCTOSEDYL*

Presentation Proctosedyl is available as smooth, off-white suppositories and as an odourless, yellowish-white, translucent, greasy ointment. Each suppository or gram of ointment contains the following active ingredients.

Cinchocaine Hydrochloride BP	5 mg
Hydrocortisone BP	5 mg
Framycetin Sulphate BP (Soframycin)	10 mg
Aesculin	10 mg

Uses The local anaesthetic cinchocaine relieves pain and relaxes sphincteric spasm. Pruritus and inflammation are relieved by hydrocortisone, which also decreases serous discharge, while Soframycin controls local infection (a cause of inflammation and irritation).

Proctosedyl is thus used for the following: internal and external haemorrhoids; prophylaxis between attacks to prevent recurrences; haemorrhoidal complications—anal pruritus, perianal eczema, proctitis, fissure; pre-operative and post-operative treatment of haemorrhoidectomy patients; post-partum haemorrhoidal conditions.

Dosage and administration A suppository is inserted morning and evening, and after each stool.

Apply the ointment in small quantity with the finger on the painful or pruritic area, morning and evening and after each stool. For deep application attach cannula to tube, insert to full extent and squeeze tube gently from lower end whilst withdrawing.

The ointment may be used separately or concurrently with the suppositories.

Contra-indications, warnings, etc Known hypersensitivity to any of the ingredients.

In pregnant animals, administration of corticosteroids can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

As with all preparations containing topical corticosteroids, the possibility of systemic absorption should be considered. In particular, long-term continuous therapy should be avoided in infants. Adrenal suppression can occur even without occlusion.

Pharmaceutical precautions Store cool.

Legal category POM.

Package quantities *Proctosedyl Suppositories* Packs of 12.

Proctosedyl Ointment: Tubes of 15 g and 30 g (with cannula).

Further information Nil.

Product licence numbers

Proctosedyl ointment 0109/5038
Proctosedyl Suppositories 0109/5039

SURGAM* ▼

Presentation White, convex tablets, 10 mm in diameter, marked SURGAM 200 on one side and  on the reverse. Each tablet contains 200 mg tiaprofenic acid.

Uses *Properties:* Surgam is a non-steroidal anti-inflammatory agent with marked analgesic properties.

Indications: Rheumatoid arthritis, osteoarthritis; low back pain; musculo-skeletal disorders such as fibrositis, capsulitis, epicondylitis and other soft-tissue inflammatory conditions; sprains and strains, post-operative inflammation and pain and other soft-tissue injuries.

Dosage and administration *Adults:* 600 mg daily in divided doses.

Children: There are insufficient data to recommend use of Surgam in children.

Contra-indications, warnings, etc

Contra-indications: Active peptic ulceration, hypersensitivity to the drug.

Precautions: Surgam should be used with care in patient with a history of peptic ulceration, severe renal or hepatic insufficiency, asthma or previous sensitivity to aspirin or other non-steroidal anti-inflammatory agents. Since Surgam is highly protein-bound, it may be necessary to modify the dosage of other highly protein-bound drugs; e.g. anticoagulants, sulphonamides, hypoglycaemic agents, phenytoin and certain potent diuretics when these are administered concurrently.

Pregnancy: Although animal studies have not revealed evidence of teratogenicity, safety in human pregnancy and lactation cannot be assumed and, in common with other non-steroidal anti-inflammatory agents, administration during the first trimester should be avoided.

Lactation: There are no data on the passage of Surgam into the breast milk.

Side effects: Surgam is generally well tolerated. However, there have been occasional reports of gastrointestinal upset, headache, drowsiness and skin rash.

Treatment of overdosage: In the event of overdosage with Surgam, supportive and symptomatic therapy is indicated.

Pharmaceutical precautions Store in a cool place and protect from light.

Legal category POM.

Package quantities 200 mg tablets in bottles of 100.

Further information Nil.

Product licence number 0109/0108.

RYTHMODAN* CAPSULES

RYTHMODAN* RETARD TABLETS ▼

RYTHMODAN INJECTION

Presentation *Oral.*

Rythmodan Capsules: Capsules with opaque green cap and opaque yellow body with 'RY' and 'RL' printed in black, containing 100 mg of disopyramide base.

Capsules with opaque white cap and body with 'RY' and '150' printed in black, containing 150 mg disopyramide base.

Rythmodan Retard Tablets: White, circular biconvex tablets, 12 mm in diameter, film-coated with a break line. Tablets are marked 'RY' and 'R' on one side and  on the reverse. Each tablet contains disopyramide phosphate equivalent to 250 mg disopyramide base in a sustained release formulation.

Intravenous Injection.

Rythmodan Injection: Ampoules for intravenous use only, 5 ml ampoules containing disopyramide phosphate equivalent to 50 mg disopyramide base in solution.

Uses Properties: Rythmodan is able to prevent and control a wide variety of cardiac arrhythmias probably by slowing conduction in the His-Purkinje system and by increasing the effective refractory period of the atria and ventricles.

Indications Oral Rythmodan is indicated in:

1. Maintenance of normal rhythm following conversion by Rythmodan Injection, other parenteral drugs or electroconversion.
2. Prevention of arrhythmias after myocardial infarction.
3. Treatment of persistent ventricular and atrial extrasystoles, paroxysmal supraventricular tachycardia, Wolff-Parkinson-White syndrome.
4. Suppression of arrhythmias during surgical procedures.
5. Control of arrhythmias following the use of digitalis or similar glycosides.

Rythmodan Injection is intended for intravenous use only and is indicated in the following conditions:

1. Conversion of ventricular and supraventricular

arrhythmias after myocardial infarction, including those not responding to lignocaine or other i.v. treatment.

2. Control of ventricular and atrial extrasystoles, supraventricular tachycardia, and Wolff-Parkinson-White syndrome.

3. Control of arrhythmias following digitalis or similar glycosides when Rythmodan cannot be administered orally.

Dosage and administration *Oral Rythmodan*

Capsules: The recommended daily dosage in adults is 300–800 mg in divided doses adjusted according to the response of the patient.

Rythmodan Retard Tablets: The recommended dose for stabilised patients or those receiving Rythmodan for the first time is 1 to 1½ tablets (250–375 mg) twice daily. Patients being transferred from intravenous therapy with Rythmodan should be stabilised on standard Rythmodan capsules for the first 24 hours (see below). Tablets should be swallowed and not crushed or chewed.

Intravenous Injection/Rythmodan Injection: The recommended dosage can be given by two different regimes.

1. An initial direct intravenous injection of 2 mg/kg (but not exceeding 150 mg (15 ml) irrespective of body weight) should be given SLOWLY OVER NOT LESS THAN FIVE MINUTES, i.e. the rate of injection must not exceed 30 mg (3 ml) per minute in order to reduce or avoid unwanted haemodynamic effects. If conversion occurs during this time the injection should be stopped. If the arrhythmia is to respond to Rythmodan it will usually do so within 10–15 minutes after completion of the injection.

Transfer to oral maintenance therapy is accomplished by giving 200 mg orally, immediately on cessation of intravenous administration, followed by 200 mg every 8 hours for 24 hours. Most patients may be maintained subsequently on a daily dosage of 500–750 mg of Rythmodan, preferably administered as 1 to 1½ Rythmodan Retard tablets (250–375 mg) twice daily. Where the need for lower dosage outweighs the convenience of twice daily administration, appropriate doses of conventional capsules (100 to 150 mg) may be administered.

If conversion is achieved by intravenous Rythmodan but the arrhythmia subsequently recurs, a further slow direct intravenous injection over not less than five minutes may be administered cautiously and preferably under ECG control. The total administration by the intravenous route should not exceed 4 mg/kg (maximum 300 mg) in the first hour, nor should the combined administration by the intravenous and oral routes exceed 800 mg in 24 hours.

2. An initial direct intravenous injection as above, i.e. over not less than five minutes, maintained by intravenous infusion by drip of 20–30 mg/hour (or 0.4 mg/kg/hour) up to a maximum of 800 mg daily. This regime should be employed if the patient is unable to take oral medication or in particularly serious arrhythmias being treated in coronary care units.

Heart failure: In determining the intervals between administration of Rythmodan capsules it should be borne in mind that whilst the elimination half-life in normal volunteers is approximately seven hours, in patients with heart failure, half-life values of 12 hours or more have been recorded.

Impaired renal function: Standard capsules should be used in patients in renal failure. A reduced dosage,

preferably accompanied by assay of disopyramide plasma levels in cases of severe renal failure (creatinine clearance <8 ml/min) is recommended. The following table may be helpful as a guide.

<i>Creatinine clearance (ml/min)</i>	<i>Dosage 100 or 150 mg capsules</i>
Normal	Normal dosage
20–60	100 mg 8-hourly or 150 mg 12-hourly
8–20	100 mg 12-hourly
<8	150 mg daily

Children: There are insufficient data to recommend the use of Rythmodan in children.

Contra-indications, warnings, etc

Contra-indications: Disopyramide is contra-indicated in second or third degree heart block and sinus node disease if no pacemaker is present, cardiogenic shock and severe uncompensated heart failure and hypersensitivity to disopyramide.

Warnings and precautions: There have been reports of ventricular tachycardia or ventricular fibrillation or Torsade de Pointes in patients receiving disopyramide. These have been usually, but not always, associated with significant widening of the QRS complex or prolonged QT interval. If these ECG changes or arrhythmias develop the drug should be discontinued.

Disopyramide should be used only with caution in patients with atrial flutter or atrial tachycardia with block as conversion of a partial AV block to a 1:1 response may occur. Accordingly, the need for prior digitalisation should be considered.

Owing to its negative inotropic effect, disopyramide should be used with caution in patients suffering from significant cardiac failure. Such patients should be fully digitalised or controlled with other therapy before initiating treatment with disopyramide.

The occurrence of hypotension following disopyramide administration, which has been observed especially in patients with cardiomyopathy or inadequately compensated congestive heart failure, requires prompt discontinuation of the drug. Any resumption of therapy should be at a lower dose with close patient monitoring.

The use of disopyramide in combination with other negative inotropic drugs such as beta adrenoceptor antagonists is not recommended especially in intravenous therapy.

In view of the serious nature of many of the conditions being treated it is suggested that *Rythmodan Injection should only be used when facilities exist for cardiac monitoring or defibrillation, should the need arise.*

Disopyramide should be used with caution in patients receiving concurrent therapy with diuretics likely to give rise to hypokalaemia since this may reduce patient response to disopyramide.

Disopyramide should be used with caution in the treatment of digitalis intoxication.

Care should be taken when prescribing disopyramide for patients with bundle branch block as the effect of disopyramide in this condition is unpredictable. If first degree heart block develops in a patient receiving disopyramide, dosage should be reduced and may require discontinuation if the block persists.

Since disopyramide is eliminated predominantly by glomerular filtration the dose administered to patients with significant renal impairment may require adjustment. Patients with renal impairment should not be treated with sustained release disopyramide.

Hepatic impairment causes an increase in the plasma half-life of Rythmodan and a reduced dosage may be required.

Due to its anticholinergic properties, patients with glaucoma, a tendency to urinary retention, or any patient receiving a drug with anticholinergic activity may be unsuitable for Rythmodan therapy.

Pregnancy: Although Rythmodan has undergone animal tests for teratogenicity without evidence of any effect on the developing foetus, the benefits of using Rythmodan in the first trimester of pregnancy should be weighed against possible risks.

Lactation: There are no data on the excretion of Rythmodan into human milk. However, animal studies have shown a higher concentration of Rythmodan in milk than in plasma. Therefore, if the drug is considered essential, an alternative method of infant feeding should be used.

Side effects: Rythmodan is usually well tolerated. Most common side effects (dry mouth, blurred vision, urinary hesitancy) are attributable to the drug's mild anticholinergic action. Exceptionally this may be marked. Gastrointestinal irritation may also occur. Very rarely, disopyramide therapy has been associated with acute psychosis, cholestatic jaundice and hypoglycaemia. Side effects usually disappear rapidly with reduction of dosage or cessation of therapy. Profuse sweating may indicate too rapid intravenous injection.

Overdosage: Animal studies indicate that overdosage may lead to cardiac arrest or atrio-ventricular block or to disorders of ventricular excitability leading to terminal ventricular fibrillation. Intracardiac conduction defect and ventricular hyperexcitability may be controlled by general intensive supportive therapy.

Infusion studies in dogs and man have shown the effectiveness of isoprenaline in restoring any marked fall in blood pressure.

Pharmaceutical precautions Store in a cool place. Rythmodan Injection is physically compatible with the following: Sodium Chloride Injection BP, Dextrose Injection BP, Compound Sodium Chloride Injection BP, Compound Sodium Lactate Injection BP.

Legal category POM.

Package quantities

Rythmodan Capsules 100 mg	Packs of 100
Rythmodan Capsules 150 mg	Packs of 100
Rythmodan Retard 250 mg	Packs of 100
Rythmodan Injection 50 mg/5 ml	Packs of 5 ampoules

Further information Nil.

Product licence numbers

Rythmodan Capsules 100 mg	0109/0022
Rythmodan Capsules 150 mg	0109/0075
Rythmodan Retard Tablets 250 mg	0109/0094
Rythmodan Injection	0109/0060

***Trade Mark**

(PRESOLINE®)

Representation Apresoline Tablets each containing 5 mg hydralazine hydrochloride, circular, polished, sugar-coated tablets, pale yellow in colour, marked CIBA on one side and the letters GF on the other.

Apresoline Tablets each containing 50 mg hydralazine hydrochloride, circular, polished, sugar-coated tablets, violet-red in colour, marked CIBA on one side and the letters HG on the other.

Ampoules each containing 20 mg hydralazine hydrochloride, presented as a white lyophilised powder in a clear glass 2 ml ampoule (requiring reconstitution before use – see 'Dosage' below).

Uses *Mode of action:* Apresoline lowers blood pressure apparently by exerting an arteriolar dilating effect through a direct relaxation of vascular smooth muscle. Although the precise mechanism of action of Apresoline is not fully understood, the major effects are on the cardiovascular system, with no important effects on the central nervous system. Apresoline exerts a moderate but significant antihypertensive effect (diastolic more than systolic). Because of its selective dilating effect on arterioles, it tends to improve renal, uterine and cerebral blood flow. The effect results in a decrease in arterial blood pressure and peripheral vascular resistance, and in increase in heart rate, stroke volume and cardiac output. The rise in cardiac output accompanies the fall in blood pressure, probably as a reflex response. In patients with heart failure, these reflexes are attenuated and the improvement in cardiac output is due to afterload reduction, without accompanying tachycardia or hypotension; it also serves to improve renal blood flow and renal function.

Indications *Hypertension: Oral:* Apresoline is indicated, usually in conjunction with other anti-hypertensive agents for the treatment of moderate to severe hypertension. Especially good results are obtained in combination with a beta-adrenergic blocker such as propranolol, with base-line diuretic therapy in addition.

Parenteral: Apresoline is used intravenously to control hypertensive emergencies, particularly those associated with pre-eclampsia and toxemia of pregnancy, and in hypertension with renal complications. (See Contraindications, warnings, etc.). In hypertensive patients with normal kidneys who are treated with Apresoline, there is evidence of increased renal blood flow and a maintenance of glomerular filtration rate. In some instances improved renal function has been noted where control values were below normal prior to the administration of Apresoline.

Chronic congestive cardiac failure Apresoline is recommended in the management of moderate to severe congestive cardiac failure in patients in whom optimal doses of diuretics and cardiac glycosides are proving insufficient.

In patients with high left ventricular filling pressure, it is advisable to combine Apresoline with a nitrate.

Dosage and administration *Hypertension: Oral:* The initial dose of Apresoline is 25 mg, two or three times daily in combination with a beta-blocker plus thiazide diuretic. This may be increased to a maximum of 200 mg daily given in two or three divided doses.

Parenteral: In hypertensive emergencies, 20–40 mg should be given by slow intravenous injection or intravenous drip and repeated as necessary. The contents of the vial should be reconstituted with 1 ml of water for injection and then diluted with saline. Once reconstituted the injection must be given immediately and any remainder discarded. It is inadvisable to use dextrose solution as a vehicle for the parenteral administration of hydralazine. Apresoline for infusion can be used with a 5% sorbitol solution, or isotonic inorganic infusion solutions such as sodium chloride or Ringer's solution.

Chronic congestive cardiac failure: It is advisable to initiate therapy in hospital, with a starting dose of 25 mg three or four times daily. Dependent on the clinical response, this dose may need to be increased every second day up to a dose of 50–75 mg three to four times daily. In acute heart failure, single initial doses of 100 mg or possibly 200 mg may be required. Occasionally, where oral therapy is inappropriate, 20 mg may be given intravenously and repeated at hourly intervals depending on response.

Because of the known association of a reversible lupus like syndrome with high or prolonged dosage of Apresoline, acetylator status should be determined when maintenance therapy is established, and where appropriate ANF titre should be monitored periodically.

Contra-indications, warnings, etc *Side-effects:* Tachycardia, headache, flushing, anorexia, nausea and vomiting can occur. All these side effects may be minimised by the prior administration of a beta-blocker.

Contra-indications: Apresoline has been found to be teratogenic in mice, producing a small incidence of cleft palate and certain other minor bony malformations, in oral doses ranging from 20–120 mg/kg. Its use should therefore be avoided in the first half of pregnancy that is, during the period of organogenesis.

Apresoline should also be avoided in patients with tachycardia.

Precautions: Occasionally patients on Apresoline develop symptoms suggestive of rheumatoid arthritis. Also skin reactions and fever may occur producing a syndrome similar to systemic lupus erythematosus. This is much more likely to occur with high doses and is rare below doses of 200 mg. In cardiac failure, where higher doses may be necessary, the precautions indicated in the 'Dosage and Administration' section should be observed. If such symptoms do develop, the drug should be gradually withdrawn, when remission will usually occur. Only rarely is it necessary to treat the reaction with corticosteroids.

Apresoline should not be prescribed in cases of left ventricular heart failure due to severe aortic or mitral

stenosis or in constrictive pericarditis. Apresoline should be used with caution in patients with coronary disease or undergoing anaesthesia (which may precipitate severe hypotension), or in patients taking tricyclic antidepressants or MAO inhibitors.

Treatment of overdose: Gastric lavage or, in the absence of coma, emetic treatment should be instituted as soon as possible. If hypotension is present, an attempt should be made to raise the blood pressure without increasing the tachycardia. Adrenaline should therefore be avoided. Supportive measures such as intravenous fluids and elevation of foot of bed are also indicated. Cautious administration of angiotensin or noradrenaline intravenously may be of use.

Pharmaceutical precautions The tablets should be protected from heat and moisture.

Legal category POM.

Package quantities *Apresoline Tablets 25 mg:* Securitainers of 100.

Apresoline Tablets 50 mg: Securitainers of 100.

Apresoline Ampoules 20 mg: Dry hydralazine hydrochloride in boxes of 5.

Further information Apresoline improves the renal and uterine blood flow. This makes it ideally suited for use in toxemia of pregnancy, and in hypertension with renal complications. Apresoline also improves cerebral blood flow and is useful especially in combination with a beta-blocking drug in elderly patients.

Apresoline lowers blood pressure by a reduction in peripheral resistance, but when used as monotherapy, this beneficial effect is counterbalanced to some extent by a reflex tachycardia. The concomitant use of a beta-blocking drug like oxprenolol will prevent this associated increase in cardiac output and enhance the antihypertensive effect considerably.

Product licence numbers

Apresoline Tablets 25 mg	0008/5002
Apresoline Tablets 50 mg	0008/0029
Apresoline Ampoules 20 mg	0008/5065

DESFERAL*

Presentation A sterile, lyophilised powder available in vials containing 500 mg of desferrioxamine mesylate.

Uses A highly specific iron chelating agent recommended for the treatment of acute iron poisoning, chronic iron accumulation, primary haemochromatosis and secondary haemochromatosis (haemosiderosis); for the diagnosis of iron storage disease and certain anaemias; and for the management of corneal rust stains and ocular siderosis.

Dosage and administration When administered parenterally, the drug should be employed in the form of a 10% solution, e.g. by dissolving the contents of one vial (500 mg) in 5 ml of distilled water. If the solution is slightly opalescent, it can still safely be given intramuscularly or subcutaneously. The 10% Desferal solution can be diluted with routinely employed infusion solutions (saline, glucose, dextrose or dextrose-saline). For intravenous infusions, however, only clear solutions should be used.

The dosage recommendations are the same for adults and children.

Treatment of pathological iron overload: As a rule,

treatment with Desferal should be continued for at least several months, possibly on an intermittent basis. To assess the response, urinary iron excretion should initially be monitored daily, and later at longer intervals (but no less than once every 2 weeks).

Although Desferal can be given by intramuscular injection, in most cases it exerts a considerably greater effect when administered – preferably with the aid of a portable, light-weight, infusion pump – by continuous intravenous or subcutaneous infusion. Intravenous infusions usually prove somewhat more effective than subcutaneous infusions, which are particularly suitable for ambulant patients.

However, since the iron excretion rates obtained with the above mentioned modes of administration vary from patient to patient, one should first individually determine which of them yields the best results before embarking on long-term medication.

For the purposes of infusion treatment the average daily dose is 1.5–4 g administered intravenously or subcutaneously over a period of approximately 12 hours. In some cases it is possible to achieve a further increase in iron excretion by infusing the same daily dose over a 24-hour period.

For intramuscular treatment the average initial dose is 0.5–1 g daily, given in 1–2 injections. The maintenance dose to be selected will depend on the patient's iron excretion rate.

Treatment of acute iron poisoning: In this indication larger doses, administered both orally and parenterally are usually required. Speed is essential.

Gastric lavage should be carried out as quickly as possible using, if readily available, 1% sodium bicarbonate solution. This should be followed by the oral administration, by stomach tube if necessary, of 5–10 g (the contents of 10–20 vials) of Desferal in 50–100 ml of fluid. This will chelate any iron remaining in the stomach and prevent any further absorption.

To eliminate the iron that has already been absorbed 1–2 g Desferal should be injected intramuscularly every 3–12 hours; alternatively, Desferal should be infused either subcutaneously or – particularly if the patient is seriously ill and already in a state of shock – intravenously at a rate of not more than 15 mg/kg/h, the maximum dose in any 24 hours being 80 mg/kg. Duration of treatment will depend on the patient's condition.

Further measures, e.g. sodium bicarbonate, sedatives, oxygen, etc., may be given as necessary. The patient's progress should be checked by serum iron determinations.

It should be noted that the serum iron level may rise sharply when the iron is released from the reticuloendothelial system.

Theoretically 100 mg of Desferal can chelate approximately 8.5 mg of iron, thus 5 g can chelate the iron contained in about 10 tablets of ferrous sulphate or ferrous gluconate.

Desferal test for iron overload: This test is based on the principle that normal subjects do not excrete more than a fraction of a milligram of iron in their urine daily and a standard intramuscular injection of 500 mg of Desferal does not increase this above 1 mg. In iron storage diseases, however, the increase may be well over 1.5 mg.

Procedure:

1. The haemoglobin, serum iron and total iron binding capacity are estimated.

2. 500 mg of Desferal are given intramuscularly and 400 ml of water are drunk.

3. All urine is collected over the next six hours.
4. The urinary iron is estimated in the six hour urine specimen.

An excretion of 1–1.5 mg (18–27 μmol) of iron during this 6-hour period is suggestive of an iron-storage disease; values of more than 1.5 mg (27 μmol) can be regarded as definitely pathological. The test yields reliable results only in cases where renal function is normal.

Contra-indications, warnings, etc *Contra-indications:* None.

Precautions: Desferal should only be used with caution in patients with renal dysfunction.

In acute iron poisoning requiring treatment with Desferal in patients suffering from severe renal dysfunction, dialysis might help to eliminate the chelated iron.

Rapid intravenous injections of Desferal may give rise to hypotonic shock. This seems to be due to too rapid injection of the material. It is therefore wiser to adhere to the recommendation to give Desferal by intravenous infusion.

Where an iron-storage disease is associated with scorbutic acid deficiency, oral administration of vitamin C in the standard dosage (130–250 mg daily, given in fractional doses) may serve to enhance excretion of the iron complex in response to Desferal; larger doses of vitamin C fail to produce an additional effect. In patients with severe chronic iron-storage disease undergoing combined treatment with Desferal and high doses of vitamin C (more than 500 mg daily) impairment of cardiac function has been encountered; this proved reversible when the vitamin C was withdrawn. Monitoring of cardiac function is indicated during such combined therapy.

Pregnancy: Desferal should not be given during pregnancy unless, in the judgment of the physician, the expected benefits outweigh the potential risk.

Side-effects: There have been only rare reports of allergic skin reactions and cardiovascular (e.g. hypotension, shock), neurological (e.g. dizziness, convulsions), and gastro-intestinal disturbances, impairment of hepatic and renal function, as well as changes in the blood picture (e.g. thrombocytopenia). Some of these manifestations, however must be considered as signs and symptoms of the underlying disease. The iron complex excreted under treatment with Desferal may cause reddish-brown discoloration of the urine.

Opacities of the lens have been observed in animal experiments after prolonged administration of very high doses. Patients should therefore have their eyes examined both prior to the institution of long-term treatment with Desferal and also from time to time during medication.

Local pain may occur after intramuscular injection.

Pharmaceutical precautions Desferal should be stored at 4°C or below.

Legal category POM.

Package quantities Available in packs of 10 vials, each containing 500 mg. Desferal.

Further information Desferal is readily soluble in water so that it can be rapidly administered both orally and parenterally in situations where speed is essential. It is highly specific for trivalent iron and the resulting chelate is stable and non-toxic. The intestinal chelate is not absorbed and that formed systemically as a result of

parenteral administration is rapidly excreted via the kidneys without deleterious effects. Desferal mobilises and removes iron from all human organs, tissues and proteins excepting haemoglobin and undesirable effects on erythropoiesis have not been reported.

Method for preparing desferrioxamine eye drops:

1. **Preparation of solvent:** Formula:

Methyl cellulose 4,000 cps	25 mg	0.5%
Benzyl alcohol	50 mg	1.0%
Water for Injection q.s.	5.0 ml	100%

Method: The methyl cellulose is dispersed in water for injection at 90°C. This is cooled with continuous stirring. When the temperature reaches 35°C, benzyl alcohol is added and the solution diluted to volume with water for injection. The solution should be filtered through a No 1, then No 2 sintered glass filter. 5 ml of this solution are filled into brown/amber eye drop bottles, stoppered and autoclaved at 110°C for 20 minutes.

2. **Preparation of drops:** To be carried out under aseptic conditions.

- (a) Remove foil disc from Desferal vial containing 500 mg Desferal.
- (b) Unscrew eye drop bottle cap and take up 5 ml of solvent into a sterile syringe; replace cap.
- (c) Inject solvent into vial and shake to dissolve the Desferal. Care should be taken to dissolve all the Desferal.
- (d) Withdraw the solution into the sterile syringe; remove cap from bottle; transfer solution to bottle and replace cap.

The drops are now ready for use.

Note: Desferal (desferrioxamine mesylate) is unstable in solution and thus the eye drops should be prepared at the time of use. The solution should be discarded at the end of one week from the date of preparation.

Product licence number 0008/5073

DORIDEN*

Presentation Doriden Tablets each containing 250 mg of glutethimide as a circular, flat, white tablet with bevelled edges, having the monogram CIBA on one side and the letters GA and a break line on the other.

Uses *Mode of action:* Doriden is an effective oral, general-purpose, non-barbiturate hypnotic, with a prompt action and a medium duration of effect. The active constituent, glutethimide, is lipid soluble which ensures rapid and effective penetration of the central nervous tissue, whilst its metabolites are completely soluble in water and hence completely and easily excreted by the kidneys.

Indications: Doriden is recommended for the treatment of insomnia (including disturbed and restless sleep).

Dosage and administration *Adults:* For insomnia, initially 1 or 2 tablets a quarter to half an hour before retiring. It may be possible to reduce the dosage to 1 tablet subsequently.

Children: aged 1–6 years: $\frac{1}{2}$ tablet.

Over 6 years: 1 tablet.

Contra-indications, warnings, etc *Side-effects:* Doriden has been known occasionally to produce skin rashes, nausea and hyperexcitability, and more infre-

quently, acute hypersensitivity reactions, blood dyscrasias and peripheral neuropathy have been reported.

Prolonged use of Doriden may lead to the development of dependence and to toxic confusional states.

Contra-indications: Use in patients hypersensitive to glutethimide.

Precautions: Doriden should be used with caution in epileptic patients. Withdrawal after a prolonged period of administration in high doses or after an overdosage may lead to epileptic fits.

Doriden may cause drowsiness. Patients receiving this medication should not drive or operate machinery unless the drug has been shown not to interfere with physical or mental ability.

Doriden potentiates the effect of phenothiazines, tricyclic antidepressants, alcohol and diminishes the action of coumarin anticoagulants.

In common with all drug therapy, Doriden should not be used during pregnancy unless considered essential by the physician.

Overdosage: Mild to moderate intoxication as judged by the clinical condition of the patient, or size of the ingested dose (less than 10 g) or blood levels (less than 2.5 mg%) may be treated symptomatically. The standard measures for the care of the unconscious patient, namely gastric lavage, airway care, and the maintenance of respiration and circulation, should be instituted.

Severe intoxication where there is a deep coma, or a history of ingestion of more than 10 g or blood levels of more than 3 mg% may require haemodialysis, which should be considered early. If haemodialysis is undertaken it should be continued until the patient is awake. Careful observation for a further 24 hours is then recommended since Doriden shows affinity for body fat depots, and in response to a rapid lowering of blood levels, it may be released into the blood stream thus precipitating further coma. Sudden episodes of apnoea or hypotension have been reported, possibly related to developing cerebral oedema. Osmotic diuresis by prompt intravenous infusion of 20% mannitol solution has been shown in some cases to abort these episodes.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Tablets of Doriden 250 mg in Securainers of 100 and 500.

Further information Nil.

Product licence number 0008/5005.

ESIDREX*

Presentation Tablets containing 25 mg hydrochlorothiazide, circular, flat, white, with bevelled edges, impressed with the monogram CIBA on one side and the letters CE and a break line on the other.

Tablets containing 50 mg of hydrochlorothiazide, circular, flat, white, with bevelled edges impressed with the monogram CIBA on one side and the letters UT and a break line on the other.

Uses *Mode of action:* Esidrex is a thiazide diuretic which exerts its diuretic effect in inhibiting the reabsorption of sodium, chloride and water, probably at the proximal renal tubules.

Indications: It is indicated for the treatment of oedema associated with acute and chronic heart failure, various

hepatic conditions, renal disorders; such as chronic glomerular nephritis and nephrotic syndrome, the premenstrual syndrome and fluid retention associated with obesity, diabetes insipidus or drug therapy (e.g. with corticosteroids.) It is also recommended for the treatment of hypertension, including hypertension occurring during pregnancy. It is also used to potentiate other antihypertensives such as guanethidine and reserpine.

Dosage and administration Esidrex is given orally. The dosage for adults is:

In acute and chronic heart failure – initially 50–100 mg daily, reducing to a maintenance dose of 25–50 mg three or four days weekly.

Chronic glomerular nephritis, nephrotic syndrome, ascites and hepatic cirrhosis, initially 50–75 mg daily. This may be reduced to a maintenance dose of 25–50 mg on alternate days.

Pre-menstrual oedema – 25 mg daily from the onset of symptoms until menstruation begins.

Drug-induced oedema, 25–50 mg on alternate days.

Hypertension – 25 mg increasing gradually to 75 mg daily according to the response.

Hypertension and oedema of pregnancy, mild symptoms, 25–50 mg daily, moderate hypertension – 50–100 mg daily initially and then reducing to a lower dose when control is achieved.

In all indications the total daily dose may be given as a single dose after breakfast. As Esidrex increases sodium excretion it is usually possible to relax dietary salt restrictions.

Children: At the discretion of the physician.

Contra-indications, warnings, etc

Side-effects: Side-effects such as mild anorexia, nausea, constipation and diarrhoea, skin rashes and photosensitivity may occur. There have been reports of blood dyscrasias including thrombocytopenia, but these are rare.

Contra-indications: Esidrex, in common with other thiazides is contra-indicated in the presence of precoma associated with hepatic cirrhosis, or Addison's disease or advanced renal failure.

Precautions: In patients with some degree of renal impairment, a rise in blood urea can occur and in extreme cases result in an oliguric crisis. In such cases, either the dose should be reduced or the treatment interrupted temporarily.

Prolonged doses may bring about a decrease in glucose tolerance and precipitate a diabetic condition. In known diabetics the addition of Esidrex to the treatment regime will almost certainly alter the insulin requirement.

In common with other thiazide diuretics hyperuricaemia may be induced by Esidrex. Gout may be exacerbated in patients with a previous history or family history of this condition.

Patients who are being treated with this preparation may require regular monitoring of fluid and electrolyte balance particularly when diuresis is substantial or in patients suffering from renal impairment. Potassium supplements may be required. Particular caution is needed with this preparation in the elderly since electrolyte balance is more likely to be precarious due to bowel or renal dysfunction. Also urinary retention is more likely.

Esidrex should only be used during pregnancy considered essential by the physician.

The concomitant administration of this preparation

with cardiac glycosides or hypotensive agents may necessitate adjustment of the dosage of those drugs.

Drug interactions: The action of tricyclic antidepressants and MAO inhibitors may be potentiated by Esidrex.

Overdosage: Esidrex is self-limiting in its action and toxic effects have not been observed.

Pharmaceutical precautions Esidrex should be protected from heat and moisture and should preferably be dispensed in a moisture-proof container.

Legal category POM.

Package quantities Esidrex 25 mg and 50 mg Tablets are available in Securitainers of 100 and 500.

Further information Esidrex has a powerful saluretic and diuretic action, is well tolerated and remains effective when administered for long periods.

Esidrex acts on the renal tubules, inhibiting the reabsorption of sodium and chloride. Low-salt diets may therefore be relaxed during Esidrex therapy.

Esidrex reduces high blood pressure and potentiates the action of other antihypertensives but has no effect on the blood pressure in normotensive individuals.

Product licence numbers

Esidrex Tablets 25 mg 0008/5045

Esidrex Tablets 50mg 0008/5046

SIDREX[®]-K

Description Round white, sugar-coated tablets, 2.1 mm in diameter with a maximum height of 7.7 mm. The inner, slow-release wax core contains 600 mg potassium chloride (8.06 mEq) and the outer coat contains 12.5 mg hydrochlorothiazide.

Uses *Mode of Action:* Esidrex-K is a thiazide diuretic which exerts its diuretic effect by inhibiting the reabsorption of sodium, chloride and water, probably at the proximal renal tubules.

Indications: It is indicated for the treatment of oedema associated with acute and chronic heart failure; various hepatic conditions; various renal disorders, such as chronic glomerular nephritis and nephrotic syndrome, pre-menstrual syndrome and fluid retention associated with obesity, diabetes insipidus or drug therapy (e.g. with corticosteroids). It is also recommended for the treatment of hypertension, including hypertension occurring during pregnancy. It is also used to potentiate other antihypertensives such as guanethidine and reserpine.

Dosage and administration Esidrex-K is given orally and the tablets should be swallowed whole. The dosage for adults is:

In acute and chronic heart failure – initially 50–100 mg daily (4–8 tablets), reducing to a maintenance dose of 5–50 mg (2–4 tablets) three or four days a week.

Chronic glomerular nephritis, nephrotic syndrome, cirrhosis and hepatic cirrhosis – initially 50–75 mg (4–6 tablets) daily. This may be reduced to a maintenance dose of 25–50 mg (2–4 tablets) on alternate days.

Pre-menstrual oedema: 25 mg daily from the onset of symptoms until menstruation begins.

Drug-induced oedema – 25–50 mg (2–4 tablets) on alternate days.

Hypertension – 25 mg increasing gradually to 75 mg daily according to the response.

Hypertension and oedema of pregnancy, mild symp-

oms – 25–50 mg daily (2–4 tablets), moderate hypertension – 50–100 mg (4–8 tablets), daily initially, reducing to a lower dose when control is achieved.

In all indications the total daily dose may be given as 1 dose before breakfast, or 2 equally divided doses after breakfast and lunch. As Esidrex-K increases salt excretion, it is usually possible to relax dietary salt restrictions.

Children: At the discretion of the physician.

Contra-indications, warnings, etc

Side-effects: Side-effects such as mild anorexia, nausea, constipation and diarrhoea, skin rashes and photosensitivity may occur as a result of treatment with Esidrex-K. In common with other thiazides, there have been reports of thrombocytopenia, but these are rare.

Esidrex-K tablets are designed to avoid the risks of gastro-intestinal irritation. However, if a patient under treatment with Esidrex-K develops severe vomiting, severe abdominal pains or flatulence or gastro-intestinal haemorrhage, the preparation should be withdrawn at once, because in the presence of an obstruction it could conceivably give rise to ulceration or perforation.

Contra-indications: Esidrex-K is contra-indicated in the presence of hyperkalaemia or precoma associated with hepatic cirrhosis, Addison's disease or advanced renal failure.

All solid forms of potassium medication are contra-indicated in the presence of obstructions in the digestive tract (e.g. resulting from compression of the oesophagus due to dilation of the left atrium or from stenosis of the gut).

Precautions: In patients with some degree of renal impairment, a rise in blood urea can occur and in extreme cases result in an oliguric crisis. In such cases, either the dose should be reduced or the treatment interrupted temporarily.

Prolonged doses of thiazides may bring about a decrease in glucose tolerance and precipitate a diabetic condition. In known diabetics the addition of Esidrex-K to the treatment regime will almost certainly alter the insulin requirement.

In common with other thiazide diuretics, hyperuricaemia may be induced by Esidrex-K. Gout may be exacerbated in patients with a previous history or family history of this condition.

Patients who are being treated with this preparation may require regular monitoring of fluid and electrolyte balance particularly when diuresis is substantial or in patients suffering from renal impairment. Potassium supplements may be required. Particular caution is needed with this preparation in the elderly since electrolyte balance is more likely to be precarious due to bowel or renal dysfunction. Also urinary retention is more likely.

Esidrex-K should only be used during pregnancy if considered essential by the physician.

The concomitant administration of this preparation with cardiac glycosides or hypotensive agents may necessitate adjustment of the dosage of those drugs.

Drug interactions: The action of tricyclic antidepressants and MAO inhibitors may be potentiated by Esidrex-K.

Overdosage: Esidrex-K is self-limiting in its action and toxic effects have not been observed.

Pharmaceutical precautions Esidrex-K should be protected from heat and moisture and should preferably be dispensed in a moisture-proof container.

Legal category POM.

Package quantities Esidrex-K Tablets are available in Securainers of 100 and 500.

Further information Esidrex-K has a powerful saluretic and diuretic action, is well tolerated and remains effective when administered for long periods.

Esidrex-K acts on the renal tubules inhibiting the reabsorption of sodium and chloride. Low salt diets should therefore be relaxed during Esidrex-K therapy.

Esidrex-K reduces high blood pressure and potentiates the action of other antihypertensives but has no effect on the blood pressure in normotensive individuals.

Product licence number 0008/5035.

ISMELIN*

Presentation Ismelin Tablets each containing 10 mg guanethidine sulphate. Circular, flat, white tablets with bevelled edges, impressed with the monogram CIBA on one side and Ismelin 10 on the other.

Ismelin Tablets each containing 25 mg guanethidine sulphate. Circular, flat, pink tablets with bevelled edges, impressed with the monogram CIBA on one side and Ismelin 25 on the other.

Ismelin Ampoules each containing 10 mg/ml clear, colourless solution of guanethidine sulphate in a clear glass 1 ml ampoule. When Ismelin is given by intravenous infusion, the contents of the ampoule should be added to saline or dextrose saline.

Uses *Mode of action:* Ismelin is a peripheral sympathetic blocking drug which lowers blood pressure by inhibiting vasoconstrictive mechanisms.

Recommended for the treatment of all grades of hypertension. The parenteral formulation is intended for control of hypertensive crises and to obtain more rapid blood-pressure control.

Dosage and administration *Adults: oral:* Ismelin has a sustained length of action in excess of 24 hours, and can therefore be given as a single daily dose which has to be titrated to the patient's particular needs. In mild to moderate hypertension, dosage should begin at 20 mg daily, increasing if necessary to 30 mg daily. A daily dose in excess of 30 mg is rarely required in the milder grades of hypertension.

In patients with more severe hypertension, the majority will be adequately controlled and free from hypertensive symptoms on a daily dose of 40 mg or less. Occasionally, a daily dose of up to 100 mg may be required and, in exceptional cases, even more.

Increments in dosage should not exceed 10 mg and an interval of at least one week should be allowed to elapse before a further increase in dosage is introduced.

Frequent adjustment of dosage during the stabilisation period is not necessary, and according to individual assessment the interval between consultations may be up to one month.

Parenteral: In the management of hypertensive crises, including toxæmia of pregnancy, Ismelin should be given by intramuscular injection. One injection of 10–20 mg will generally cause a fall of blood pressure within 30 minutes which reaches a maximum in one to two hours and is maintained for four to six hours. If a further dose of 10–20 mg is deemed necessary, then three hours should be allowed to elapse between doses.

Children: Ismelin has been used in children, but dosage needs to be established.

Contra-indications,

Side-effects are often an exaggeration of the drug's action. By adhering to the dose and giving small increments where necessary, these effects should be avoided. Should fainting occur, the patient should be advised against rising from a sitting position, the dose should be reduced and the drug discontinued until the next visit.

If diarrhoea proves a problem, the action can be taken: (a) lower the daily dose; (b) lower the daily dose of codeine phosphate to the minimum.

Failure of ejaculation, effects on rare occasions on exertion, nasal congestion, myalgia or muscle weakness, intermittent claudication.

Toxic effects have not been reported with prolonged dosage.

Contra-indications: The drug is contraindicated in the presence of heart failure. In practice, this is rarely a problem in the treatment of hypertension by the use of Ismelin.

Precautions: Ismelin should be used with care in treating patients with renal impairment. Ismelin may increase the effect of a diuretic. As is the case with other agents, Ismelin may increase the risk of bleeding by lowering blood platelet counts or myoclonic activity.

Caution should be exercised in patients with a history of recent cerebral or myocardial infarction.

When patients have been treated with Ismelin, it should be remembered that treatment may be delayed for a day of operation. As the drug is not excreted during anaesthesia with larger doses of atropine.

N.B. Intravenous injection should be given by slow i.v. drip.

Interaction with other drugs: Ismelin, like other tricyclic antidepressants, tends to potentiate the actions of Ismelin: this is particularly true in treating patients already receiving sedatives, or those classes. The hypotensive effect is enhanced by alcohol or other depressants.

Additive effects. The tricyclic antidepressants, such as Rauwolfia alkaloids, potentiate the effects of Ismelin, bearing in mind the effects of reserpine and thiazides potentiate its action. More than normal will be required when Ismelin is given with reserpine, such as 10 mg weekly, at the same time as previous compounds.

Treatment of overdosage

tatic collapse, which usually requires no treatment other than keeping the patient recumbent. Occasionally pressor agents may be required in severe cases.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Tablets 10 mg and 25 mg of smelin in bubble packs of 100 (10 modules of 10 tablets).

Also ampoules of 1 ml containing 10 mg in boxes of 1.

Further information Ismelin can be relied upon to lower blood pressure in almost all patients with hypertension. It is widely used in those patients whose blood pressure needs lowering more than can be achieved with diuretic alone. Such patients can be managed on a simple regime of two Navidrex[®] K and two Ismelin 10 mg tablets daily. Response to Ismelin is usually reliable and predictable for long periods, as tolerance requiring adjustment of dosage is not normally a problem.

Product licence numbers

smelin Tablets 10 mg 0008/5006

smelin Tablets 25 mg 0008/5007

smelin Ampoules 0008/5077

LIORESAL[®]

Representation Lioresal tablets each containing 10 mg aclofen; circular, flat, white tablets, uncoated, with bevelled edges, having the monogram CIBA on one side and the letters KJ and a break line on the other.

Uses Lioresal is chemically unrelated to any other antispastic agent and acts at spinal level, reducing spasticity and spasm and thereby improving the activities of daily living.

Lioresal is indicated for the relief of spasticity of voluntary muscle resulting from such disorders as: multiple sclerosis, other spinal lesions e.g. tumours of the spinal cord, syringomyelia, motor neurone disease, ankylosing myelitis, traumatic partial section of the cord.

Lioresal is also indicated in adults and children for the relief of spasticity of voluntary muscle arising from e.g. cerebrovascular accidents, cerebral palsy, meningitis, traumatic head injury.

Patient selection is important when initiating Lioresal therapy; it is likely to be of most benefit in patients whose spasticity constitutes a handicap to activities and/or physiotherapy. Treatment should not be commenced until the spastic state has become stabilized.

Dosage and administration Before starting treatment with Lioresal it is prudent to realistically assess the overall extent of clinical improvement that the patient may be expected to achieve. Careful titration of dosage is essential (particularly in the elderly) until the patient is stabilised. If too high a dosage is initiated or if dosage is increased too rapidly side-effects may occur. This is particularly relevant if the patient is ambulant, in order to minimise muscle weakness in the unaffected limbs or where spasticity is necessary for support.

Dulcis: The following gradually increasing dosage regime is suggested but should be adjusted to suit individual patient's requirements.

5 mg three times a day for three days

10 mg three times a day for three days

15 mg three times a day for three days

20 mg three times a day for three days

Satisfactory control of symptoms is usually obtained with doses up to 60 mg daily, but a careful adjustment is often necessary to meet the requirements of each individual patient. The dose may be increased slowly if required, but a maximum daily dose of more than 100 mg is not advised unless the patient is in hospital under careful medical supervision. Small frequent dosage may prove better in some cases than larger spaced doses. Also some patients benefit from the use of Lioresal only at night to counteract painful flexor spasm. Similarly a single dose given approximately 1 hour prior to the performance of specific tasks such as washing, dressing, shaving, physiotherapy, will often improve mobility.

Once the maximum recommended dose has been reached, if the therapeutic effect is not apparent within 6 weeks a decision whether to continue Lioresal should be taken.

Children: In children under eight years of age the starting dose may need to be as low as 5–10 mg daily in three or four divided doses, increasing gradually over a two week period to a maximum of 40 mg daily in divided doses. For children over eight years a starting dose of 10 mg daily in divided doses and a maximum dose of 60 mg daily are recommended.

There have been no reports of tolerance.

Contra-indications, warnings, etc Side-effects:

Nausea, vomiting, daytime sedation and confusion, as well as muscle hypotonia and fatigue, have been observed after treatment with Lioresal. The incidence of these effects may be reduced by lowering the dosage with little or no loss of therapeutic effect. Should nausea persist then it is recommended that Lioresal be ingested with food or a milk beverage.

Visual hallucinations have been reported on sudden withdrawal of Lioresal.

Precautions: Lioresal should be used with extreme care in patients already receiving antihypertensive therapy.

It should be noted that psychotic states and epileptic manifestations may be exacerbated by treatment with Lioresal.

The customary practice of avoiding drugs during the first three months of pregnancy whenever possible should also apply to Lioresal. Although Lioresal passes into breast milk, the concentrations are so low that the use of therapeutic doses should generally entail no risk for the child.

Treatment of overdose: In cases of overdose the induced hypotonia can involve the muscles of respiration. Muscular flaccidity may persist for up to three days following recovery of consciousness.

As Lioresal is principally excreted via the kidneys, it is important to maintain a high urinary output by means of an increased fluid intake and, if necessary, the use of diuretics.

There is no specific antidote to Lioresal. Symptomatic measures should be applied as required.

Pharmaceutical precautions Lioresal should be protected from heat.

Note: Details of a suitable formula for the extemporaneous preparation of a paediatric oral suspension of Lioresal are available on request to the manufacturer.

Legal category POM.

Package quantities Securitainers of 100 × 10 mg tablets of Lioresal.

Further information The major benefits of Lioresal

stem from its ability to reduce painful flexor or extensor spasms and spontaneous clonus thereby facilitating the mobility of the patient, increasing his independence and helping rehabilitation. General well being is often improved and sedation is less often a problem than with centrally acting drugs.

Product licence number 0008/0053.

LUDIOMIL*

Presentation Ludiomil tablets each containing 10 mg maprotiline hydrochloride, pale yellow, circular, film-coated tablets with CIBA on one side and the letters CO on the reverse.

Ludiomil Tablets each containing 25 mg maprotiline hydrochloride, greyish-red, circular, film-coated tablets with CIBA on one side and the letters DP on the reverse.

Ludiomil Tablets each containing 50 mg maprotiline hydrochloride; light orange, circular, film-coated tablets with CIBA on one side and the letters ER on the reverse.

Ludiomil Tablets each containing 75 mg maprotiline hydrochloride; brownish-orange, circular, film-coated tablets with CIBA on one side and the letters FS and a break line on the reverse.

Uses *Indications:* Symptoms of depressive illness.

Dosage and administration The optimum dose depends on the severity of the depression and the individual patient response to treatment. The usual dose range is 25–75 mg daily which may be given in 1 dose or in 3 divided doses.

Clinical evidence suggests that Ludiomil given once daily is effective and well tolerated, especially when given at night. Dosage at night should reduce the need for hypnotics or tranquillisers to be prescribed with Ludiomil.

Pharmacokinetic studies show that virtually the same steady-state blood levels are produced whether Ludiomil is given in once daily or divided doses.

For moderate or severe depression, treatment should start with 75 mg daily, increasing if necessary, to a maximum of 150 mg daily. Initially the patient should be closely monitored and dosage adjusted after one to two weeks according to the response. Treatment will need to be maintained until natural remission of the depression permits weaning off Ludiomil or the use of a lower dose for maintenance.

It may be advisable in elderly patients, or those who may be sensitive to this type of drug, to start treatment with lower doses such as 30 mg at night or 10 mg three times a day. This should then be adjusted in one to two weeks according to the response.

Children: Not recommended.

Contra-indications, warnings, etc *Side-effects:* Convulsions have been reported as occurring in patients both with and without a history of epilepsy.

Skin rashes are not uncommon.

Anticholinergic side-effects such as dry mouth, disturbances of accommodation, tachycardia, constipation and hesitancy of micturition have been reported less frequently with maprotiline than with standard tricyclic antidepressants.

The following adverse effects, although not necessarily all reported with Ludiomil, have occurred with tri/tetracyclic antidepressants:

Possible adverse effects include drowsiness, dizziness, sweating, postural hypotension, tremor, paraesthesia,

vivid dreams and skin rash. Interference with sexual function may occur. The incidence and severity of these side-effects does not prejudice treatment in the majority of patients.

Serious adverse effects are rare and have included depression of the bone marrow, agranulocytosis, cholestatic jaundice, hypomania.

Psychotic manifestations, including mania and paranoid delusions may be exacerbated.

Withdrawal symptoms may occur on abrupt cessation of therapy and include insomnia, irritability and excessive perspiration.

Withdrawal symptoms in neonates whose mother received tri/tetracyclic antidepressants during the third trimester have also been reported.

Contra-indications: Ludiomil is contra-indicated in severe liver or renal disease, history of epilepsy, narrow angle glaucoma, retention of urine, recent myocardial infarction.

Precautions: Do not use during pregnancy, or during lactation, especially during the first and last trimesters unless there are compelling reasons. There is no evidence as to drug safety in human pregnancy, nor is there evidence from animal work that it is free from hazard. Ludiomil is excreted in the breast milk. Nursing mother should be advised to cease breast feeding.

In common with other substances in this therapeutic group, Ludiomil should be used with caution in patient with cardiovascular disease, such as any degree of heart block or other cardiac arrhythmias.

The elderly are particularly liable to experience side effects. The initial dosage should be increased with caution under close supervision (see dosage).

Ludiomil should be administered with caution to patients with symptoms suggestive of bladder neck obstruction.

Patients posing a high suicidal risk require close initial and continuing supervision.

In common with all other substances in this therapeutic group, Ludiomil may modify patients' reactions (e.g. driving ability, operating machinery, etc.) to a varying degree, depending on dosage and individual susceptibility. Patients should be warned of this possible hazard.

Drug interactions: Ludiomil should not be given concurrently with or within 2 weeks of cessation of therapy with monoamine oxidase inhibitors.

Ludiomil may decrease the antihypertensive effect of guanethidine, debrisoquine, bethanidine and possibly clonidine. It would be advisable to review all antihypertensive therapy during treatment with tri/tetracyclic antidepressants.

Ludiomil should be used with caution in patient receiving sympathomimetic agents such as ephedrine, isoprenaline, noradrenaline, phenylephrine and phenylpropanolamine.

Barbiturates may decrease whilst neuroleptics and methylphenidate may increase the plasma levels of Ludiomil.

The effects of alcohol may be potentiated by Ludiomil. Anaesthetics given during tri/tetracyclic antidepressant therapy may increase the risk of arrhythmias and hypotension. If surgery is necessary, the anaesthetist should be informed that a patient is being so treated.

Treatment of overdosage: There is no specific antidote to Ludiomil. Major signs of overdosage include convulsions and cardiovascular disturbances. The stomach should be emptied as quickly as possible by gastric lavage or emesis and unconscious patients should be

ospitalised in a unit where full support of vital functions and cardiac monitoring are possible. Treatment is symptomatic.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Ludiomil Tablets are available in our strengths, 10 mg, 25 mg and 50 mg in containers of 100 tablets, 75 mg in containers of 28 tablets. All tablets are packed in PVC/foil bubble packs.

Further information Ludiomil is a novel compound with a tetracyclic nucleus belonging to the chemical class of dibenzo-bicyclo-octadienes. It shows a broad spectrum of antidepressant activity, being highly effective in both endogenous and reactive depression. Ludiomil works quickly, some symptoms, such as insomnia, anxiety and mood, begin to improve within three to four days. This, coupled with the good tolerability of once daily dosage, makes Ludiomil a very worthwhile treatment for all forms of depression. The 75 mg tablets of Ludiomil are packed in daily reminder packs of 28 tablets, making it simple for the patient to remember to take them.

Product licence numbers

Ludiomil Tablets 10 mg	0008/0117
Ludiomil Tablets 25 mg	0008/0118
Ludiomil Tablets 50 mg	0008/0119
Ludiomil Tablets 75 mg	0008/0129

METOPIRONE*

Presentation Metopirone Capsules each containing 50 mg metyrapone in an opaque cylindrical soft gelatine capsule, coloured white.

Uses Mode of action: Metopirone inhibits the enzyme responsible for the 11 β -hydroxylation stage in the synthesis of hydrocortisone (cortisol) and to a lesser extent aldosterone.

When used as a diagnostic test of anterior pituitary function, one is relying upon its inhibiting effect on cortisol production. The consequent fall in plasma concentration of circulating glucocorticoids stimulates the anterior pituitary to produce more corticotrophin. This in turn stimulates the production of more of the precursors which are then excreted in the urine where they can be measured.

Indications: As a diagnostic aid in:

- Investigation of anterior pituitary function in hypopituitarism.
- Evaluation of the effect of prolonged corticosteroid therapy upon the hypothalamic-pituitary-adrenal axis.

or the management of patients with Cushing's syndrome.

In conjunction with glucocorticoids, in the treatment of resistant oedema due to increased aldosterone secretion in patients suffering from cirrhosis, nephrosis and congestive heart failure.

Dosage and administration *Oral dose when used as diagnostic test:* The urinary 17-oxygenic steroid excretion is determined on complete 24-hour collections for four consecutive days. The first two days serve as a control period. On the third day the subject is given by mouth a total of 6 doses, at four hourly intervals of 3 capsules (750 mg).

Children should be given a smaller amount based upon 6 four-hourly doses of 15 mg per kg, with a minimum dose of 250 mg.

For the treatment of resistant oedema 2.5 g to 4.5 g (10–18 capsules) should be given daily in divided doses.

Contra-indications, warnings, etc Side-effects: Metopirone may give rise to nausea and vomiting which can be controlled to some extent by taking a biscuit and milk at the same time as the capsule.

Note: Failure to absorb the drug due either to vomiting or malabsorption may give false results.

Precautions: Metopirone should be used with extreme caution in patients where gross hypopituitarism is suspected because of the risk of precipitating acute adrenal failure.

Because of the risk that Metopirone can impair the biosynthesis of foetal-placental steroids, it would seem unwise to administer it during pregnancy.

Treatment of Overdosage: The clinical picture of acute Metopirone poisoning is characterised by gastro-intestinal symptoms and acute adreno-cortical insufficiency. General measures should be taken to reduce the absorption and increase the elimination of the drug. A large dose of hydrocortisone should be administered, together with i.v. saline and glucose. This should be repeated as necessary in accordance with the patient's clinical condition.

Pharmaceutical precautions The capsules should be protected from heat and moisture.

Legal category POM.

Package quantities 250 mg capsules of Metopirone in Securitainers of 100.

Further information Since the response to Metopirone involves the adrenal cortex, it is necessary to ensure that the adrenal function is adequate (by means of ACTH or 'Synacthen') before ascribing a subnormal response to hypothalamic or pituitary dysfunction. It must be emphasised that this procedure assesses only the feedback control mechanism, and a normal response does not necessarily indicate the ability of the HPA axis to respond to stress.

Product licence number 0008/5078

MONASPOR* ▼

Presentation Vials containing dry active substance corresponding to 0.5 g and 1 g cefsulodin sodium for intramuscular and intravenous use.

Uses Mode of action: Monaspor is a semi-synthetic bactericidal beta-lactam antibiotic for parenteral use which displays marked activity against *Pseudomonas aeruginosa*. The minimum inhibitory concentrations (MIC) are very low, lying within the range of 0.25–8 mcg/ml for 88% of the *Pseudomonas* strains investigated.

Monaspor is stable against the majority of relevant beta-lactamases and is also active against most strains of *Pseudomonas aeruginosa* resistant to carbenicillin and gentamicin.

Indications: Monaspor is indicated for the treatment of infections caused by sensitive strains of *Pseudomonas aeruginosa*. These include:

Chronic recurrent urinary tract infections e.g. pyelo-

nephritis, infections accompanying obstructions of the urinary tract (e.g. in the presence of neoplasms; calculi of the urinary tract, or following surgery), prostatitis.

Respiratory tract infections e.g. pneumonia, chronic purulent bronchitis and infections associated with mucoviscidosis.

A number of cases of *Pseudomonas* infection of bone and soft tissue, such as osteomyelitis, and infected wounds and burns have been treated successfully with Monaspor.

Dosage and administration *Adults:* In adults with normal renal function the usual daily dose is 1–4 grams daily in 2–4 fractional doses.

In urinary tract infections, and chronic bronchitis, 1–3 grams daily in 2–4 fractional doses usually suffices.

In critical cases (e.g. severe pneumonia, osteomyelitis) daily doses of 6 grams or more may be necessary.

Children: The recommended daily dose is 20–50 mg/kg bodyweight.

Administration: Intramuscular: The dry powder should be dissolved using the accompanying 0.5% lignocaine solution before intramuscular administration.

Intravenous: The dry powder should be reconstituted with Water for Injection to a concentration of 1 g in 10 ml and slowly injected either directly into a vein or into the tube of an intravenous drip.

Infusion: Monaspor can be dissolved in the routinely employed solutions e.g. Sodium Chloride Intravenous Infusion BP, Ringer's Injection USP, Dextrose Intravenous Infusion BP, Dextran 40 Intravenous Infusion BP (10%). It must not be mixed with sodium bicarbonate.

When administering an infusion lasting more than 30–60 minutes and in order to obtain high initial blood levels, it is advisable to inject the first dose as a slow bolus injection.

If Monaspor is infused intermittently via a Y-attachment to another infusion, administration of the latter should be interrupted while the Monaspor infusion is in progress.

Monaspor can be administered in combination with other antibiotics such as gentamicin or carbenicillin. They can either be infused together or injected in the same syringe (diluted with Water for Injection to a total volume of 10 ml). Monaspor, however, should not be pre-mixed with tobramycin but they may be administered separately.

Aqueous solutions of the drug take on a yellow colouration. This has no effect on the drug's antibiotic activity.

Solutions displaying clouding or precipitation after admixing of the drug should not be used.

Only freshly prepared Monaspor solutions should be employed. Monaspor infusion solutions should not be used if they have been stored for longer than 24 hours in a refrigerator (5°C) or 12 hours at room temperature (23°C). Mixtures containing Monaspor and other drugs in the same syringe should not be stored for more than 4 hours at room temperature. The stability of Monaspor solutions is greatest between pH 4–7. Solutions with a pH of greater than 7 should be administered immediately after they have been prepared.

Contra-indications, warnings, etc *Contra-indications:* Hypersensitivity to cephalosporins.

Precautions: In chronic infections it is important that the treatment should be of sufficiently long duration to obtain a successful clinical result.

In cases where lengthy treatment with large doses of

Monaspor is required, blood counts and tests of renal function should be performed.

As with any type of antibiotic therapy, it is advisable to determine the sensitivity of the causative micro-organisms before initiating treatment.

In patients known to be allergic to penicillin, caution should be exercised when employing Monaspor, since cross-sensitivity with cephalosporins may be encountered. If allergic reactions occur, Monaspor should be withdrawn and suitable countermeasures taken.

In patients with renal failure, the priming dose should be the same as in patients without renal disease. Repeat doses, however, must be reduced in size or the interval between them prolonged. The recommendations in the following table may be used as a guide. The elimination of the drug in dialysis fluid is about 45% of the dose and it is suggested that a normal dose be given at the beginning and end of the dialysis period.

<i>Creatinine clearance</i>	<i>Maintenance doses in % of normal doses at following intervals:</i>			
<i>ml/min</i>	<i>6 h</i>	<i>8 h</i>	<i>12 h</i>	<i>24 h</i>
50	90	90	95	—
30	75	80	90	—
20	65	70	80	—
10	55	60	70	—
5	45	55	65	—
2.5	40	45	60	—
0	—	—	—	75

In patients suffering from severe liver damage and in those allergic to local anaesthetics, Monaspor should be given intramuscularly with sterile Water for Injection or intravenously (i.e. without lignocaine).

When determining urinary sugar levels, enzymatic methods should be used because other techniques may yield false positive results.

Pregnancy: As with other drugs, the use of Monaspor during pregnancy is advised only if there are compelling reasons.

Side-effects: Monaspor is generally well tolerated. The following have been observed as rare side effects: nausea, dizziness, allergic skin reactions, and eosinophilia, as well as occasional increases in the values for transaminases, alkaline phosphatase, non-protein nitrogen, and serum creatinine. Intravenous injections of Monaspor are usually painless when administered slowly. Local pain occurring as a reaction to intramuscular injections can be prevented by employing the accompanying ampoules of 0.5% lignocaine solution.

Pharmaceutical precautions The vials should be stored below 25°C and protected from light.

Legal category POM.

Package quantities *For intramuscular injection:* Vial containing 0.5 g or 1 g of active substance with ampoule of 0.5% lignocaine solution (3 ml).

For intravenous injection: Vials containing 0.5 g or 1 g of active substance.

Further information Nil.

Product licence numbers

500 mg vials for intramuscular injection	0008/0158
500 mg vials for intravenous injection	0008/0159
1 g vials for intramuscular injection	0008/0160
1 g vials for intravenous injection	0008/0162

NAVIDREX®

Presentation Navidrex Tablets containing 0.5 mg of cyclopenthiiazide as white, flat, circular tablets with bevelled edges, bearing the monogram CIBA on one side, and the letters AO on each side of a breakline on the other.

Uses *Mode of action:* Navidrex is a thiazide diuretic which exerts its diuretic effect by inhibiting the reabsorption of sodium, chloride and water, probably at the proximal renal tubules.

Indications: Navidrex is indicated for the treatment of mild to moderate hypertension, in more severe hypertension it may be used in conjunction with other anti-hypertensive agents. It is also indicated for the treatment of acute and chronic heart failure, cardiac asthma, oedema associated with renal disease, pre-menstrual tension, liver disease, drug therapy and obesity, oedema and hypertension associated with pregnancy.

Dosage and administration *Adults:* Hypertension 0.25 mg to 0.5 mg daily, increasing rarely to a maximum of 1.5 mg. For best results in hypertension doses should be given seven days a week, the entire dose being taken in the morning.

In acute and chronic heart failure, cardiac asthma, oedema associated with renal or liver disease, obesity, or drug induced oedema, an initial dose of 0.5 mg to 1 mg until a satisfactory clinical response is attained. The maximum effective dose is 1.5 mg daily although this is rarely required. When a satisfactory clinical response is achieved a dose of 0.5 mg on alternate days is usually adequate.

Pre-menstrual tension 0.25 mg to 0.5 mg daily from the onset of symptoms until menstruation begins.

Since Navidrex increases salt excretion it is usually possible to relax dietary salt restriction.

Contra-indications, warnings, etc *Side-effects:* Side-effects such as mild anorexia, nausea, constipation and diarrhoea, skin rashes and photosensitivity may occur. There have been reports of blood dyscrasias including thrombocytopenia, but these are rare.

Contra-indications: Navidrex is contra-indicated in the presence of precoma associated with hepatic cirrhosis or Addison's disease or advanced renal failure.

Precautions: In patients with some degree of renal impairment, a rise in blood urea can occur and in extreme cases result in an oliguric crisis. In such cases, either the dose should be reduced or the treatment interrupted temporarily.

Prolonged doses may bring about a decrease in glucose tolerance and precipitate a diabetic condition. In known diabetics the addition of Navidrex to the treatment regime will almost certainly alter the insulin requirement.

In common with other thiazide diuretics hyperuricaemia may be induced by Navidrex. Gout may be exacerbated in patients with a previous history or family history of this condition.

Patients who are being treated with this preparation may require regular monitoring of fluid and electrolyte balance particularly when diuresis is substantial or in patients suffering from renal impairment. Potassium supplements may be required. Particular caution is needed with this preparation in the elderly since electrolyte balance is more likely to be precarious due to bowel or renal dysfunction. Also urinary retention is more likely.

Navidrex should only be used during pregnancy if considered essential by the physician.

The concomitant administration of this preparation with cardiac glycosides or hypotensive agents may necessitate adjustment of the dosage of those drugs.

Pharmaceutical precautions Usual storage precautions apply.

Legal category POM.

Package quantities Navidrex is available in Securitainers of 100 and 500.

Further information After a single oral dose diuresis starts within one or two hours reaching a maximum in four to eight hours, lasting up to 12 hours. If taken in the morning the clearly defined duration of action ensures that the patient can sleep undisturbed at night. It is important that the patient be encouraged to take a potassium rich diet during treatment with Navidrex. For routine use, it is advisable to give supplementary potassium, e.g. 'Slow-K' or alternatively to use 'Navidrex-K' which contains 'Slow-K'.

Product licence number 0008/5047.

NAVIDREX-K®

Presentation Yellow-ochre, polished, sugar coated tablets, about 12 mm in diameter, having an inner slow-release wax core containing Potassium Chloride BP 600 mg (8.06 mEq) and an outer coat containing 0.25 mg cyclopenthiiazide.

Uses Navidrex-K is a thiazide diuretic, which exerts its diuretic effect by inhibiting the reabsorption of sodium, chloride and water, probably at the proximal renal tubules. It is indicated for the treatment of mild to moderate hypertension. In more severe hypertension it may be used in conjunction with other antihypertensive agents. Navidrex-K is also indicated for the treatment of acute and chronic heart failure, cardiac asthma, oedema associated with renal disease, pre-menstrual tension, liver disease, drug therapy and obesity, oedema and hypertension associated with pregnancy.

Dosage and administration *Adults: Oral:* In hypertension, 0.25–0.5 mg (1 or 2 tablets) daily is usually sufficient. Rarely, 1.5 mg (6 tablets) daily may be required. For best results in hypertension doses should be given seven days a week. In acute and chronic heart failure, cardiac asthma, oedema associated with renal or liver disease and oedema associated with obesity or drug-induced oedema, an initial dose of 0.5–1 mg (2–4 tablets) daily until a satisfactory clinical response is attained.

The maximum effective dose is 1.5 mg (6 tablets) daily, although this is rarely required.

When a satisfactory clinical response is achieved, a maintenance dose of 0.25–0.5 mg (1 or 2 tablets) daily or 0.5 mg (2 tablets) on alternate days is usually adequate.

Pre-menstrual tension, 0.25–0.5 mg (1 or 2 tablets) daily from the onset of symptoms until menstruation begins.

The entire daily dose should be taken in the morning and it is important that the tablet be swallowed whole.

Children: Oral: At the discretion of the physician.

Note: Since Navidrex-K increases salt excretion it is usually possible to relax dietary salt restrictions.

Contra-indications, warnings, etc *Side-effects:* Side-effects such as mild anorexia, nausea, constipation and diarrhoea, skin rashes and photosensitivity may occur as a result of treatment with Navidrex-K. In common with other thiazides, there have been reports of thrombocytopenia, but these are rare.

Navidrex-K tablets are designed to avoid the risks of gastro-intestinal irritation. However, if a patient under treatment with Navidrex-K develops severe vomiting, severe abdominal pains or flatulence or gastro-intestinal haemorrhage, the preparation should be withdrawn at once, because in the presence of an obstruction it could conceivably give rise to ulceration or perforation.

Contra-indications: Navidrex-K is contra-indicated in the presence of hyperkalaemia or precoma associated with hepatic cirrhosis, Addison's disease or advanced renal failure.

All solid forms of potassium medication are contra-indicated in the presence of obstructions in the digestive tract (e.g. resulting from compression of the oesophagus due to dilation of the left atrium or from stenosis of the gut).

Precautions: In patients with some degree of renal impairment, a rise in blood urea can occur and in extreme cases result in an oliguric crisis. In such cases, either the dose should be reduced or the treatment interrupted temporarily.

Prolonged doses of thiazides may bring about a decrease in glucose tolerance and precipitate a diabetic condition. In known diabetics the addition of Navidrex-K to the treatment regime will almost certainly alter the insulin requirement.

In common with other thiazide diuretics, Navidrex-K may precipitate an attack of gout in patients predisposed to this condition.

Patients who are being treated with this preparation may require regular monitoring of fluid and electrolyte balance particularly when diuresis is substantial or in patients suffering from renal impairment. Potassium supplements may be required. Particular caution is needed with this preparation in the elderly since electrolyte balance is more likely to be precarious due to bowel or renal dysfunction. Also urinary retention is more likely.

Navidrex-K should only be used during pregnancy if considered essential by the physician.

The concomitant administration of this preparation with cardiac glycosides or hypotensive agents may necessitate adjustment of the dosage of those drugs.

Pharmaceutical precautions Navidrex-K Tablets should be protected from heat and moisture. The tablets should be dispensed in a moisture-proof container.

Legal category POM.

Package quantities Navidrex-K Tablets are available in Securitainers of 100 and 500.

Further information The low absolute doses required with Navidrex-K, compared to other thiazide diuretics, make it economical in all appropriate indications. After a single dose, diuresis starts within 1–2 hours, reaches a maximum in 4–8 hours and lasts about 12 hours. Thus a morning dose will permit the patient to sleep undisturbed at night. Hypertension is also controlled by a single daily dose. The built-in potassium supplement is based on

Slow-K* and compared with other potassium supplements, is less likely to produce an unpalatable taste, gastro-intestinal irritation or inadequate absorption.

Product licence number 0008/5036.

ORIMETEN* ▼

Presentation White to yellowish white tablets, round with slightly convex faces and slightly bevelled edges, printed with 'CIBA' on one side, and 'GG' with score on the other side. Each tablet contains 250 mg aminogluthetimide.

Uses *Mode of action:* Orimeten inhibits steroid biosynthesis in the adrenal cortex, thereby producing a medical adrenalectomy. This inhibition occurs at a very early stage, i.e. the conversion of cholesterol to Δ^5 pregnenolone. Suppression of oestrogen production in peripheral tissue may also play a part in the response to Orimeten in patients with carcinoma of the breast.

Indications: Metastatic carcinoma of the breast in post-menopausal or oophorectomised women (especially where the tumours are oestrogen-sensitive), including in particular patients in whom adrenalectomy or hypophysectomy would otherwise be indicated.

In many cases, metastases or recurring tumours diminish in size or even disappear during treatment with Orimeten. Such remission may be maintained for several years. Bone metastases attributable to breast cancer respond particularly well, the patient often experiencing marked relief of pain.

Dosage and administration Treatment should commence at 250 mg twice daily for 2 weeks. In the absence of severe unwanted effects, the dose may then be increased to 250 mg four times daily. Doses greater than 1 g daily should be avoided as side effects may occur more frequently.

Supplementary therapy: In addition to its effect on oestrogen synthesis, Orimeten suppresses the production of glucocorticoids, and in patients with carcinoma of the breast supplementary glucocorticoids will be needed (e.g. 20 mg hydrocortisone b.d.). It should be noted that Orimeten accelerates the metabolism of dexamethasone, hence if this glucocorticoid is used, a relatively high dose (up to 3 mg daily) is required.

In some patients the suppression of aldosterone synthesis may lead to hyponatraemia, hyperkalaemia, hypotension and dizziness, in which case a mineralocorticoid (e.g. fludrocortisone 0.1–0.15 mg daily or on alternate days) should be given.

Contra-indications, warnings, etc

Precautions: The patients blood count and plasma electrolytes should be checked regularly. Occasionally, Orimeten has been found to diminish thyroid function. If, during treatment for carcinoma of the breast signs of Cushing's Syndrome (due to concomitant glucocorticoid medication) appear, the dosage of the glucocorticoid should be reduced.

Orimeten may increase the rate of metabolism of some drugs, e.g. coumarin anti-coagulants, oral anti-diabetic agents, dexamethasone, whose dosage may need to be adjusted.

Use in pregnancy: Since foetal abnormalities have been observed in animals and there have been cases of pseudohermaphroditism in newborn infants of women treated with Orimeten, use during pregnancy and lactation is contra-indicated.

Side-effects: The tolerability of Orimeten varies greatly from patient to patient. Central nervous side effects, such as dizziness, somnolence and lethargy, are relatively common and dose dependent; unsteadiness occurs only in the higher dosage range. Gastrointestinal effects such as nausea, vomiting or diarrhoea, are less frequent and likewise dose-dependent. Drug rash – accompanied sometimes by fever – may develop after 7–14 days; it usually subsides within 7–10 days despite continued treatment, but if it fails to do so, the treatment must be reduced or temporarily withdrawn or the dosage of the corticosteroid raised. There have been rare reports of pancytopenia, leucopenia and agranulocytosis.

Accidental overdosage: No serious outcome following overdosage of aminogluthethimide has been reported. However, gastric lavage will be useful when indicated, together with full supportive measures to maintain respiration and circulation in the unconscious patient. In severe cases, haemodialysis or charcoal haemoperfusion may aid removal of the drug. In all cases steroid replacement must be maintained.

Pharmaceutical precautions Protect from heat, light and moisture.

Legal category POM.

Package quantities Securitainers of 100 tablets.

Further information Medical adrenalectomy with Orimeten carries significant advantages over surgical adrenalectomy. Corticosteroid secretion is inhibited in a reversible and controllable manner with none of the risks associated with surgery.

Product licence number 0008/0147

OTRIVINE* NASAL DROPS OTRIVINE* NASAL SPRAY OTRIVINE* NASAL DROPS PAEDIATRIC

Presentation Clear, colourless, odourless solutions. Otrivine Nasal Drops and Spray contain 0.1% w/v xylometazoline hydrochloride. Otrivine Nasal Drops Paediatric contain 0.05% w/v xylometazoline hydrochloride.

Uses Otrivine has a local vasoconstrictor action producing relief of nasal congestion lasting for up to 12 hours. It is indicated in the treatment of nasal congestion, perennial and allergic rhinitis, including hay fever and sinusitis.

Dosage and administration Since Otrivine clears nasal congestion in a few minutes and the effect persists for up to 12 hours, it is only necessary to administer the drops or spray twice, or at the most, three times, a day. Patients may prefer one application at night to ensure a clear nasal airway and avoid sleep disturbance.

Adults: 2 or 3 drops of the 0.1% solution or one or two applications of spray in each nostril, two or three times daily.

N.B. The 0.1% solution should not be used for children under the age of 12 years.

Infants and children under 12: 1 or 2 drops of Otrivine Paediatric Solution 0.05% once or twice daily for average cases. The specially designed paediatric dropper bottle limits the volume of each application to prevent accidental overdosage. Otrivine Paediatric Solution can be used in infants where nasal congestion is interfering with feeding.

Contra-indications, warnings, etc *Side-effects:* Side-effects are infrequent with Otrivine and are generally mild, but may include local stinging and discomfort, sneezing, dryness of the nose, headache, insomnia, drowsiness or palpitations.

Precautions: The prolonged use of vasoconstrictors is not recommended in chronic rhinitis. It should be noted that excessive use or abuse of Otrivine may cause rebound congestion or drug-induced rhinitis.

Treatment of overdosage: Treatment will only be necessary in infants and young children when they could be expected to fall into a deep sleep followed by recovery within 12 hours. In addition to gastric lavage symptomatic treatment of convulsions or respiratory depression should be given if these arise.

Pharmaceutical precautions None.

Legal category P.

Package quantities Otrivine 0.1% Nasal Spray and Drops 10 ml. Otrivine 0.05% Nasal Drops Paediatric 10 ml.

Further information Otrivine has been shown to provide much more prolonged relief from nasal congestion than ephedrine. In contrast to the effect of the latter, the vasoconstrictor action is not intense, therefore decongestion is achieved without local discomfort and rebound nasal congestion is unlikely to occur.

Product licence numbers

Otrivine Nasal Drops	0008/5023
Otrivine Nasal Spray	0008/5024
Otrivine Nasal Drops Paediatric	0008/5022

OTRIVINE*-ANTISTIN* NASAL DROPS OTRIVINE*-ANTISTIN* NASAL SPRAY

Presentation A clear, colourless, odourless solution containing xylometazoline hydrochloride 0.05% w/v antazoline sulphate 0.5% w/v.

Uses Otrivine-Antistin is a combined long-acting vasoconstrictor and antihistamine for the prompt relief of rhinitis associated with seasonal or perennial allergies, such as hay fever.

Dosage and administration For local administration to the nose.

Adults: Nasal spray or drops, one application from the spray or two or three drops applied to each nostril two or three times daily. One application at bedtime if necessary.

Contra-indications, warnings, etc *Side effects:* Side effects are infrequent with Otrivine-Antistin and are generally mild. They may include local stinging and discomfort, sneezing, dryness of the nose, headache, insomnia, drowsiness or in sensitive patients tachycardia. Prolonged use of Otrivine-Antistin may cause rebound congestion and drug-induced rhinitis.

Precautions: The prolonged use of vasoconstrictors is not recommended in chronic rhinitis. Antihistamines may cause drowsiness, if affected do not drive or operate machinery. Avoid alcoholic drink.

Contra-indications: Nil.

Pharmaceutical precautions The preparation should be protected from heat.

Legal category P.

Package quantities

Nasal Spray 10 ml.

Nasal dropper bottle 10 ml.

Further information Otrivine-Antistin is a gentle, long-acting combination, which, used in accordance with the recommended dosage, is free from rebound effects.

Product licence numbers

Otrivine-Antistin Nasal Drops 0008/5026

Otrivine-Antistin Nasal Spray 0008/5117

RIMACTANE*

Presentation Rimactane Capsules each containing 150 mg rifampicin. An opaque, two-piece, hard gelatine capsule size 2, reddish-brown in colour, marked with the monogram CIBA on each half and the code JZ 150. The capsule has a diameter of 6.2 mm approx. and is 17.8 mm approx. in length.

Rimactane Capsules each containing 300 mg rifampicin. An opaque, two-piece, hard gelatine capsule size 1, coloured reddish-brown and dark brown, marked with the monogram CIBA on each half and the code CS 300. The capsule is approx. 6.8 mm in diameter and 18.7 mm approx. in length.

Rimactane Syrup: An opaque, red-coloured suspension having the odour and taste of raspberry; each 5 ml contains 100 mg rifampicin.

Uses *Mode of action:* Rimactane is a semi-synthetic antibiotic with bactericidal activity against most groups of mycobacteria.

Indications: Rimactane is a major drug in the management of tuberculosis and certain opportunist mycobacterial infections. It is effective in cases resistant to other anti-tuberculous agents and shows no cross-resistance outside the rifamycin group of drugs. It is effective in combination with isoniazid, streptomycin, pyrazinamide, ethambutol and the majority of second-line drugs.

Dosage and administration Rimactane should be given as a single dose, preferably on an empty stomach, at least 30 minutes before breakfast to ensure a high peak serum concentration. Dosage should be adjusted according to body weight of patients.

Adults: Oral: 450–600 mg daily as a single dose (based on approximately 10 mg per kg body weight). (Those patients 50 kg (8 stone) and over should take 600 mg rifampicin daily, whilst patients under 50 kg should take 450 mg).

Children: Oral: Up to 20 mg per kg body weight daily to a maximum of 600 mg as a single dose.

Premature and newborn infants: Oral: 10 mg/kg once daily. Do not exceed this dosage. These infants, in whom the liver enzyme system is not yet fully developed, should be given Rimactane only in grave emergencies.

Rimactane must always be given in association with at least one and preferably two other anti-tuberculosis drugs, to prevent the emergence of resistant strains. Especially good results have been reported when Rimactane has been used in combination with isoniazid and ethambutol. Whilst it is not generally recommended that rifampicin be used in combination with PAS, if for any reason this regimen is used, the drugs should be given not less than eight hours apart to ensure satisfactory blood levels.

Use in pregnancy and lactation: Rifampicin has been

shown to have teratogenic effects in animals on very high doses, therefore during pregnancy the use of Rimactane should, if possible, be avoided. Particularly during the first 3 months of pregnancy, the drug's possible risks for the foetus must be carefully weighed against its therapeutic benefits for the mother.

When administered during the last few weeks of pregnancy, Rimactane can cause post-natal haemorrhages in mother and infant, for which treatment with vitamin K may be indicated.

Rifampicin is excreted in breast milk. Mothers in whom its use proves unavoidable should refrain from breast-feeding their infants.

Contra-indications, warnings, etc. *Contra-indications:* Rimactane is contra-indicated in patients with jaundice or where there is known hypersensitivity to rifamycins.

Precautions: As Rimactane is excreted principally by the biliary tract, caution should be exercised in treating patients with hepatic disorders. Such patients should have liver function monitored during treatment.

In the presence of complete renal failure rifampicin is excreted entirely in the bile, provided hepatic function is not impaired the dosage of rifampicin need not be adjusted.

The occurrence of liver function abnormalities is more common when rifampicin and isoniazid are used in combination, special care is therefore required in patients with pre-existing liver impairment, or in the elderly, malnourished or very young patient.

When resuming treatment with Rimactane after a temporary or a prolonged interval, the drug should be given in small, gradually increasing doses. In adults an initial dose of 75 mg daily should be administered raised subsequently by 75 mg per day until the desired dosage level is attained. If, as may happen in exceptional cases the patient develops renal failure, thrombocytopenia, purpura or haemolytic anaemia, treatment with Rimactane should be stopped at once and not re-instituted at a later date.

Microbiological techniques for assaying the serum concentrations of folic acid and vitamin B₁₂ are not suitable for use during treatment with rifampicin.

Drug interactions: Rifampicin is a potent inducer of liver enzymes which may increase the metabolism of concomitantly administered drugs such as corticosteroids, oral contraceptives, oral anti-coagulants, oral anti-diabetic agents, dapsone, phenytoin, some digitalis preparations, quinidine and methadone. The dosage of these drugs may need considerable review when Rimactane is being prescribed, larger doses usually being needed when Rimactane is introduced and a reduction on withdrawal.

In women receiving treatment with rifampicin it has been found that the contraceptive activity of oral contraceptives may be impaired. In such cases, additional non-hormonal methods should be employed.

Side-effects: Occasionally, gastrointestinal disturbances and skin rashes have been reported after treatment with Rimactane.

Side-effects to rifampicin, probably of immunological/allergic origin have been reported, particularly in connection with intermittent, interrupted or repeated treatment; e.g. influenza-like symptoms and rarely skin rashes, fever and dyspnoea have occurred. If serious complications arise such as thrombocytopenia, purpura, renal failure or haemolytic anaemia, rifampicin should be stopped at once and never restarted.

There may be an elevation of serum bilirubin levels, SGOT and SGPT levels and more rarely alkaline phosphatase during the early stages of treatment. In patients with previously normal liver function these changes are transient and usually revert towards normal pre-treatment levels in about two weeks even when Rimactane is continued. Routine liver function tests during treatment are unnecessary unless the patient becomes unwell or exhibits frank jaundice. The occurrence of jaundice may call for temporary cessation of treatment however in most patients it is possible to resume therapy. (See Precautions).

In common with other antibiotics, mild leucopenia and eosinophilia have been reported in a few patients, but appear to be of no particular clinical significance and no causal relationship has been established.

Treatment of overdosage: There is no specific antidote to Rimactane. In cases of severe overdosage gastric lavage may be undertaken and general supportive treatment administered.

Pharmaceutical precautions This product should be protected from heat and moisture.

The syrup to be stored below 25°C. Both capsules and syrup have a shelf-life of four years.

Legal category POM.

Package quantities Capsules of 150 mg Rimactane (red) and 300 mg Rimactane (red and brown) in securitainers of 100.

Syrup containing 100 mg in 5 ml; in bottles of 100 ml.

Further information Rimactane is orally active, very well tolerated and its activity is comparable with that of isoniazid. In combination, these two agents are commonly used as first-line therapy and offer the greatest chance of rapid eradication of the infection. It is usual, however, to employ a third drug during the first two months of treatment or at least until the results of sensitivity tests are known. The orange-red colour imparted to the urine, sputum and tears by rifampicin is a valuable guide to adherence to the drug regime. Rifampicin may also permanently discolour soft contact lenses.

Product licence numbers

Rimactane Capsules 150 mg	0008/5080
Rimactane Capsules 300 mg	0008/5081
Rimactane Syrup	0008/0106

RIMACTANE* INFUSION

Presentation 10 ml vial containing 300 mg rifampicin (red lyophilised powder) with an accompanying 5 ml ampoule of clear colourless solvent solution (Water for Injection BP + polysorbate 81).

20 ml vial containing 600 mg rifampicin (red lyophilised powder) with an accompanying 10 ml ampoule of clear colourless solvent solution (Water for Injection BP + polysorbate 81).

Uses Rimactane Infusion is indicated in patients with all forms of tuberculosis who are unable to tolerate oral therapy, e.g. post operative or comatose patients or patients in whom gastro-intestinal absorption is impaired.

Dosage and administration *Treatment of tuberculosis* with Rimactane Infusion should concurrently include the use of other effective anti-tuberculous drugs to prevent the emergence of rifampicin-resistant strains of Mycobacteria.

Adults: In tuberculosis daily administration of 600 mg when given in an intravenous drip over two to three hours has been found to be effective and well tolerated for the majority of adult patients. Serum concentrations following this dosage regimen are similar to those obtained after 600 mg by mouth. Lower doses are recommended for small, or frail and elderly patients. A daily dose of 8 mg/kg bodyweight should not be exceeded in patients with impaired liver function.

Transfer to oral therapy: When patients are able to accept oral medication, they should be transferred to Rimactane capsules or syrup. Oral dosage would be expected to be the same as that used with the infusion (see oral Rimactane data sheet).

Children: Paediatric usage has not yet been established. However, the following regimens are suggested:

In tuberculosis, a single daily dose of up to 20 mg/kg bodyweight is recommended, although total daily dose should not usually exceed 600 mg.

Preparation of Infusion: Rimactane Infusion is prepared for use by aseptically adding the solvent to the vial of rifampicin powder and shaking vigorously and continuously for about 30 seconds.

When the powder has completely dissolved, the solution should be immediately diluted in 500 ml (600 mg of rifampicin) or 250 ml (300 mg of rifampicin) of 5% glucose solution or other suitable infusion fluid (see Pharmaceutical Precautions). It is suggested that the infusion is administered over a period of 2-3 hours. The preparation should be used within 6 hours.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to rifamycins.

Although not recommended for use in patients with jaundice, the therapeutic benefit of Rimactane Infusion should be weighed against the possible risks.

During pregnancy the use of Rimactane should if possible be avoided. Particularly during the first 3 months of pregnancy the drug's possible risks for the foetus must be carefully weighed against its therapeutic benefits for the mother.

When administered during the last few weeks of pregnancy, Rimactane can cause post-natal haemorrhages in the mother and infant, for which treatment with vitamin K may be indicated.

Rimactane passes into the breast milk. Mothers in whom its use proves unavoidable should refrain from breast-feeding their infants.

Precautions: As rifampicin is excreted principally by the biliary tract, caution should be exercised in treating patients with hepatic disorders. Such patients should have liver function monitored during treatment and lower doses of Rimactane Infusion may be necessary.

The occurrence of liver function abnormalities is more common when rifampicin and isoniazid are used in combination and special care is therefore required when these are used in patients with pre-existing liver impairment or in the elderly, malnourished or very young patients.

Rifampicin is a potent inducer of liver enzymes which may increase the metabolism of concomitantly administered drugs such as corticosteroids, oral contraceptives, oral anticoagulants, oral antidiabetic agents, dapsone, digitalis preparations, quinidine, and methadone. The dosage of these drugs may need considerable review when rifampicin is being prescribed, larger doses usually being needed when rifampicin is introduced and a reduction when it is withdrawn.

Women taking oral contraceptives should use additional non-hormonal means of contraception.

When resuming treatment with rifampicin after a prolonged interval, renal function should be closely monitored. If, as may happen in exceptional cases, the patient develops renal failure, thrombocytopenia, purpura, or haemolytic anaemia, treatment with rifampicin should be stopped at once and not re-instituted at a later date.

Notes: In the presence of complete renal failure, rifampicin is excreted entirely in the bile; provided hepatic function is not impaired the dosage of rifampicin need not be adjusted.

Microbiological techniques for assaying the serum concentrations of folic acid and Vitamin B₁₂ are not suitable for use during treatment with rifampicin.

Side-effects: Rimactane Infusion is generally very well tolerated and accepted by patients, although hypersensitivity reactions have been described, and occasionally patients have experienced fever, skin rashes and nausea/vomiting. A few cases of broncho-spasm, occurring mainly in chronic asthmatics, have been reported; no causal relationship has been established.

Local tolerability: occasional instances of phlebitis and pain at the infusion site have been reported.

Side-effects to rifampicin, probably of immunological/allergic origin have been reported, particularly in connection with intermittent, interrupted or repeated treatment; for example, influenza-like symptoms, and, rarely skin rashes, fever and dyspnoea have occurred. If serious complications arise such as thrombocytopaenia, purpura, renal failure or haemolytic anaemia, rifampicin should be stopped at once and never restarted.

In patients with previously normal liver function, experience has shown that in many cases changes in liver function are transient and usually revert towards normal pre-treatment levels in about two weeks, even when rifampicin is continued. Routine liver function tests during treatment are unnecessary unless the patient becomes unwell or exhibits frank jaundice. An isolated report showing a moderate rise in the serum bilirubin and/or transaminase or more rarely alkaline phosphatase level is not usually itself an indication for interrupting treatment. The decision should be made after repeating the tests, noting the trends in the levels and considering them in conjunction with the patient's clinical condition. It has been possible in most patients in whom alterations to liver function caused interruption of Rimactane Infusion therapy, to carefully reinstate the drug.

In common with other antibiotics, mild leucopenia, and eosinophilia have been reported in a few patients, but appear to be of no particular clinical significance and no causal relationship has been established.

Rifampicin may produce a reddish discolouration of the urine, sputum and tears; soft contact lenses may also be discoloured.

Pharmaceutical precautions Rimactane Infusion should be freshly prepared. Rifampicin powder and the solvent as supplied have a shelf life of 3 years when stored at room temperature.

Compatibility: Rimactane Infusion is compatible with the following infusion solutions for up to 6 hours: Mannitol 10% and 20%. Macrodex with saline solution, Macrodex with glucose solution, Rheomacrodex, sodium bicarbonate 1.4%, laevulose 5% and 10%, Ringer lactate, Ringer acetate, dextrose 5% and 10%, saline solution.

Incompatibility: Rimactane Infusion is incompatible with

the following: Perfudex, sodium bicarbonate 5%, sodium lactate 0.167M, Ringer acetate with dextrose.

Rimactane Infusion should not be mixed with other drugs as precipitation may occur; concurrent intravenous therapy should be administered via a different site of injection.

Legal category POM.

Package quantities

Rimactane Infusion 300 mg: Combined pack of 1 vial + 1 × 5 ml solvent ampoule.

Rimactane Infusion 600 mg: Combined pack of 1 vial + 1 × 10 ml solvent ampoule.

Product licence numbers

Rimactane Infusion 300 mg 0008/0151

Rimactane Infusion 600 mg 0008/0152

RIMACTAZID* COMBINED TABLETS

Presentation Rimactazid 150 Tablets each containing 150 mg rifampicin (Rimactane*) and 100 mg isoniazid, pink, round, bi-convex, sugar-coated tablets, marked with the monogram CIBA on one side and the letters EI on the other.

Rimactazid 300 Tablets each containing 300 mg rifampicin (Rimactane*) and 150 mg isoniazid; brownish orange, capsule-shaped, bi-convex, sugar-coated tablets, marked with the monogram CIBA on one side and the letters DH on the other.

Uses *Mode of action:* Rimactazid contains the semi-synthetic antibiotic Rimactane, which has bactericidal activity against most groups of Mycobacteria, and isoniazid, which is an effective anti-bacterial agent against Mycobacterium tuberculosis.

Indications: Rimactane and isoniazid are both major drugs in the management of tuberculosis and in certain opportunist mycobacterial infections. This combination has been shown to eradicate tuberculosis infection faster and more effectively than any previous regimen. Extensive UK experience has led to the routine use of Rimactane and isoniazid as basic therapy supported in the first six to eight weeks, or until cultures are negative, by a third drug, e.g. streptomycin, pyrazinamide, ethambutol and the majority of second-line drugs. Whilst it is not generally recommended that rifampicin be used in combination with PAS, if for any reason this regimen is used, the drugs should be given not less than eight hours apart to ensure satisfactory blood levels. Rifampicin is effective in cases resistant to other anti-tuberculous agents and shows no cross-resistance outside the rifamycin group of drugs.

Dosage and administration Rimactazid should be given as a single dose, preferably on an empty stomach, if possible 30 minutes before breakfast to ensure a high peak serum concentration. Dosage should be adjusted according to body weight of patients.

Adults: Oral: The combined tablets of Rimactazid provide Rimactane and isoniazid in the accepted ratios to provide the currently recommended adult dose of these two drugs. Thus, 2 tablets daily of Rimactazid 300 are recommended for patients of 50 kg (8 stone) and over and 3 tablets daily of Rimactazid 150 for patients under 50 kg (i.e. the usual daily dosage of 600 mg or 450 mg Rimactane, each with 300 mg isoniazid).

Use in pregnancy and lactation: Rifampicin has been shown to have teratogenic effects in animals on very high doses, therefore during pregnancy the use of Rimactazid should, if possible, be avoided. Particularly during the first 3 months of pregnancy the drug's possible risks to the foetus must be carefully weighed against its therapeutic benefits for the mother.

When administered during the last few weeks of pregnancy, Rimactane can cause post-natal haemorrhages in mother and infant, for which treatment with vitamin K may be indicated.

Rifampicin is excreted in breast milk. Mothers in whom its use proves unavoidable should refrain from breast-feeding their infants.

Contra-indications, warnings, etc *Contra-indications:* Rimactazid is contra-indicated in patients with jaundice or where there is known hypersensitivity to rifamycins and/or isoniazid. The causative agent should be replaced by another antituberculous drug in combination therapy.

Psychotic states characterised by mania and hypomania are contra-indications for isoniazid.

Precautions: As Rimactane and isoniazid are metabolised in the liver, patients with impaired liver function should be treated with caution. Such patients should have liver function monitored during treatment. Any deterioration in liver function in these patients is an indication for stopping treatment.

The occurrence of liver function abnormalities is more common when rifampicin and isoniazid are used in combination and special care is therefore required in patients with pre-existing liver impairment or in the elderly, malnourished or very young patients.

In the presence of complete renal failure rifampicin is excreted entirely in the bile, provided hepatic function is not impaired the dosage of rifampicin need not be adjusted.

When resuming treatment with rifampicin after a temporary interruption or a prolonged interval, the drug should be given in small gradually increasing doses. For this purpose, rifampicin and isoniazid should temporarily be administered in free combination. In adults an initial dose of rifampicin 75 mg daily should be administered, raised subsequently by 75 mg per day until the desired dosage level is attained. During this period, renal function should be closely monitored. If as may happen in exceptional cases the patient develops renal failure, thrombocytopenia, purpura or haemolytic anaemia, treatment with rifampicin should be stopped at once and not re-instituted at a later date. Normal dosage of isoniazid should be continued over this period.

Microbiological techniques for assaying the serum concentrations of folic acid and Vitamin B₁₂ are not suitable for use during treatment with rifampicin.

Care should be taken in giving isoniazid to patients suffering from convulsive disorders, chronic alcoholism or impaired liver or kidney function. Pyridoxine may be useful in preventing the occurrence of peripheral neuritis.

Drug Interactions: Rifampicin is a potent inducer of liver enzymes which may increase the metabolism of concomitantly administered drugs such as corticosteroids, oral contraceptives, oral anti-coagulants, oral anti-diabetic agents, dapsone, some digitalis preparations, quinidine and methadone. The dosage of these drugs may need considerable review when Rimactazid or Rimactane is being prescribed, larger doses being needed when

Rimactazid or Rimactane is introduced and a reduction when either is withdrawn.

In women receiving treatment with rifampicin it has been found that the contraceptive activity of oral contraceptives may be impaired. In such cases, additional non-hormonal methods should be employed.

In patients under treatment with phenytoin, the dosage of this drug should be individually readjusted, because isoniazid raises, and rifampicin lowers its plasma concentration.

It is not advisable to administer isoniazid concomitantly with disulphiram, although the mechanism of this interaction is unclear.

Side effects: *Associated with Rimactane.* Occasionally gastrointestinal disturbance and drug rashes have been reported after treatment with Rimactane.

There may be an elevation of serum bilirubin levels, SGOT and SGPT levels and more rarely alkaline phosphatase during the early stages of treatment.

In patients with previously normal liver function these changes are transient and usually revert towards normal pre-treatment levels in about two weeks even when Rimactane is continued. Routine liver function tests during treatment are unnecessary unless the patient becomes unwell or exhibits frank jaundice. The occurrence of jaundice may call for temporary cessation of treatment however in most patients it is possible to resume therapy. (See Precautions).

In common with other antibiotics, mild leucopenia and eosinophilia have been reported in a few patients, but appear to be of no particular clinical significance and no causal relationship has been established.

Associated with isoniazid: Side-effects with isoniazid are not common, but hypersensitivity reactions characterised by fever, rash and lymphadenopathy do occur. Isoniazid can cause a mood elevating effect in high dosage which can result in more severe manic disturbances. Occasionally peripheral neuritis has been described, also liver function disturbances, blood dyscrasias, rheumatic syndrome and lupus erythematosus – like signs and symptoms. Hyperglycaemia and gynecomastia have also been associated with isoniazid treatment.

Treatment of overdose: There is no specific antidote to Rimactane. In cases of severe overdose gastric lavage may be undertaken and general supportive treatment administered.

Severe overdose of isoniazid has been treated with phenobarbitone given intravenously, pyridoxine and oxygen. Peritoneal dialysis has also been used.

Pharmaceutical precautions Rimactazid Tablets should be protected from heat and moisture. The combined tablets have a shelf-life of four years.

Legal category POM.

Package quantities Rimactazid 150 Tablets (pink) and Rimactazid 300 Tablets (brownish orange) in securitainers of 100.

Further information Rimactane is orally active, very well tolerated and its activity is comparable with that of isoniazid. In combination, these two agents are commonly used as first-line therapy and offer the greatest chance of rapid eradication of the infection. It is usual, however, to employ a third drug during the first two months of treatment or at least until the results of sensitivity tests are known. Continuation therapy with rifampicin and isoniazid has been shown to eradicate the infection in almost all patients faster and with a lower

relapse rate than any alternative regime. The combined tablets of Rimactazid thus make the most effective combination simpler to take. The orange-red colour imparted to the urine, sputum and tears by rifampicin is a valuable guide to drug adherence; rifampicin may also permanently discolour soft contact lenses.

Product licence numbers

Rimactazid 150 mg 0008/0121

Rimactazid 300 mg 0008/0120

RITALIN*

Presentation Ritalin Tablets each containing 10 mg of methylphenidate hydrochloride, as a circular, flat, white tablet with bevelled edges. The monogram CIBA is impressed on one face and the other is marked with the letters AB and a break line.

Ritalin Ampoules each containing 20 mg methylphenidate hydrochloride as a white lyophilised mass in a clear glass 2 ml ampoule.

Uses Mode of Action: Ritalin has a stimulant effect on the central nervous system.

Indications: Functional behavioural problems in children (Minimal brain dysfunction, hyperkinesia). Narcolepsy.

In anaesthesia for the management of post anaesthetic tremors, including those induced by halothane.

Dosage and administration Adults: Orally the average dose is 20–30 mg daily in 2 doses, 1 before breakfast and 1 before lunch. Parenterally Ritalin may be given subcutaneously, intramuscularly or intravenously, the dose being 10–20 mg to be repeated as required by the clinical response.

For parenteral use the contents of the ampoule should be dissolved in 1 ml of Water for Injection BP. The resulting solution is isotonic.

Note: The parenteral solution should not be injected through tubing or a syringe which contains a barbiturate or a strongly alkaline solution, as a heavy precipitate will be formed.

Children: (over 6 years) Orally 5–10 mg three times daily, increasing if necessary by weekly increments of 5–10 mg in the daily dosage. Doses above 60 mg daily are not recommended. To obviate the risk of insomnia, the last dose should be taken not later than 4 p.m. Ritalin is not indicated in children less than 6 years. Ampoules not recommended for paediatric use.

Contra-indications, warnings, etc Side-effects: Nervousness, insomnia and anorexia are the most common adverse reactions of Ritalin. On rare occasions hypersensitivity reactions, nausea, dizziness, palpitations, headache, dyskinesia, drowsiness and skin rash have been reported. Blood pressure and pulse changes, both raising and lowering, may occur.

Contra-indications: The presence of marked anxiety or tension is a contra-indication to the use of Ritalin, as it may aggravate these symptoms. Ritalin is also contra-indicated in patients with severe angina pectoris, glaucoma, tachyarrhythmias and thyrotoxicosis.

Ritalin should not be used for severe depression of either exogenous or endogenous origin. Ritalin should not be used in patients suffering from epilepsy, or in those with a propensity for dependence on drugs including alcohol. Ritalin should not be given together with pressor agents, MAO inhibitors or tricyclic antidepressants.

Precautions: Ritalin should only be used with extreme caution in patients receiving antihypertensive agents of the adrenergic neurone blocking type, e.g. debrisoquine, guanethidine. High dosage may induce cardiac arrhythmias. Ritalin has also been reported as inhibiting the metabolism of coumarin, anticonvulsants such as phenobarbitone, phenylhydantoin, primidone and also phenylbutazone.

Ritalin may cause dependence so it should be given cautiously to emotionally unstable patients. Chronic abuse can lead to marked tolerance and psychic dependence with varying degrees of abnormal behaviour. Frank psychotic episodes can occur, especially with parenteral abuse.

Overdosage: There is no specific antidote to Ritalin overdosage. Management consists of appropriate supportive measures. Gastric contents may be evacuated by induction of emesis or gastric lavage. Signs and symptoms may include respiratory depression, hypotension and shock, cardiac arrhythmias, hypertension, convulsions or excitation states, hyperthermia. In the treatment of hypotension sympathomimetic agents should not be used. Hypertension may be treated with an alpha-blocker such as Rogitine or a vasodilator such as Apresoline. Convulsions and excitation states may be controlled by the cautious use of diazepam, however this may aggravate respiratory depression. Cardiovascular function, respiration and body temperature should be monitored for several days following the onset of improvement.

Pharmaceutical precautions Protect from light.

Legal category POM: MDA.

Package quantities 10 mg tablets of Ritalin in Securitainers of 100.

20 mg dry ampoules of methylphenidate hydrochloride in boxes of 6 for hospital use only.

Further information Nil.

Product licence numbers

Ritalin Tablets 10 mg 0008/5049

Ritalin Ampoules 20 mg 0008/5082

ROGITINE*

Presentation Clear glass ampoules each containing 50 mg phentolamine mesylate presented as a colourless to pale yellow solution in 5 ml water for injection. Each box contains 5 × 5 ml ampoules. Also available as ampoules containing 10 mg phentolamine mesylate in 1 ml water for injection. Each box contains 6 × 1 ml ampoules.

Uses Mode of Action: Acute, severe cardiac insufficiency is often characterised by a high degree of sympathico-adrenergic stimulation which leads to a pronounced increase in the myocardial oxygen requirement. Marked peripheral vasoconstriction and a rise in left-ventricular filling pressure, accompanied by pulmonary congestion or pulmonary oedema, are usually also present.

In patients with acute, severe cardiac insufficiency, particularly when due to recent myocardial infarction, parenteral administration of Rogitine elicits a prompt improvement in the clinical picture. By acting directly on vascular smooth muscle, by blocking the alpha-receptors, and by indirectly stimulating the beta-receptors,

Rogitine exerts a rapid and potent vasodilator effect which also extends to the venous system. Systemic and pulmonary vascular resistance, as well as left-ventricular filling pressure, are reduced. The work load on the heart is thus diminished – alternatively the level of cardiac performance attained at a given work load is improved. Stroke volume and cardiac output are increased, which has the effect of limiting the fall in blood pressure.

Moreover, the positive inotropic activity of Rogitine also helps to enhance cardiac performance. Rogitine, however, does not unduly accelerate the heart rate; on the contrary, the net result of its various effects is a marked easing of the strain on the heart. Besides its direct haemodynamic effect, the drug also stimulates secretion of insulin, which is reduced in the presence of severe cardiac insufficiency; this stimulant action tends to have a favourable influence on myocardial metabolism. The anti-arrhythmic properties possessed by Rogitine may diminish the occurrence of ventricular or supra-ventricular extra systoles.

Indications: Acute left ventricular failure (cardiogenic shock) particularly following myocardial infarction.

Paroxysmal hypertension associated with phaeochromocytoma or interaction of foodstuffs with MAOI's; and as prophylactic treatment (in combination with a beta-blocker) before and during surgical removal of phaeochromocytoma.

As a diagnostic agent in cases of suspected phaeochromocytoma.

Dosage and administration *Cardiogenic Shock:* The dosage should be individually adapted to the patient's requirements and will depend on the severity of the cardiac insufficiency and on the blood pressure.

Rogitine should be administered in the form of an intravenous infusion in 5% sterile glucose, saline or dextrose saline solution. A dose of 5–60 mg Rogitine should be given over a period of 10–30 minutes at an infusion rate of 0.1–2 mg per minute. If necessary, especially in cases where the systemic arterial blood pressure is elevated, the infusion rate during the first minute can be raised up to 5 mg per minute.

Systolic blood pressure should be carefully monitored during the infusion and a fall below 100 mm Hg is an indication for reducing the infusion rate (see Precautions).

Depending on the patient's response, the treatment can either be continued for several hours or repeated at intervals.

Paroxysmal hypertension: 5–10 mg intramuscularly or intravenously to be repeated if necessary. When used prior to surgical removal of phaeochromocytoma, administer the injection 2 hours before surgery and repeat if necessary during the operation. In children during surgery for the removal of phaeochromocytoma, the dosage is 1 to 5 mg given intravenously according to age.

As a diagnostic test for phaeochromocytoma: This test is based upon the fact that Rogitine produces a fall in blood pressure when it is caused by excess circulating adrenaline and/or noradrenaline, so it is of value only in the hypertensive phase of the paroxysmal type of case. False positives may result from patients suffering from uraemia, or who have received sedatives or narcotics during the twenty-four hours prior to the test.

The initial step in the test is to determine the basal blood pressure of the patient – this is essential for the

correct interpretation of the test. An intravenous injection of 5 mg of Rogitine (1 mg in children) is then administered. As the insertion of the needle may involve a pressor response the blood pressure should be allowed to drop back to within 3 to 4 mm of the basal level before injecting Rogitine.

In the event of a positive response the blood pressure will fall rapidly, and quickly return to basal levels. The blood pressure must be measured at 30 second intervals for 3 minutes after injections, and then every 60 seconds for 7 more minutes.

An immediate marked drop in both systolic and diastolic blood pressure is the typical positive response in patients having a phaeochromocytoma which is discharging adrenaline or noradrenaline at the time of the test. The maximum depressor effect usually occurs within two minutes and usually involves a fall in systolic pressure of about 60 mm and the diastolic fall usually exceeds 25 mm. The blood pressure remains low for only a relatively short time and may return to pre-injection levels within 10–15 minutes. Positive results should be confirmed by either estimation of catecholamines in the urine or by another diagnostic procedure.

False positive results may be seen in patients with uraemia and those having taken sedatives prior to the test.

Whilst false negative results may be seen:

- if at the time of injection the tumour is not discharging sufficient adrenaline or noradrenaline to elevate the blood pressure significantly;
- when a phaeochromocytoma is present in a patient also having essential hypertension, the test may not cause such a marked fall in blood pressure.

The other clinical findings and tests would usually assist in interpreting such results.

The intravenous administration of Rogitine may cause tachycardia in rare instances, weakness, dizziness or flushing, but are not considered serious in relation to the test.

Further details available on request from CIBA Laboratories, Horsham, West Sussex.

Contra-indications, warnings, etc *Contra-indication:* Severe hypotension.

Precautions: Monitoring of the patient's blood pressure, heart rate, and clinical condition is necessary not only to ensure correct selection of cases suitable for treatment with Rogitine but also to decide upon the appropriate dosage and duration of parenteral therapy. As a general rule, a systolic pressure of 80 mmHg should be regarded as the lowest limit at which the drug can still be employed.

Side-effects: When administered in the recommended dosages, Rogitine is generally well tolerated. Hypotension, tachycardia and dizziness may occur, particularly if the drug is given parenterally. Nausea, diarrhoea, and nasal congestion have been reported in response to fairly high doses, but they subside again following discontinuation of the infusion.

Treatment of Overdosage: In the event of overdosage (as evidenced by an excessive fall in blood pressure, or by tachycardia) it is usually sufficient simply to discontinue the infusion; if necessary, the effect of Rogitine can be attenuated by giving noradrenaline.

Pharmaceutical precautions Protect from heat and light.

Legal category POM.

Package quantities

- (a) Ampoules each containing 50 mg Rogitine in 5 ml Water for Injection. Boxes of 5.
- (b) Ampoules each containing 10 mg Rogitine in 1 ml Water for Injection. Boxes of 6.

Further information Nil.

Product licence numbers

Rogitine Ampoules 50 mg/5 ml 0008/0145
Rogitine Ampoules 10 mg/1 ml 0008/5070.

SLOW-K®

Presentation Pale orange, polished, sugar-coated tablets about 12 mm in diameter, printed with the name Slow-K, containing 600 mg (8.06 mEq) of Potassium Chloride BP.

Uses Mode of Action: The potassium chloride in Slow-K is finely distributed in a neutral wax base, from which it is gradually released over a period of 3–6 hours during its passage through the digestive tract. This special form of potassium substitution therapy is designed to avoid high localised concentrations of potassium chloride which might irritate or damage the mucosa. The potassium chloride present in Slow-K is completely absorbed in the intestinal tract.

Indications: For the treatment and specific prevention of hypokalaemia especially in cases of the following kinds.

Where protracted or intensive diuretic medication is being given as treatment for hypertension or cardiac failure, and where diuretics have been prescribed to resolve massive oedema. Potassium substitution is of particular importance in patients undergoing concomitant digitalisation because hypokalaemia may cause hypersensitivity to digitalis.

Renal disease associated with increased potassium excretion e.g. nephrotic syndrome.

Liver cirrhosis, especially during diuretic therapy.

Gastro-intestinal disorders accompanied by potassium depletion e.g. chronic diarrhoea, repeated vomiting, ulcerative colitis, status post ileostomy.

Hypochlorhaemic alkalosis, cases in which a low salt diet or prolonged fasting have been imposed and patients receiving an unbalanced diet deficient in potassium.

Protracted or intensive treatment with corticosteroids, ACTH or carbenoxolone, Cushing's syndrome.

Initial treatment for megaloblastic anaemia.

Diabetic ketosis.

In these conditions Slow-K is particularly indicated if a diet rich in potassium cannot be guaranteed.

Dosage and administration Adults: The dosage of Slow-K should be adapted to the cause, degree and duration of potassium depletion. 2–6 tablets are usually an adequate supplement. It is important that the tablets should be swallowed whole, and to ensure the tablets enter the stomach, taken with meals or with a tumbler of water.

In states of severe potassium deficiency, a higher dose of 9–12 tablets daily may be needed. According to the dosage of diuretic used and the needs of the individual patient, a dose ratio of one Slow-K tablet with each tablet of thiazide diuretic will usually suffice when administered as a potassium supplement. However, when the more potent diuretics such as frusemide are used, larger doses of Slow-K may be required. Where

intermittent diuretic therapy is being used it is probably best to continue the Slow-K on the days between the diuretic administration.

Children: At the discretion of the physician.

Contra-indications, warnings, etc Side-effects: Side-effects are rare with Slow-K, as any excess potassium is rapidly excreted in the urine.

In rare cases, oral potassium preparations may provoke gastro-intestinal disturbances (nausea, vomiting, abdominal pains, diarrhoea) necessitating either a reduction in dosage or withdrawal of medication (see Precautions).

Contra-indications: Advanced renal failure, untreated Addison's disease, acute dehydration, hyperkalaemia. All solid forms of potassium medication are contra-indicated in the presence of obstructions in the digestive tract (e.g. resulting from compression of the oesophagus due to dilation of the left atrium or from stenosis of the gut).

Precautions: If a patient under treatment with Slow-K develops severe vomiting, severe abdominal pains or flatulence, or gastro-intestinal haemorrhage, the preparation should be withdrawn at once, because in the presence of an obstruction it could conceivably give rise to ulceration or perforation.

In patients suffering from impaired renal function, special care should be exercised when prescribing potassium salts owing to the risk of their producing hyperkalaemia. Monitoring of the serum electrolytes is particularly necessary in patients with diseases of the heart or kidneys.

To guard against the risk of hyperkalaemia, one should also refrain from administering potassium salts together with potassium-sparing diuretics such as aldosterone antagonists or triamterene.

In cases of metabolic acidosis, the hypokalaemia should be treated not with potassium chloride but with an alkaline potassium salt (e.g. potassium bicarbonate).

Pharmaceutical precautions Slow-K Tablets should be protected from heat, light and moisture. The tablets should be dispensed in moisture-proof containers.

Legal category GSL.

Package quantities Slow-K Tablets (600 mg Potassium Chloride BP in a special slow-release core, equivalent to 8.06 mEq K⁺) Securitainers of 500.

Further information The potassium chloride in Slow-K has been shown to be completely absorbed, but occasionally patients may notice 'ghost' tablet cores in the faeces, these have been shown not to contain any potassium. The administration of Slow-K does not obviate the need to encourage the patient to take an adequate potassium-containing diet.

Product licence number 0008/5039.

SLOW-TRASICOR®

Presentation Slow-Trasicor Tablets each containing 160 mg oxprenolol hydrochloride in a special sustained-release formulation. Circular, slightly bi-convex, white film-coated tablets, having the monogram CIBA impressed on one side and Slow-Trasicor on the other.

Uses Mode of action: Slow-Trasicor Tablets release oxprenolol hydrochloride (a non-selective beta-adren-

ergic receptor blocking drug) gradually from a special sustained release formulation, thus prolonging the pharmacological action.

Slow-Trasicor protects the heart and cardiovascular system against excessive adrenergic stimulation caused by either physical or emotional activity. Accordingly, under conditions of sympathetic drive, heart rate, force of contraction and output are reduced, leading to a fall of myocardial work and oxygen consumption. The extra-cardiac effect of Slow-Trasicor include attenuation of both renin and free fatty acid release.

Slow-Trasicor has partial agonist activity (PAA) also known as intrinsic sympathomimetic activity (ISA). This property means that some degree of stimulation of the beta receptors is maintained. Under conditions of rest, this tends to counterbalance the reduction in heart rate and force of contraction.

Indications: *Hypertension:* All grades of hypertension in once-daily dosage. The concomitant use of a thiazide diuretic will enhance the antihypertensive effect of Slow-Trasicor, resulting in better control from reduced dosage.

Angina pectoris: For continuous prophylaxis in once-daily dosage to improve exercise tolerance and reduce the frequency and severity of anginal attacks. Beta-blocking agents have been shown to improve the medium-term prognosis, by reducing the rate of recurrent complications and death in patients after myocardial infarction.

Anxiety: For the control of anxiety and anxiety tachycardia.

Dosage and administration Slow-Trasicor Tablets release oxprenolol gradually from a special sustained-release formulation. This provides a considerably longer pharmacological action from a given dose, thus allowing once-daily dosage.

Adults: *Hypertension:* Initially one tablet daily, given in the morning. If necessary, this dose can be raised to two or more tablets, usually given once daily until satisfactory blood pressure control is achieved. However, when used as monotherapy, dosage should not exceed 3 tablets daily, i.e. 480 mg Slow-Trasicor, since experience has shown that hardly any increase in the response can be achieved by this means. The addition of a diuretic will often give a quicker and more satisfactory response. Usually, patients respond to a dose of one or two tablets of Slow-Trasicor in combination with a diuretic and most of the antihypertensive effect is achieved within 2-3 days. The addition of a vasodilator will often enable control to be achieved in the minority of patients who might otherwise fail to respond.

Angina pectoris: Initially one tablet daily, given in the morning. This can be increased to two or three tablets, usually given once daily depending on patient response. An evening dose may be beneficial in nocturnal angina. Increased dosage is related to increased exercise tolerance, but doses higher than three tablets should not normally be required. Slow-Trasicor is compatible with glyceryl trinitrate and the two drugs are complementary since they reduce heart work by different mechanisms. It may be possible, however, to reduce the use of glyceryl trinitrate when the patient has become established on Slow-Trasicor.

As with other beta-blocking drugs, sudden withdrawal of treatment may induce severe and continuous angina. Patients should, therefore, be advised to avoid interrup-

tion of established therapy and if withdrawal becomes necessary it should be done gradually.

Anxiety states: One tablet daily. Although no evidence of habituation or tolerance has been observed with Trasicor its effectiveness in the long term treatment of anxiety has not been established. In the treatment of transient situational anxiety it may be appropriate to prescribe a single dose of 40-80 mg conventional Trasicor. Trasicor can be administered concurrently with benzodiazepines. When withdrawal of pre-existing anxiolytic therapy is indicated this should take place gradually.

Contra-indications, warnings, etc *Side-effects:* Slow-Trasicor is well tolerated. However, dizziness, drowsiness, headache, insomnia, excitement and gastrointestinal disturbance may occur particularly at the start of treatment. Like other beta-blockers, isolated cases of excessive bradycardia and thrombocytopenia have been reported. As with other beta-blockers, bronchospasm and heart failure may occasionally be precipitated in susceptible patients (see Precautions) and exertional tiredness and feelings of coldness in the extremities have been reported on rare occasions. However, the incidence of these side-effects is low, possibly due to the partial protection afforded by the sympathomimetic effect of Slow-Trasicor.

Slow-Trasicor possess antihypertensive effects but these are unlikely to be noted in normotensive subjects.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic blocking drugs. The reported incidence is small, and in most cases the symptoms have cleared when the treatment was withdrawn. Discontinuance of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-adrenergic blocker should be gradual.

Contra-indications: Slow-Trasicor is contra-indicated in patients with atrio-ventricular block, marked bradycardia, uncontrolled heart failure and cardiogenic shock.

Precautions: If there is evidence of cardiac failure this must be controlled by digitalis and/or diuretics before and during Slow-Trasicor therapy. Should the pulse rate fall below 50 per minute, then treatment should be restarted at a lower dose. Caution should be observed when treating asthmatics, chronic bronchitis or other individuals where bronchospasm may be provoked. Slow-Trasicor should be given cautiously to patients with metabolic acidosis, or anaesthesia with ether or chloroform. For anaesthesia the agent selected should be one exhibiting as little negative inotropic activity as possible e.g. halothane, nitrous oxide. Treatment with a beta-blocker is liable to mask symptoms of hypoglycaemia and also to affect carbohydrate metabolism. In patients with labile or insulin dependent diabetes in particular, it may therefore be necessary to readjust the dosage of anti-diabetic medication.

Beta-blockers may cause bradycardia in the fetus which can also persist after birth. During pregnancy, in the course of labour and during lactation beta-blockers should only be employed after the needs of the mother have been weighed against the possible risks to the fetus.

Treatment of overdosage: Overdosage with Slow-Trasicor may lead to excessive bradycardia, hypotension, coma and convulsions. It should also be noted that severe toxicity may develop rapidly and that there may be severe hypotension and bradycardia despite a normal

ECG. For sinus bradycardia and hypotension 0.5–2.0 mg of atropine should be slowly administered by intravenous infusion. If this does not raise the heart rate sufficiently isoprenaline may be necessary. The dose of isoprenaline needs to be sufficient to reverse the blockade and should be assessed by the clinical response. A reasonable starting dose would be 25 mcg of isoprenaline hydrochloride.

In severe cardiogenic shock the treatment of choice appears to be glucagon. The initial dose should be 5–10 mg intravenously, further boluses or an infusion can be used according to the patient's condition. Transvenous pacing has been used, sometimes with success. If bronchospasm develops bronchodilators should be used. Patients should be monitored for several days as the beta-blocking effects of Slow-Trasicor exceed its plasma half-life.

Pharmaceutical precautions The tablets have no special storage requirements.

Legal category POM.

Package quantities Cartons of 28 Slow-Trasicor Tablets consisting of two reminder calendar foils of 14. (Each carton of 28 represents 2–4 weeks' treatment, depending on whether storage is one or two tablets daily).

Further information Slow-Trasicor is a sustained release preparation of Trasicor* (oxprenolol hydrochloride) designed to release oxprenolol so that maximal response is obtained within 1–2 hours (as with plain Trasicor tablets), whilst the pharmacological action is sustained for 24 hours. Thus Slow-Trasicor produces a smoother absorption of Trasicor and by levelling out peak serum concentrations, avoids 'wastage' and minimises unwanted effects of beta-blockade. Accordingly, there is greater utilisation of Trasicor (oxprenolol) mg for mg (i.e. greater distance walked by an anginal patient before the onset of pain) with Slow-Trasicor.

Trasicor protects the cardiovascular system from excess adrenergic discharge and the resulting elevation of catecholamine levels which are a known risk factor in coronary heart disease and which in the long term, may contribute to the secondary effects of hypertension.

Trasicor prevents emotional tachycardia during environmental stress. In anxiety, Trasicor does not produce sedation or cause dependence. The best response is seen in patients who have not previously received benzodiazepines.

Slow-Trasicor is presented in day-of-the-week calendar packs to improve patient compliance.

Product licence number 0008/0130.

SYNACTHEN*

Presentation A clear, colourless, sterile solution containing 0.25 mg tetracosactrin per ml. This preparation is available in 1 ml ampoules.

Uses *Mode of action:* Synacthen is a synthetic polypeptide with corticotrophic activity and a short duration of action. Synacthen consists of the first 24 amino acids occurring in natural adrenocorticotrophin.

Indications: Since Synacthen has all the properties of natural ACTH it can be used in all situations where a short acting ACTH preparation is indicated, e.g. bronchial asthma, but only if other therapeutic measures have failed and under strict medical supervision. Also as a

diagnostic test for the investigation of adrenocortical insufficiency.

Dosage and administration Synacthen may be given by intravenous or intramuscular or subcutaneous injection.

Adult dosage for therapeutic use: Intravenously 0.25 mg of Synacthen in 500 ml of infusion fluid (isotonic dextrose or other electrolyte solution) over a six-hour period. By intramuscular injection 0.25 mg every three to four hours.

As a diagnostic aid: Withdraw 5–8 ml of venous blood into a heparinised tube, then inject intramuscularly 0.25 mg of Synacthen. After 30 minutes withdraw a further 5–8 ml into a heparinised tube, centrifuge the blood specimen, measure plasma hydroxycorticoids and interpret the results. (The Mattingly method is suitable.)

For a normal test the initial level of plasma cortisol should be greater than 5 mcg/100 ml (138 nmol/l), provided that the patient has not received a glucocorticoid within the previous 12 hours. The plasma cortisol level 30 minutes after the injection of Synacthen should be greater than 18 mcg/100 ml (500 nmol/l) irrespective of the initial level, and should have risen by at least 7 mcg/100 ml (200 nmol/l).

Synacthen should not be added to blood or plasma transfusions as it is liable to be inactivated by the enzymes.

When administering Synacthen for a therapeutic effect the route of choice is by intravenous infusion in isotonic dextrose or electrolyte solution. The route of infusion is important. It is suggested that 500 ml containing 0.25 mg of Synacthen should be given over six hours at the rate of approximately 24 drops per minute. When given intravenously 1 mg of Synacthen is equivalent in activity to approximately 100 units of corticotrophin.

Contra-indications, warnings, etc *Contra-indications:* Hypersensitivity reactions may occur in response to Synacthen particularly in patients with allergic disorders or with an allergic diathesis. In rare cases these may be of a serious nature and take the form of anaphylactic reactions, which normally occur within 30 minutes. Such reactions should be considered an absolute contra-indication to further treatment with this polypeptide.

Milder reactions of an allergic or hypersensitive nature should also be considered as an indication that the course of treatment should be stopped and not restarted, since a trivial reaction may be followed by a more serious event if further injections are given. These milder reactions include urticaria, pruritis, flushing and faintness and dyspnoea. Since some reactions have occurred without warning wherever possible patients should remain at the hospital or doctor's surgery for a recovery period following an injection.

As with any treatment that may carry an allergic risk injections of Synacthen should be administered under medical supervision and in the event of a severe anaphylactic reaction occurring despite these precautions, the following measures are recommended: administer 0.5 mg adrenaline s.c. or i.m. as well as a large i.v. dose of corticosteroid for example 50–100 mg prednisolone as prednisolone sodium phosphate BP, repeating the dose if necessary.

The doctor should routinely enquire about possible previous reactions to Synacthen or drugs in general and about a past history of allergic disorders.

Synacthen is contra-indicated in patients allergic or sensitive to Synacthen Depot; in acute psychoses, in the

presence of systemic infections without specific anti-infective therapy, in Cushing's syndrome and in patients with peptic ulcer and heart failure. Synacthen is also contra-indicated during pregnancy.

Precautions: Synacthen should be used cautiously in patients hypersensitive to ACTH of animal origin; and in patients suffering from diabetes mellitus or hypertension, where the dosage of concomitant medication may need adjustment.

Side-effects: When employed as a therapeutic agent, Synacthen is liable to give rise to side-effects which are due to the drugs hormonal activity e.g. sodium and water retention, raised blood pressure, hypokalaemia, hyperglycaemia, increased susceptibility to infection, Cushing's syndrome, hyperpigmentation and psychological disturbances. The more serious side-effects usually associated with steroids, peptic ulcer, osteoporosis, retarded wound healing and myopathy are less frequent. Troublesome side-effects are often an indication of overdosage.

Pharmaceutical precautions Synacthen should be protected from heat and light.

Legal category POM.

Package quantities Synacthen Ampoules 0.25 mg per ml in boxes of 6.

Further information Nil.

Product licence number 0008/0034.

SYNACTHEN* DEPOT

Presentation Tetracosactrin Acetate BP with zinc injection. A sterile white suspension, which settles on standing, containing 1 mg of Synacthen per ml. The preparation is intended for intra-muscular injection, and is available in 1 ml ampoules and 2 ml multi-dose vials.

Uses *Mode of action:* Synacthen is a synthetic polypeptide consisting of the first 24 amino acids of the naturally occurring anterior pituitary hormone ACTH. These 24 amino acids are the ones responsible for the corticotropic activity. Those numbering 25 to 39, some of which vary from one species to another, but which do not appear necessary for corticotropic activity, are omitted. Synacthen thus has the same biological action as natural human ACTH. Synacthen is a hexa-acetate. In the depot form it is adsorbed on to a zinc phosphate complex, to prolong its action.

Indications: For the treatment of rheumatoid arthritis and other allied rheumatic conditions, including juvenile rheumatoid diseases and rheumatic fever, acute gout, psoriatic arthropathy, dermatomyositis, asthma but only in exceptional cases (see contra-indications, warnings, etc.), chronic skin disorders such as pemphigus, generalised bullous or exfoliative dermatitis, dermatitis herpetiformis and erythrodermia, nephrotic syndrome, ulcerative colitis, Crohn's Disease, acute neurological conditions such as exacerbations of multiple sclerosis, Guillain-Barré syndrome, Bell's paralysis, optic neuritis, systemic lupus erythematosus, hypsarrhythmia and periorthritis nodosa. To transfer or wean patients from corticosteroid therapy.

Dosage and administration Synacthen Depot should be given intramuscularly, preferably into the buttock.

Adults: Usually 0.5–1 mg twice a week (sometimes less or at longer intervals according to response). For best results the dosage regime should be tailored to individual requirements.

In acute cases, 1 mg i.m. daily for three days. A maintenance regime should be adopted as soon as an adequate response is obtained. The cortisol response is rapid and lasts about 28 hours, the clinical response usually lasts longer.

Infants: Initially 0.25 mg daily by i.m. injection. Maintenance dose 0.25 mg every two to eight days.

Small children: Initially 0.25–0.5 mg daily by i.m. injection. Maintenance dose 0.25–0.5 mg every two to eight days.

Children of school age: Initially 0.25–1 mg daily by i.m. injection. Maintenance dose 0.25–1 mg every two to eight days.

If secondary adrenocortical atrophy has occurred, Synacthen Depot can restore adrenal responsiveness over three or four days. This effect may be utilised in weaning patients from corticosteroid therapy. 1 mg of Synacthen Depot being given daily for three days, the steroid dosage being reduced by a quarter each day. If desired the adrenal responsiveness may be checked, using the 30-minute Synacthen test. A further course of Synacthen Depot may be given if necessary.

Contra-indications, warnings, etc Hypersensitivity reactions may occur in response to Synacthen Depot, particularly in patients with allergic disorders or with an allergic diathesis. In rare cases these may be of a serious nature and take the form of anaphylactic reactions, which normally occur within 30 minutes. Such reactions should be considered an absolute contra-indication to further treatment with this polypeptide. Milder reactions of an allergic or hypersensitive nature should also be considered as an indication that the course of treatment should be stopped and not restarted, since a trivial reaction may be followed by a more serious event if further injections are given. These milder reactions include urticaria, pruritus, flushing and faintness and dyspnoea. Since some reactions have occurred without warning wherever possible patients should remain at the hospital or doctor's surgery for a recovery period following an injection. As with any treatment that may carry an allergic risk, injections of Synacthen Depot should be administered under medical supervision and in the event of a severe anaphylactic reaction occurring despite these precautions, the following measures are recommended: administer 0.5 mg adrenaline s.c. or i.m. as well as a large i.v. dose of corticosteroid for example 50–100 mg prednisolone as Prednisolone Sodium Phosphate BP, repeating the dose if necessary.

The doctor should routinely enquire about possible previous reactions to Synacthen Depot or drugs in general and about a past history of allergic disorders.

Synacthen Depot is also contra-indicated in acute psychoses, in the presence of systemic infections without specific anti-infective therapy, in Cushing's Syndrome, in patients with peptic ulcer, heart failure and during pregnancy. Synacthen Depot is contra-indicated for use by the intravenous route.

Side-effects: Glucocorticoid effects such as 'moon face', raised blood sugar, psychological disturbances and decreased resistance to infection may occur with Synacthen Depot. Mineralocorticoid and androgenic effects such as hypertension, water retention, and weight gain, acne, hirsutism, skin pigmentation and disturbances of

the menstrual cycle can sometimes be troublesome. On the other hand the more serious side-effects usually associated with steroids – such as gastric pain and ulcer formation, skin atrophy, bruising, retarded wound healing, osteoporosis and myopathy – are less frequent. Troublesome side-effects are often an indication of overdosage.

Provided the dosage is carefully individualised, Synacthen Depot is unlikely to inhibit growth in children. Nevertheless in children undergoing long-term treatment, growth should be monitored.

Precautions: Synacthen Depot should be used cautiously in patients hypersensitive to ACTH of animal origin and in patients suffering from diabetes mellitus or hypertension, where the dosage of concomitant treatment may need adjustment.

Overdosage: Overdosage may temporarily lead to fluid retention and signs of excessive adrenocorticotrophic activity (Cushing's Syndrome). In such cases the interval between injections should be extended or dosage reduced as necessary. An oral diuretic may be given, but it is wise to give a potassium supplement, e.g. 'Slow-K'.

Pharmaceutical precautions Synacthen Depot should be stored in a refrigerator (2–6°C) and protected from light. Before administration, it should be well shaken.

Legal category POM.

Package quantities Ampoules of 1 mg in 1 ml packed in boxes of 10.

Multi-dose vials of 2 mg in 2 ml, packed singly.

Further information Synacthen Depot is a free-flowing, fine suspension which can be easily injected using a fine needle.

Since it contains a shorter chain molecule which is not 'foreign' to the human species it may often be well tolerated by patients who are sensitive to animal-extracted ACTH.

The Depot formulation, an inorganic complex, is much longer acting than the gel or CMC forms of ACTH. Thus injections of Synacthen Depot can be more widely spaced. The therapeutic effect far outlasts the cortisol response.

Long-term treatment with Synacthen Depot does not cause adrenal suppression. In fact Synacthen Depot is frequently used to wean patients off steroids. Many cases have been reported where it has eventually been possible to withdraw the Synacthen Depot also, even in patients who initially showed evidence of considerable adrenal atrophy.

Product licence numbers

Ampoules 1 mg 0008/5071

Vials 2 mg 0008/5072

TRASICOR®

Presentation Trasicor Tablets each containing 20 mg oxprenolol hydrochloride. Circular, flat, white, film-coated tablets with bevelled edges, having the monogram CIBA impressed on one side and Trasicor 20 on the other.

Trasicor Tablets each containing 40 mg oxprenolol hydrochloride. Circular, flat, white, film-coated tablets with bevelled edges, having the monogram CIBA impressed on one side and Trasicor 40 on the other.

Trasicor Tablets each containing 80 mg oxprenolol

hydrochloride. Circular, pale yellow, slightly bi-convex, film-coated tablets having the monogram CIBA impressed on one side and Trasicor 80 on the other.

Trasicor Tablets each containing 160 mg oxprenolol hydrochloride. Circular, pale orange, slightly bi-convex, film-coated tablets, having the monogram CIBA impressed on one side and Trasicor 160 on the other.

Trasicor Ampoules each containing 2 mg oxprenolol hydrochloride. A white lyophilised mass supplied in a clear glass 2 ml size ampoule.

Uses Mode of action: Trasicor is a beta-adrenergic receptor blocking drug. Its principal effects are seen on the heart where the rate is slowed (negative chronotropic effect) with consequent reduction in heart work and myocardial oxygen consumption.

Trasicor provides effective prophylactic control of angina throughout the day in the majority of patients. The frequency and severity of anginal attacks are reduced, whether precipitated by exercise or emotional stress, and exercise tolerance is improved. ST segment depression seen on exercise is also reduced.

Trasicor has partial agonist activity (PAA) also known as intrinsic sympathomimetic activity (ISA). This property means that some degree of stimulation of beta receptors is maintained. Under conditions of rest this tends to balance the negative chronotropic and negative inotropic effects. Trasicor blocks the effects of excessive catecholamine stimulation resulting from stress.

The mechanism of the antihypertensive effect of Trasicor is not clearly understood. Whilst haemodynamic effects on cardiac output and peripheral resistance appear to be factors, effects on plasma renin and/or the central nervous system may be of significance.

Indications: For the treatment of angina pectoris, all grades of hypertension and sympathetically induced cardiac arrhythmias. For the control of anxiety and anxiety tachycardia. Subsidiary indications include functional heart disorders, hypertrophic obstructive cardiomyopathy, as an adjunct to the treatment of thyrotoxicosis and dysrhythmias associated with anaesthesia.

Dosage and administration Adults: Angina pectoris: Most patients respond to 40–160 mg three times daily. Individual patients may require more, but only rarely are doses above 480 mg daily required.

Trasicor is compatible with glyceryl trinitrate and they are complementary since they reduce heart work by different mechanisms. It is usually possible, however, to reduce or even discontinue the use of glyceryl trinitrate when the patient has become established on Trasicor.

As with other beta-blocking drugs, sudden withdrawal of treatment with Trasicor may induce severe and continuous angina. Patients should, therefore, be advised to avoid interruption of established therapy and if withdrawal becomes necessary it should be done gradually.

Hypertension: Initially 80 mg twice daily. If necessary this daily dose can be increased at convenient intervals (e.g. weekly or fortnightly) until satisfactory blood-pressure control is achieved. When used as monotherapy doses of 480 mg/day should not be exceeded, since experience has shown that hardly any increase in the response can be achieved by this means. The addition of a diuretic will often give a quicker and more satisfactory response. Usually, patients respond to a dose of 80–320 mg Trasicor in combination with a diuretic and most of the antihypertensive effect is achieved within 2–3 days. The addition of a vasodilator will often enable

control to be achieved in the minority of patients who might otherwise fail to respond.

Cardiac arrhythmias: Initial dose 20–40 mg three times daily. This may be increased if necessary to achieve the desired effect.

Trasicor Ampoules 2 mg for parenteral use. Trasicor may be given intramuscularly or intravenously for the emergency treatment of severe cardiac arrhythmias. The recommended starting dose is 2 mg dissolved in 10 ml Water for Injection BP or Injection of Sodium Chloride BP and given slowly, i.e. over 30 seconds, by intravenous injection. If there has been no adequate response within 5 minutes, additional doses of 2 mg, followed by 4 mg, then 8 mg can be given at 5-minute intervals, giving a maximum cumulative dosage of 16 mg in cases of persistent atrial arrhythmias.

N.B. Parenteral administration should be restricted to patients in hospital, preferably under ECG control.

Anxiety states: The majority of patients will respond to a total daily dose of 160 mg. Although no evidence of habituation or tolerance has been observed with Trasicor, its effectiveness in the long term treatment of anxiety has not been established. In the treatment of transient situational anxiety a single dose of 40–80 mg of Trasicor may be prescribed. Trasicor can be administered concurrently with benzodiazepines. When withdrawal of pre-existing anxiolytic therapy is indicated, this should take place gradually.

Hyperthyroidism: 40–120 mg daily in 2 or 3 divided doses.

Pre-operatively: Patients with thyrotoxicosis and phaeochromocytoma may be managed on 60 mg daily in three divided doses. Atropine must always be used pre-operatively.

Anaesthesia: 2 mg ampoules. For the management of prophylaxis of anaesthetic arrhythmias up to 2 mg should be given by slow intravenous injection. Patients should be fully atropinised. Further doses of up to 2 mg at a time may be administered cautiously as required for the management of resistant cases or to maintain the effect.

In patients undergoing elective surgery, it may be considered desirable to employ a beta-blocker as pre-medication, by shielding the heart against the effects of stress, the beta-blocker may serve to guard against excessive sympathetic stimulation, which is liable to provoke such cardiac disturbances as arrhythmia or acute coronary insufficiency. In a patient under beta-blockade, the anaesthetic selected should be one exhibiting as little negative inotropic activity as possible, e.g. halothane, nitrous oxide. If, on the other hand, inhibition of sympathetic tone during the operation is regarded as undesirable, the beta blocker can be withdrawn gradually prior to surgery.

Children: Occasionally Trasicor has been given to children and infants to control arrhythmias. No dosage scheme has been worked out but oral Trasicor has been given empirically on a body-weight basis of approximately 1 mg/kg.

Contra-indications, warnings, etc *Side-effects:* Trasicor is well tolerated. However dizziness, drowsiness, headache, insomnia, excitement and gastro-intestinal disturbance may occur particularly at the start of treatment. Isolated cases of excessive bradycardia and thrombocytopenia have been reported.

As with other beta-blockers, bronchospasm and heart failure may occasionally be precipitated in susceptible

patients (see 'Precautions') and exertional tiredness and feelings of coldness in the extremities have been reported on rare occasions. However, the incidence of these side-effects is low, possibly due to the partial protection afforded by the sympathomimetic effect of Trasicor.

Trasicor possesses antihypertensive effects, but these are unlikely to be noted in normotensive subjects.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic blocking drugs. The reported incidence is small, and in most cases the symptoms have cleared when the treatment was withdrawn. Discontinuation of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-adrenergic blocker should be gradual.

Contra-indications: Trasicor is contra-indicated in patients with atrioventricular block, marked bradycardia, uncontrolled heart failure and cardiogenic shock.

Precautions: If there is evidence of cardiac failure, this must be controlled by digitalis and/or diuretics before and during Trasicor therapy. Should the pulse rate fall much below 50 per minute, then treatment should be withdrawn and re-started at a lower dose. Caution should be observed when treating asthmatics, chronic bronchitis or other individuals where bronchospasm may be provoked. Trasicor should be given cautiously to patients with metabolic acidosis or anaesthesia with ether or chloroform (see Dosage and Administration). Treatment with a beta-blocker is liable to mask symptoms of hypoglycaemia and also to affect carbohydrate metabolism. In patients with labile or insulin dependent diabetes in particular, it may therefore be necessary to readjust the dosage of anti-diabetic medication. Like other beta-blockers, Trasicor should not be given in combination with calcium antagonists of the verapamil type, because their concomitant use may result in bradycardia, hypotension or even cardiac arrest.

Beta-blockers may cause bradycardia in the fetus which can also persist after birth. During pregnancy and in the course of labour and during lactation beta-blockers should only be employed after the needs of the mother have been weighed against the possible risks to the fetus.

Treatment of overdosage: Overdosage with Trasicor may lead to excessive bradycardia, hypotension, coma and convulsions. It should also be noted that severe toxicity may develop rapidly and that there may be severe hypotension and bradycardia despite a normal ECG. For sinus bradycardia and hypotension 0.5–2.0 mg of atropine should be administered slowly by intravenous infusion.

If this does not raise the heart rate sufficiently isoprenaline may be necessary. The dose of isoprenaline needs to be sufficient to reverse the blockade and should be assessed by the clinical response. A reasonable starting dose would be 25 mcg of isoprenaline hydrochloride.

In severe cardiogenic shock the treatment of choice appears to be glucagon. The initial dose should be 5–10 mg intravenously, further boluses or an infusion can be used according to the patient's condition. Transvenous pacing has been used, sometimes with success. If bronchospasm develops bronchodilators should be used. Patients should be monitored for several days as the beta-blocking effects of Trasicor exceed its plasma half-life.

Pharmaceutical precautions The ampoules should

be protected from light; the tablets have no special storage requirements.

Legal category POM.

Package quantities

20 mg Tablets: 100s and 500s.

40 mg Tablets: 100s and 500s.

80 mg Tablets: 100s.

160 mg Tablets: 100s.

All Trascor Tablets packed in Securitainers.

Ampoules 2 mg: Boxes of 5.

Further information In hypertension, Trascor blocks only the beta-receptors and does not share the problems usually associated with other antihypertensive therapy, e.g. postural effects, failure of ejaculation, diarrhoea. Mental and physical lethargy is not a problem with Trascor, many patients reporting an increased sense of well-being.

Trascor protects the cardiovascular system from excess adrenergic discharge and the resulting elevation of catecholamine levels, which are a known risk factor in coronary heart disease and which, in the long term, may contribute to the secondary effects of hypertension.

Trascor prevents emotional tachycardia during environmental stress. In anxiety, Trascor does not produce sedation or cause dependence. The best response is seen in patients who have not previously received benzodiazepines.

Product licence numbers

Trascor Tablets 20 mg 0008/0124

Trascor Tablets 40 mg 0008/0125

Trascor Tablets 80 mg 0008/0122

Trascor Tablets 160 mg 0008/0123

Trascor Ampoules 2 mg 0008/5068

TRASIDREX ▼

Presentation Trasidrex tablets each contain 160 mg oxprenolol hydrochloride in a sustained release core and 0.25 mg cyclopenthiiazide in the coat. The tablets are circular, with a red sugar coat, and printed CIBA on one side and TRASIDREX on the other, both words in black.

Uses *Mode of action:* Trascor* (oxprenolol) is a non-selective beta-adrenergic receptor blocking drug with antihypertensive properties. It exerts a competitive and reversible blockade of the beta-adrenergic receptors, thereby protecting the cardiovascular system against excessive adrenergic stimuli, such as those produced by emotional stress and environmental factors. Oxprenolol also has partial agonist activity (PAA) also known as intrinsic sympathomimetic activity (ISA). This property means that some degree of stimulation of the beta receptors is maintained. Under conditions of rest this tends to counter-balance the negative chronotropic and negative inotropic effects of beta-blockade.

The gradual release of oxprenolol from a special sustained release core in Trasidrex prolongs its pharmacological action to 24 hours.

Navidrex* (cyclopenthiiazide) is a thiazide diuretic with sustained antihypertensive activity.

The combination of cyclopenthiiazide and a slow-release formulation of oxprenolol in a single tablet has a number of advantages:

1. Since oxprenolol and cyclopenthiiazide have different modes of antihypertensive activity their therapeutic actions are complementary.

2. Once daily dosage with the combination improves patient compliance.

3. Trascor inhibits the rise in renin caused by diuretics alone. Conversely Navidrex may be expected to improve the response in low renin hypertensives.

4. The addition of Navidrex to Trascor further reduces the minimal risk of cardiac failure.

Indications: In the treatment of mild and moderate hypertension.

Dosage and administration *Adults:* Initially 1 tablet daily, usually given in the morning. Most of the antihypertensive effect of the combination is achieved within two to three days. If necessary, the dose can be increased to 2 or more tablets given once daily, until satisfactory blood pressure control is achieved. Most patients should respond to 1 or 2 tablets.

Trasidrex can be successfully combined with other single antihypertensive drugs having a different pharmacological effect. In particular, a free combination with a vasodilator will often be beneficial.

Contra-indications, warnings, etc *Side-effects:* Trasidrex is well tolerated. However dizziness, drowsiness, headache, insomnia, excitement and gastrointestinal disturbances may occur, particularly at the start of treatment. Like other beta-blockers, there have been isolated reports of bradycardia and thrombocytopenia.

As with other beta-blockers, bronchospasm, and heart failure may occasionally be precipitated in susceptible patients (see precautions) and exertional tiredness and feelings of coldness in the extremities have been reported on rare occasions. However, the incidence of these side-effects is low, possibly due to the partial protection afforded by the sympathomimetic effect of Trascor.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic blocking drugs. The reported incidence is small, and in most cases the symptoms have cleared when the treatment was withdrawn. Discontinuance of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-adrenergic blocker should be gradual.

Like other diuretics with a similar mode of action, cyclopenthiiazide may cause latent gout or latent diabetes mellitus to become manifest. In a few cases, allergic skin reactions, mild anorexia, nausea, constipation and diarrhoea have been reported. In common with other thiazides, there have been isolated reports of thrombocytopenia.

In contrast with other antihypertensive agents, Trasidrex does not cause postural hypotension, sedation or interference with sexual function.

Contra-indications: Trasidrex is contra-indicated in patients with atrio-ventricular block, marked bradycardia, uncontrolled heart failure and cardiogenic shock. Because of the cyclopenthiiazide content, it is contra-indicated in patients with marked renal insufficiency.

An antidiuretic effect has been reported following concomitant treatment with thiazide diuretics and lithium. As with all products which contain thiazide diuretics Trasidrex is contra-indicated during lithium treatment.

Pregnancy: Beta-blockers may cause bradycardia in the fetus, which can also persist after birth. During pregnancy, in the course of labour and during lactation beta-blockers should only be employed after the needs of the mother have been weighed against the possible risks to the fetus.

Precautions: If there is evidence of cardiac failure, this

must be controlled by digitalis before and during trasidrex therapy. Should the pulse rate fall below 50 per minute, treatment should be re-started at a lower dose, if feasible. Particular caution should be observed when treating asthmatics, chronic bronchitics or other individuals where bronchospasm may be provoked.

Trasidrex should be given cautiously to patients with metabolic acidosis or anaesthesia with ether or chloroform. For anaesthesia the agent selected should be one exhibiting as little negative inotropic activity as possible e.g. halothane, nitrous oxide.

Treatment with a beta-blocker is liable to mask the symptoms of hypoglycaemia and also to affect carbohydrate metabolism. In patients with labile or insulin-dependent diabetes in particular, it may therefore be necessary to readjust the dosage of anti-diabetic medication. Navidrex, a thiazide diuretic, may also decrease glucose tolerance.

Like other beta-blockers, Trasidrex should not be given in combination with calcium-antagonists of the verapamil type, because their concomitant use may result in bradycardia, hypotension or even cardiac arrest.

As with other beta-blocking drugs, sudden withdrawal of treatment with Trasidrex may induce severe and continuous angina. Patients should, therefore, be advised to avoid interruption of established therapy and if withdrawal becomes necessary it should be done gradually.

Because of its Navidrex content, Trasidrex should be used with care in patients with some degree of renal impairment, as a rise in blood urea can occur and in extreme cases result in an oliguric crisis.

During long-term treatment with Trasidrex, salt restriction is unnecessary.

The potassium sparing action of Trasacor may obviate the necessity of giving potassium supplements to counter the effects of the thiazide.

Treatment of overdosage: Overdosage with Trasidrex may lead to excessive bradycardia, hypotension, coma and convulsions. It should also be noted that severe toxicity may develop rapidly and that there may be severe hypotension and bradycardia despite a normal C.G. For sinus bradycardia and hypotension 0.5–2.0 mg of atropine should be administered slowly by intravenous fusion. If this does not raise the heart rate sufficiently isoprenaline may be necessary. The dose of isoprenaline needs to be sufficient to reverse the blockade and should be assessed by the clinical response. A reasonable starting dose would be 25 mcg of isoprenaline hydrochloride.

In severe cardiogenic shock the treatment of choice appears to be glucagon. The initial dose should be 5–10 mg intravenously, further boluses or an infusion can be used according to the patient's condition. Transvenous pacing has been used, sometimes with success. If bronchospasm develops bronchodilators should be used. Patients should be monitored for several days as the beta-blocking effects of Trasidrex exceed its plasma half-life. Because Trasidrex is a slow-release formulation, it is likely that the effects of overdosage will be more persistent than following conventional oxprenolol. Further information may be obtained from CIBA Laboratories, Horsham.

Pharmaceutical precautions The tablets should be protected from heat, light and moisture.

Legal category POM.

Package quantities Cartons of 28 tablets consisting of two reminder calendar foils of 14 tablets (each carton of 28 represents two to four weeks' treatment depending on whether dosage is 1 or 2 tablets daily).

Further information By combining a beta-blocker (Trasacor[®]) and a thiazide diuretic (Navidrex[®]) in a single tablet in a calendar pack, the management of hypertension can be greatly simplified for the majority of patients. Compliance will be improved and many of the pharmacological actions of the two components produce beneficial complementary effects.

Product licence number 0008/0138.

VARBIAN ▼

Presentation A clear, colourless solution containing 1 mg/1 ml prenalterol hydrochloride in 5 ml ampoules.

Indications: Varbian is indicated in adult patients who specifically require inotropic stimulation in the following conditions only: management of cardiac failure or hypotension associated with myocardial infarction, in open heart surgery, shock, or in the abolition or reduction of the cardiac effects of beta-adrenoceptor blockade.

Mode of action: Varbian is a β_1 -selective adrenoceptor stimulant. Varbian thus stimulates β_1 -receptors in the heart in doses which have no significant effect on β_2 -receptors in the lungs and blood vessels. Varbian has a more pronounced effect on cardiac contractility than on heart rate. Cardiac output increases mainly as a result of increased stroke volume. An increase of heart rate may be seen. Varbian increases the systolic blood pressure with little or no effect on diastolic pressure. Since Varbian rapidly reverses the haemodynamic effects of β -blockers, the compound may be used to abolish or reduce the cardiac action of β -blockers where this is desirable.

Dosage and administration 1. To abolish or reduce the cardiac effects of β -adrenoceptor blockade, Varbian should be given in doses of 2–5 mg i.v. Varbian should be administered cautiously, generally over a 5-minute period depending on the acuteness of the situation. The optimal effect of each dose is generally achieved within 2–5 minutes, after which further doses may be given to a maximum of 20 mg total. Larger doses of Varbian may be necessary in patients who have taken β -adrenoceptor blocking agents in excess of the recommended dose.

2. For the management of cardiac failure or hypotension associated with myocardial infarction, in open heart surgery, or shock, Varbian should be given by slow intravenous infusion, at a rate of 0.5 mg/minute. However, the rate of administration and duration of therapy should be adjusted according to the patient's response as determined by heart rate, blood pressure and, if possible, cardiac output. The maximum total dose used in clinical trials has been 20 mg.

Contra-indications, warnings, etc *Side effects:* Palpitations and nervousness may occur. Isolated ventricular ectopic beats have been observed. In some patients with a history of angina pectoris Varbian has caused an increase in anginal attacks.

Precautions: Hypovolaemia should be corrected before giving Varbian. Varbian should be used with caution in patients with angina pectoris and recent myocardial infarction (during the first 6 weeks post-infarct). Varbian should be used with caution in patients with hypokalaemia. Patients with uncontrolled or insulin-dependent

diabetes should be kept under careful observation. Varbian should be used with great caution in patients with obstructive subvalvular cardiomyopathy, as inotropic agents may exacerbate the obstruction to flow in these patients.

If an excessive increase in blood pressure or heart rate occurs and it is desired to counteract the effects of Varbian, a β -adrenoceptor blocking agent should be given intravenously.

Pregnancy: Animal toxicity studies at high doses have indicated an increased occurrence of foetal abnormalities of the thoracic cage and cardiovascular system. However, the significance of this in man is uncertain. Nevertheless, benefit-risk should be considered before administering Varbian to pregnant women or women of child-bearing potential.

Contra-indications: Varbian should not be given to patients with serious ventricular arrhythmias.

Treatment of overdose: In the event of overdose,

the infusion should be discontinued. Symptomatic measures, combined if necessary with the cautious intravenous administration of a β -adrenoceptor blocking agent, should be employed.

Pharmaceutical precautions Recommended diluents are: sterile saline, Ringer's or 5.0% anhydrous glucose solution.

Legal category POM.

Package quantities Packs of 1 ampoule.

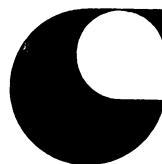
Further information Varbian has a half-life in plasma of about 2 hours. Varbian is excreted mainly via the kidneys and 60% of the dose is recovered in the urine as unchanged drug after intravenous administration in healthy subjects.

Product licence number 0008/0150

***Trade Mark**

Concept Pharmaceuticals Limited

Russell House
59/61 High Street
Rickmansworth, Herts WD3 1EZ



BARITOP* 100

Presentation White suspension containing Barium sulphate BP 100% w/v.

Uses X-ray contrast medium for radiography of the gastro-intestinal tract.

Dosage and administration The volume of Baritop 100 used will depend on the procedure and technique involved. The following dosages represent a basic guide to the quantities suitable for routine examinations:

Barium swallow	40–60 ml
Double-contrast examination of stomach and duodenum	100–150 ml
Follow-through examination of small bowel	150–300 ml
Barium enema	200–300 ml
	diluted with 600–900 ml water

Contra-indications, warnings, etc Suspected perforation of the gastro-intestinal tract. Caution should be exercised if the possibility of a lower small-bowel obstruction exists.

Pharmaceutical precautions Store in a warm place.

Legal category P.

Package quantities Sealed cans of 300 ml with 'ring-dill' opening.

Further information Baritop 100 contains carbon dioxide gas under pressure which is fully liberated at body temperature, providing a double contrast potential of its own for certain procedures. This unique property allied to excellent fluidity so that the suspension is capable of demonstrating exceptionally fine detail in the gastro-intestinal tract.

Product licence number 0603/5000.

BARITOP* EFFERVESCENT TABLETS

Presentation White tablets each containing:

Sodium Bicarbonate BP	35 mg
Calcium Carbonate BP	5 mg
Ascorbic Acid BP	35 mg
Methicone BPC	3 mg

Uses Supplementary gas-producing agent for double-contrast radiography of the gastro-intestinal tract.

Dosage and administration Twenty–thirty tablets for examination. The tablets should be swallowed with little water or barium suspension at the beginning of the examination. Ideally the tablets should be used in conjunction with a technique in which the stomach wall is 'washed' with the barium suspension by rolling the patient from side to side. The tablets should be swallowed as a single dose. Release of the gas will be proceeding while the patient is being turned from side to side and the full

volume will be available by the time the series of films is commenced.

The films should be taken as rapidly as possible after 'washing' the stomach wall, and it is essential for the patient to retain the gas in the stomach. The patients should, therefore, always be instructed to suppress eructation, at least until the series of films has been completed.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Store in a cool, dry place.

Legal category P.

Package quantities Supplied in containers of 500 tablets.

Further information Baritop Effervescent Tablets contain a defoaming ingredient to prevent excessive bubble formation during release of the gas. This reduces the possibility of mucosal detail being obscured by barium foam.

Product licence number 0603/0014.

BARITOP* G POWDER

Presentation White granular powder containing 97% Barium Sulphate BP.

Uses X-ray contrast medium for radiography of the gastro-intestinal tract.

Dosage and administration Baritop G powder may be used to prepare barium suspensions of any required concentration.

It should be used when a concentration greater than that of the ready-made barium suspensions is required for visualisation of the upper GI tract, or when a slightly more viscous preparation is required for a barium swallow.

The powder is intended particularly for barium enemas, which may be mixed to the preferred concentration.

The following volumes and concentrations of suspension prepared from Baritop G Powder represent a basic guide for standard procedures, but may be varied according to individual preference.

	<i>Volume</i>	<i>Concentration</i>
Double contrast examination of stomach and duodenum	100–200 ml	100–150% w/v
Barium swallow	40–50 ml	130–150% w/v
Follow through examination of small bowel	300 ml	70–110% w/v
Barium enema (double contrast)	400–500 ml	70–150% w/v

Measure the quantity of water indicated on the pack to produce the required concentration, add the contents of the sachet, and stir or shake to give a smooth suspension.

Contra-indications, warnings, etc Suspected perforation of the gastro-intestinal tract.

Caution should be exercised if the possibility of a lower small-bowel obstruction exists.

Pharmaceutical precautions Store under dry conditions.

Legal category P.

Package quantities Sachets containing 200 g and 1 kg of powder.

Further information Nil.

Product licence number 0603/0020.

ELUDRIL* MOUTHWASH

Presentation Clear red solution containing:

Chlorhexidine digluconate	0.1% w/v
Chlorbutol	0.1% w/v
Chloroform	0.5% v/v

Uses For local treatment of the mouth and throat in conditions such as gingivitis, stomatitis, aphthous and dental ulcers, tonsillitis, pharyngitis and minor infections of the mouth and throat.

After operative or dental procedures in the mouth or throat, and for general oral hygiene.

Dosage and administration 10 ml in half a glass of lukewarm water used as a mouthwash or gargle three or four times a day.

Not suitable for use in infants.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Bottles of 90 ml and 500 ml.

Further information Nil.

Product licence number 0603/0012.

ELUDRIL* SPRAY

Presentation Clear solution in pressurised spray containing:

Chlorhexidine digluconate	0.05% w/v
Amethocaine hydrochloride	0.015% w/v

Uses For local treatment of the mouth and throat in conditions such as gingivitis, stomatitis, aphthous and dental ulcers, tonsillitis, pharyngitis and minor infection of the mouth and throat. As adjuvant treatment in Vincent's angina and oral thrush. Also after operative or dental procedures in the mouth or throat, and for general oral hygiene.

Dosage and administration For routine use spray the mouth and throat three or four times a day.

For treatment of acute conditions the spray may be used up to once an hour.

When swallowing is painful, spray the throat thoroughly a few minutes before eating.

The spray bottle should be shaken before use, and the end of the nozzle positioned just inside the mouth. Direct the spray towards the affected area of mouth or throat and activate the spray for two or three seconds.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Spray contains 55 ml of solution

Further information Nil.

Product licence number 0603/0013.

* Trade Mark

Consolidated Chemicals Limited

The Industrial Estate

Wrexham

Clwyd LL 13 9PS

PP* STOMACH POWDER AND TABLETS

Presentation Available as a white powder and a plain tablet 12 mm in diameter.

Powder: Contains in 100 g:

alium Carbonate BP	37.82%
lagnesium Carbonate BP	37.50%
lagnesium Trisilicate BP	19.48%
ismuth Carbonate BP	2.00%
el. Alum. Hydrox. BP	3.00%
apaverine Hyd. BP	0.10%
omatropine Methyl Bromide USP	0.10%

Tablets: Each tablet contains:

alium Carbonate BP	180.5 mg
lagnesium Carbonate BP	195.0 mg
lagnesium Trisilicate BP	92.5 mg
ismuth Carbonate BP	12.5 mg
el. Alum. Hydrox. BP	15.0 mg
apaverine Hyd. BP	3.0 mg
omatropine Methyl Bromide USP	1.5 mg

Uses Dyspepsia, flatulence, nervous dyspepsia, excess acidity, heartburn biliousness, travel sickness, gastric and intestinal spasms, biliary colic, nausea and vomiting, peptic ulcer syndrome.

Dosage and administration *Powder:* 1 × 5 ml (teaspoonful) in water or milk three or four times a day.

Tablets: 1-2 tablets three or four times daily after meals.

Contra-indications, warnings, etc Glaucoma, myasthenia gravis.

Pharmaceutical precautions None.

Legal category POM.

Package quantities *Powder:* Cartons 100 g.

Tablets: Cartons of 50 and 250.

Further information Nil.

Product licence numbers

Powder 0183/5033

Tablets 0183/5013

ARDIACAP*

Presentation Slow-release capsules. Each capsule contains pentaerythritol tetranitrate (PETN) 30 mg. Blue/yellow capsule SC21 size 2 containing white and cream granules.

Uses Sustained relief in angina pectoris.

Dosage and administration One capsule to be taken every 12 hours.

Contra-indications, warnings, etc Glaucoma; should not be used in acute stages of myocardial infarction.

Pharmaceutical precautions None.

Overdosage: Treat by gastric lavage.

Legal category P.

Package quantities 30 and 200 capsules.

Further information Timed release base that provides for prolonged therapeutic effect for about 12 hours. Release pattern by diffusion.

Product licence number 0183/5018.

DEANASE*

Presentation Injectable pancreatic desoxyribonuclease as a lyophilised, white sterile, stable powder synergised with magnesium ions in vials of 1 mega and ½ mega.

Uses Haematoma, haemothorax, haematocele, mammary infections (acute puerperal mastitis) gravitational (varicose) ulcers, pressure or decubitus ulcers, other subacute or chronic ulcers, subacute cellulitis or thrombophlebitis, infected burns.

Tuberculous abscess of neck, dental abscess, intra-peritoneal abscess (subphrenic appendiceal, pelvic abscess), amoebic abscess of liver, osteomyelitis, actinomycosis, meningitis, bronchitis, unresolved pneumonia, chronic bronchial asthma, cystitis (purulent) or blood clots in bladder, virus infections (DNA) used in conjunction with cytotoxic drugs, antibiotic and radiation. In treatment of cancerous tumours. Lymphatic leukaemia.

Dosage and administration *Local therapy:* Local injection into a haematoma or superficial abscess cavity – 1,000,000 units in 2-3 ml of sterile isotonic saline. Intrathecal injection for meningitis – 1,000,000 units in 5 ml sterile isotonic saline repeated in two days as required.

Pre-urethral instillation for purulent cystitis or clots in the bladder – 1,000,000 units in 50 ml sterile water together with intramuscular systemic therapy. Aerosol inhalation spray for viscid sputum – 250,000 units in 10 ml sterile water repeated twice daily.

Systemic therapy: Is indicated in most of the above conditions and is given by intramuscular injection every second day, as required. An intramuscular injection of 1,000,000 units is effective over a period of 48 hours. In certain cases where an immediate effect is required it can be given intravenously.

Contra-indications, warnings, etc No untoward reactions have been observed in the use of this enzyme, even when injected in massive doses either systemically or locally, but possible sensitivity to beef protein should be borne in mind after a prolonged use.

Pharmaceutical precautions Store in a refrigerator at 4°C.

Under these conditions it will retain its activity for approximately two to three years. In solutions it loses its activity unless frozen. Solutions for injection should therefore be prepared at the time of use.

Legal category POM.

Package quantities $1 \times \frac{1}{4}$ million unit vial. 1×1 million unit vial + solvent.

Further information Deanaase hydrolyses highly polymerised desoxyribonucleic acid, which is chiefly responsible for the viscosity of purulent fibrinous exudates of which it forms from 30 to 70%. Its activity per unit weight is considerably greater than more commonly known enzymes.

Deanaase liquefies a) clotted blood and b) fibrinous and viscid purulent exudates following trauma or inflammation. These accumulations thereby become more readily absorbed or more fluid in consistency for easier aspiration or freer drainage. Deanaase readily removes the exudate so often resistant to the passage of antibiotics. While the absorption of a haematoma, superficial infection, or deep suppurative process may occur with Deanaase alone, resolution is often aided by preliminary antibiotic therapy and may require subsequent surgical intervention (e.g. aspiration or drainage).

Product licence number 0183/5028.

DEANASE* DC TABLETS

Presentation White, oval, enteric-coated tablet containing 10 mg of delta-chymotrypsin.

Uses In the control and reduction of inflammation in a variety of clinical conditions, e.g.:

Respiratory diseases – bronchitis, bronchiectasis, sinusitis, hay fever. Deanaase DC Oral also effectively reduces the viscosity of sputum in bronchial patients.

Trauma – contusions, haematomas, wounds, post-partum tissue reactions, sprains, fractures.

Phlebitis and thrombophlebitis.

Chronic ulcers – varicose, diabetic.

Inflammation of the eye – conjunctivitis, intra and extraocular trauma.

Inflammation following surgery – cellulitis, ulcerations, plastic surgery.

Dosage and administration Two tablets twice daily for three days and 1 tablet twice daily as maintenance dose.

Contra-indications, warnings, etc No known reaction reported, but protein sensitisation similar to pollen allergy cannot be entirely disregarded.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities 16 and 200 tablets.

Further information Delta-chymotrypsin has approximately 50% greater activity than the more common alpha-chymotrypsin and therefore is markedly more effective in its anti-inflammatory action.

Product licence number 0183/5010.

DELIMON* TABLETS

Presentation Analgesic with marked anti-inflammatory activity. Flat, round, white tablet. Each tablet contains:

Morazone (2:3 Dimethyl-4- (3-methyl-2-phenyl morpho- linomethyl)- 1-phenylpyrazol-5-ONE hydrochloride)	0.15 g
Paracetamol	0.05 g

Uses The preparation is recommended in those more painful states, irrespective of cause, which are commonly treated with analgesics containing alkaloids, barbiturates or even opiates; also in influenza, headache (common colds, etc), menstrual pain, local pain (surgery), muscular or arthritic pain or rheumatism, and migraine, etc.

Dosage and administration Normally $\frac{1}{2}$ –1 tablet, if necessary several times daily; in cases of severe pain (injuries) correspondingly higher doses.

Contra-indications, warnings, etc None known.

Overdosage: Should be treated with gastric lavage followed by administration of L-methionine.

N.B. Patients may appear well for 2-3 days before developing signs of liver damage from paracetamol overdosage.

Pharmaceutical precautions None.

Legal category POM.

Package quantities Tube of 12 tablets. Dispensing pack of 200 tablets.

Further information Contains no codeine or other alkaloid, no barbiturates, and no phenacetin or caffeine. Reduces the requirement of opiates. Well tolerated by mouth, and suitable for the symptomatic treatment of pain arising in gastro-intestinal tract and biliary apparatus.

Product licence number 0183/5011.

ENTEROMIDE* TABLETS

Presentation White tablet containing 500 mg of calcium 2-(4-(hydroxymethyl)-lureido-sulphonyl phenylcarbamoyl) benzoate. The approved name is calcium sulphaloxate. A round, flat tablet 12 mm in diameter.

Uses Summer diarrhoea in children and adults, bacterial dysentery, enteritis, colitis, food poisoning, pre-operative bowel sterilisation, 'Tourist Tummy', prophylactic against intestinal infections in tropical countries.

Dosage and administration *Adults and teenagers* 3×2 tablets daily.

Children: 3×1 tablet daily.

Infants: $3 \times \frac{1}{2}$ tablet daily.

In serious infections these doses can be doubled.

Contra-indications, warnings, etc Sulphonamide sensitivity. If administration is prolonged, white blood cell count must be checked.

Overdosage: Gastric lavage. High fluid intake.

Pharmaceutical precautions None.

Legal category POM.

Package quantities 25 and 200 tablets.

Further information Enteromide exerts both a bactericidal and bacteriostatic action. Approximately 95% of the ingested Enteromide remains unabsorbed in the intestine, thus exerting maximum concentration at the site of the infection.

Product licence number 0183/5008.

ERROCAP* CAPSULES

Presentation Capsules containing time-release granules. Each capsule contains:

Errorous fumarate 330 mg

(equiv. 110 mg elemental iron)

Vitamin B1 5 mg

Green/orange capsule size 0 containing brown and white granules.

Uses Ferrocap Capsules are recommended for treatment of anaemia from iron deficiency or blood loss, especially chronic haemorrhages, such as bleeding ulcers, haemorrhoids and some gynaecological disorders, and in all cases where dietary iron supplementation is desired.

Dosage and administration One capsule daily.

Contra-indications, warnings, etc None known.

Overdosage: Induce vomiting; gastric lavage. Parenteral administration of desferrioxamine mesylate 2 g and then leave 5 g of desferrioxamine in 100 ml of fluid in the stomach.

Pharmaceutical precautions None.

Legal category P.

Package quantities 20 and 200 capsules.

Further information Ferrocap releases its active principle by diffusion rather than disintegration. This patent process ensures constant release over four hours and is independent of pH, enzymatic activity and agitation.

Product licence number 0183/5014.

ERROCAP*-F 350 CAPSULES

Presentation Capsules containing time release granules. Each capsule contains:

Errorous fumarate

(equivalent 110 mg elemental iron)

330 mg

olic acid 350 mcg

Standard pink capsule size 0 containing brown, white and yellow granules.

Uses Ferrocap-F 350 Capsules are recommended in the management of anaemia in pregnancy. For folate deficiency and where iron intolerance is a factor.

Dosage and administration One capsule daily.

Contra-indications, warnings, etc None known.

Overdosage: Induce vomiting; gastric lavage. Parenteral administration of desferrioxamine mesylate 2 g and then leave 5 g of desferrioxamine in 100 ml of fluid in the stomach.

Pharmaceutical precautions None.

Legal category POM.

Package quantities 30 and 200 capsules.

Further information Ferrocap-F 350 releases its active principle by diffusion rather than disintegration. This patent process ensures constant release over four hours and is independent of pH, enzymatic activity and agitation.

Product licence number 0183/5017.

FLAR* CAPSULES

Presentation White opaque No. 2 hard gelatine capsule containing:

Selected lactic-ferments (see specification below) 5 billion.

Vitamin B₁ 5 mg

Vitamin B₂ (riboflavin) 0.5 mg

Vitamin B₆ (pyridoxine) 0.5 mg

Vitamin B₁₂ (cyanocobalamin) 5 mcg

PP (nicotinamide) 20 mg

Sodium pantothenate 7.5 mg

Inositol 20 mg

Folic acid 200 mcg

Liver extract from 20 g fresh liver

Inert excipient to 200 mg

The selected lactic ferments totalling 5 billion consist of *Streptococcus lactis* and *Lactobacillus acidophilus* taken from special strains that are resistant to the principal antibiotics and chemotherapeutics; such as penicillin, streptomycin, Chloramphenicol, erythromycin tetracyclines, aureomycin and sulphonamides, alone or in combination.

Uses Where lactic ferments are required.

Enteritis, gastro-enteritis, colitis, enterocolitis, dyspepsia, chronic constipation, intestinal putrefaction, diarrhoea, intestinal detoxication and certain diseases of the skin, such as urticaria, eczema and acne. Is most helpful where prolonged antibiotic treatment is necessary.

Dosage and administration *Children:* 1 capsule before each meal; in severe cases increase to 2.

Adults: 1-2 capsules before each meal; double dosage in severe cases.

Contra-indications, warnings, etc None known.

Pharmaceutical precautions Store in cool place.

Legal category POM.

Package quantities 10 and 200 capsules.

Further information In addition to said classical indications, and by virtue of its unique formulation, Flar is specifically suggested for the prevention and management of antibiotics or chemotherapeutic induced untoward side-effects, notably, states of weakness and adynamia, anaemia, atrophic mucosal lesions, black tongue, fissures, atrophic gastritis and nutritional deficiencies during treatment with antibiotics.

Product licence number 0183/5016.

FOSFOR* SYRUP

Presentation Phosphorylcolamine 5% w/v in a pink, raspberry-flavoured, sugar syrup.

Uses Promotes anabolic processes of metabolism and is therefore useful in convalescence from illness or surgery and in debilitating or wasting diseases. Improved metabolism leads to increased appetite and sense of well-being, helps counteract depression and lassitude and the return of normal sleep pattern, acute and chronic hepatitis.

Dosage and administration *Adults:* 4 × 5 ml dose (1 tablespoonful). Three times daily.

Children: 2 × 5 ml doses (1 dessertspoonful). Three times daily.

Contra-indications, warnings, etc None known.

Pharmaceutical precautions None.

Legal category GSL.

Package quantities Bottles of 200 ml and 5 litres.

Further information Phosphorylcolamine is an amino acid with a high phosphorus content, easily assimilated, present as a natural product of cellular metabolism.

Product licence number 0183/5006.

FOSFOR* INJECTION

Presentation 10 ml ampoule, 25% w/v sodium phosphorylcolamine.

Uses Addition to parenteral drip in preventing post-operative body weight loss and enhancing the recovery of general well-being after surgery. In acute Liver disease, hepatic conditions and such symptoms as asthenia, anorexia and nausea.

Dosage and administration Single doses 20 ml (i.e. 5 gm) by intravenous injection. The injection to be administered daily or every other day for a period of two to three weeks, a course of 10-20 injections.

Contra-indications, warnings, etc None known.

Pharmaceutical precautions Solutions of Calcium/magnesium salt can cause precipitation.

Legal category POM.

Package quantities Boxes 5 × 10 ml ampoules. Boxes 50 × 10 ml ampoules.

Further information Phosphorylcolamine is an amino acid with a high phosphorus content.

Product licence number 0183/5027.

Mn	22.600
mw	30.000
Relative viscosity at 37°C	1.9
Iso electric point	4.5 ± 0.3
pH value of the solution	7.4 ± 0.3
Colloid osmotic	465 mm H ₂ O
Pressure	35.2 mm Hg
Gel point	0°C

Uses Gelofusine increases the circulatory volume over a sustained period of time in cases of acute blood and fluid losses (circulatory collapse, hypovolemic shock). The prolonged expanding effect suffices in most cases to allow the resumption of normal blood regeneration. The gelatine is metabolised through proteolysis and eventually excreted. It has no antigenic properties and does not influence haemostasis.

Acute blood losses, treatment of surgical and traumatic shock (vascular atony), burns and in cases of hypovolemia due to transfer of plasma into tissues (damaged capillary walls caused by infectious diseases) or increased fluid loss (diarrhoea, vomiting). In critical blood losses (exceeding approx. one-third of the total blood volume) until whole blood can be administered.

Dosage and administration Control bleeding first. The quantity to be administered depends on requirement; and blood losses: administer by drip infusion. In urgent cases administer 500 ml within 10-15 minutes to adults and children weighing more than 25 kilos.

Contra-indications, warnings, etc Repeated minor bleeding, as in cases of gastric or duodenal ulcer, or similar chronic blood loss, calls for blood transfusions, as no hypovolemia is involved.

Pharmaceutical precautions Use only sterile infusion appliances, preferably disposable sets.

It is not recommended to mix with blood or plasma. Use only clear solutions from sealed containers.

Legal category POM.

Package quantities Infusion bottle of 500 ml. Pack of 10.

Further information Water-soluble, injectable medicament can if necessary be administered simultaneously with Gelofusine.

Preparations which should take immediate effect, such as analeptics, haemostatic agents, glucose solutions should be injected directly through the rubber section of the infusion tube. Preparations which are better tolerated in dilute form, such as gas gangrene antiserum, streptanin, circulatory agents, water-soluble vitamins should be injected into the solution through the rubber stopper mixed thoroughly.

Product licence number 0183/5025.

GELOFUSINE*

Presentation 4% Gelatin in Normal Saline.

Succinyl gelatin	20.0 g/500 ml
Na ⁺ content	77 mmol/500 ml
K ⁺ content max	0.2 mmol/500 ml
Mg ⁺⁺ content max	0.2 mmol/500 ml
Ca ⁺⁺ content max	0.2 mmol/500 ml
Cl ⁻ content max	62.5 mmol/500 ml

HEPACON* B FORTE INJECTION

Presentation 2 ml ampoules liver extract 15 mcgr B₁₂, vitamin B, pyrophosphate 50 mg, folic acid 2.5 mg

Uses Defective formation and maturation of red cell. Pernicious anaemia, etc.

Dosage and administration General tonic 2 ml every four days until red blood count is maintained. Anaemia intramuscular injection of 2 ml every day for the first

week, then decreasing doses every two weeks for several months. Permanent maintenance treatment is needed in pernicious anaemia.

Contra-indications, warnings, etc Sensitivity to protein.

Pharmaceutical precautions Store in cool place.

Legal category POM.

Package quantities Boxes 50 × 2 ml and 6 × 2 ml.

Further information In all conditions where a tonic is indicated. In pernicious anaemia. Secondary anaemia following severe diseases and loss of blood.

Product licence number 0183/5023.

HEPACON* B₁₂

Presentation 1 ml ampoules of vitamin B₁₂ 50, 100, 500 or 1,000 mcg per 1 ml.

Uses Pernicious anaemia, (Addisonian) anaemia, macrocytic anaemia of sprue (tropical and non-tropical), macrocytic nutritional anaemia, megaloblastic anaemia of infancy (certain cases), neurological symptoms of pernicious anaemia and neuropathies.

Dosage and administration *In anaemia:* Therapy is initiated with injections of 15-30 mcg once or twice per week, depending upon the nature and severity of the case and the response of the patient. For maintenance, injections of 15-30 mcg may be given at intervals of 15-30 days, or as indicated.

In neurological disturbances: 1,000 mcg, daily decreasing as improvement is noted, or as determined by the physician.

Contra-indications, warnings, etc None.

Pharmaceutical precautions None.

Legal category POM.

Package quantities Boxes 6 × 1 ml, 50, 100, 500 or 1,000 mcg.

Further information Nil.

Product licence number 0183/5022.

HEPACON* LIVER EXTRACT

Presentation Ampoules 2 ml in strengths of 5, 10, 15, 50 or 1,000 mcg B₁₂.

Uses Pernicious anaemia, tropical sprue, pellagra, tropical macrocytic anaemia, anaemia of pregnancy, fish tapeworm anaemia, gastric carcinoma or resection, hepatitis cirrhosis and chronic intestinal disease with protracted diarrhoea. Convalescence and general weakness.

Dosage and administration 1/2 ampoules administered intramuscularly.

Contra-indications, warnings, etc Possible protein sensitivity.

Pharmaceutical precautions Store in cool place.

Legal category POM.

Package quantities Boxes 50 × 2 ml and 6 × 2 ml.

Further information Nil.

Product licence number 0183/5019.

HEPACON*-PLEX VITAMIN B COMPLEX

Presentation Ampoules 2 ml

Vitamin B ₁	100 mg
Vitamin B ₂	2 mg
Vitamin B ₆	5 mg
Vitamin B ₁₂	8 mcg
Nicotinamide	150 mg
Calcium pantothenate	10 mg

Uses Vitamin B complex deficiencies, neuropsychiatric diseases, gastro-intestinal diseases, cutaneous diseases of nutritional origin, etc.

Dosage and administration 1/2 ampoules intramuscularly as required.

Contra-indications, warnings, etc None.

Pharmaceutical precautions Store in cool place.

Legal category POM.

Package quantities Boxes 50 × 2 ml and 6 × 2 ml.

Further information Nil.

Product licence number 0183/5021.

MINAMINO* COMPOUND SYRUP

Presentation Pleasant palatable syrup. Each 100 ml contains:

Biologicals:

Liver extract from	70 g fresh liver
Spleen extract from	15 g fresh spleen
Gastric mucosa extract from	7 g fresh gastric mucosa

Vitamins:

Vitamin B ₁	300 mg
Vitamin B ₂	40 mg
Vitamin B ₆	35 mg
Vitamin PP	400 mg
Vitamin B ₁₂	100 mcg

Amino acids: 2,000 mg of which the following are present. Typical analysis: histidine 175 mg, Arginine 140 mg, methionine 73 mg, tryptophane 84 mg; threonine 136 mg, tyrosine 150 mg, glutamic acid 207 mg, aspartic acid 46 mg, proline 14 mg, glycine 53 mg; alanine 85 mg, valine 102 mg, phenylalanine 153 mg, isoleucine 74 mg, leucine 306 mg, lysine 194 mg.

Minerals:

Iron citrate	410 mg
Manganese sulphate	1.7 mg
Copper sulphate	2.8 mg
Flavoured excipient to	100 ml

Uses As a vitamin and mineral supplement in geriatrics and paediatrics, delayed growth in children, during convalescence following surgery or infectious diseases and recovery from burns, influenza and colds. During corticosteroid therapy, physical and mental exhaustion. During pregnancy and lactation.

Dosage and administration *Children:* 2 × 5 ml in water three times daily.

Adults: 4 × 5 ml three times daily.

Contra-indications, warnings, etc None known.

Pharmaceutical precautions None.

Legal category POM.

Package quantities Bottles of 100 ml and 500 ml.

Further information Nil.

Product licence number 0183/5003.

NU-K*

Presentation Pale Blue opaque hard gelatin capsule size 0 containing 600 mg potassium chloride BP equiv. to 315 mg K or approx. 8 mEq of K⁺, in slow release granules.

Uses Treatment or prevention of potassium depletion or hypokalaemia from any cause eg. prolonged treatment with diuretics (especially thiazides or frusemide) or corticosteroids, cirrhosis, malabsorption, conditions associated with chronic diarrhoea.

Dosage and administration Dosage depends on the degree of potassium depletion. In most patients one to six capsules per day, preferably one at a time after food. It should be remembered that the degree of depletion of tissue potassium is not accurately reflected by the serum potassium level.

Contra-indications, warnings, etc Obstruction of the alimentary tract, advanced renal failure and conditions associated with hyperkalaemia, such as untreated Addison's disease, are all contra-indications. The risk of gastro-intestinal irritation or ulceration inherent in oral administration of potassium preparations is minimised by the mode of action of the time release granules, but the occurrence of symptoms of obstruction or ulceration indicates withdrawal of oral potassium preparations. In the presence of impaired renal function, or when potassium-sparing diuretics are used, the serum potassium level should be monitored to adjust dosage.

Overdosage: Treatment should be directed to the removal of ingested material by induced emesis or gastric lavage as appropriate. Fluid intake and output should be monitored and measures directed to the restoration of fluid and electrolyte balance. Measures to combat hypotension should be taken if required.

Pharmaceutical precautions Store in a cool place.

Legal category GSL.

Package quantities 500 capsules.

Further information Nil.

Product licence number 0183/0018.

OTOTRIPS* EAR DROPS

Presentation Vial with dropper containing:

Polymixin B sulphate	16,000 i.u.
Bacitracin	20,000 i.u.
Crystalline trypsin	25,000 NF. units
Sodium chloride	27 mg
Gelatin	15 mg

One ampoule distilled water

Uses All forms of bacterial ear infections. Acute inflammatory conditions of middle and external ear.

Dosage and administration Three to four drops instilled into ear three times daily.

Contra-indications, warnings, etc Allergy to Polymixin or Bacitracin

Pharmaceutical precautions Store in cool place.

Legal category POM.

Package quantities One box with vial, dropper and ampoule solvent.

Further information Nil.

Product licence number 0183/5000.

PLEX-HORMONE* INJECTION

Presentation A sterile solution for injection. Each 1 ml contains:

Testosterone propionate	20.0 mg
Desoxycorticosterone acetate	0.5 mg
Oestradiol benzoate	0.1 mg
Tocopheryl acetate (vitamin E)	20.0 mg

Uses Deficiency of male hormone – decreased potency; male androgen deficiency; pituitary deficiency.

Dosage and administration 2-3 injections weekly for two weeks followed by 1 injection weekly for three weeks. Maintenance dosage: 1 injection weekly.

Contra-indications, warnings, etc Contra-indicated in prostatic carcinoma, and in ischaemic heart disease.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities 6 × 1 ml box.

Further information Nil.

Product licence number 0183/5024.

PLEX-HORMONE* TABLETS

Presentation Each tablet contains:

Methyl testosterone	5 mg
Desoxycorticosterone acetate	0.5 mg
Ethinyl oestradiol	0.002 mg
Tocopheryl acetate (vitamin E)	5 mg

Uses Deficiency of male hormone – decreased potency; male androgen deficiency; pituitary deficiency.

Dosage and administration Should a rapid and intensive effect be needed for only a short period, 4-5

tablets daily for 10 days will be sufficient. The same course to be repeated when necessary, leaving at least 10-day intervals between courses.

Should an intensive action be required over a prolonged period, begin with 4–5 tablets daily for a fortnight (60–70 tablets) followed by lower maintenance dosage.

Contra-indications, warnings, etc Contra-indicated in prostatic carcinoma, and in ischaemic heart disease.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Carton of 24 tablets.

Further information Nil.

Product licence number 0183/5020.

PROPER-MYL*

Presentation 1 box containing 10 ampoules and solvent. Each ampoule contains 10 million Lyophilised yeast cells equivalent to approximately 10 micrograms of dry protein.

Uses A properdin forming agent prepared from selected yeast, known to produce significant increases in the Gamma globulins associated with antibody functions and responses.

Multiple Sclerosis.

Neoplasm.

Radiation sickness and Infectious Diseases.

Dosage and administration Graduated dosage as per instruction leaflet.

Contra-indications, warnings, etc No contra-indications known.

Pharmaceutical precautions None.

Legal category POM.

Package quantities 1 box containing: 10 ampoules powder 'Proper-Myl' with 10 ampoules solvent.

Further information Nil.

Product licence number 0183/5001.

TACHOSTYPTAN* INJECTABLE HAEMOSTAT

Presentation Each 5 ml ampoule of cream coloured colloidal solution contains 2% w/v standardised thromboplastin extracted from brain tissue.

Uses Tachostyptan is indicated in not only the treatment but in the prophylaxis of haemorrhage arising from many medical and surgical conditions. It is of particular value before and after operations associated with oozing surfaces.

Medical: Blood diatheses associated with bleeding, e.g. leukaemia, Henoch's purpura, hypoprothrombinaemia, etc. Haematemesis or melaena due to oesophagitis, oesophageal varices, peptic ulcer, gastric erosion, ulcerative colitis, polyposis, carcinoma of alimentary tract, etc. Haemoptysis due to various causes. Acute pulmonary edema. Bleeding following administration of coumarin group of drugs during anticoagulant therapy.

Surgery: Especially operative procedures associated with much tissue trauma or oozing surfaces. Haemorrhage from ulcerating malignant surface lesions.

Dosage and administration The optimal therapeutic effect is obtained by slow intravenous injection. The haemostatic effect begins after several minutes and decreases gradually after four to five hours. Tachostyptan can also be injected locally into the tissue (e.g. tonsillectomy) or administered locally by swab in haemorrhage of easily accessible wounds. Especially advantageous is the combined simultaneous dosage by parenteral and local administration. It is difficult to be precise on dosage, single and daily dosage depend on the severity of haemorrhage. In general 1–2 × 5 ml ampoules are injected at intervals of three to four hours up to 12 ampoules. In severe haemorrhage the administration in an intravenous drip has been successful, 12 ampoules in 1,000 ml normal saline over a period of six hours. As a prophylactic measure in patients in whom post-operative bleeding is suspected 1–2 ampoules should be given prior to surgery. This is now routine practice with some surgeons. Even if large doses of Tachostyptan are given there is no danger of intravascular thrombosis. It can also be used locally for superficial bleeding surfaces. In cases of hypoprothrombinaemia and dicoumaril overdosage, it is administered with Vitamin K therapy.

Contra-indications, warnings, etc None known.

Pharmaceutical precautions None.

Legal category POM.

Package quantities Boxes of 6 × 5 ml ampoules. Hospital packs of 50 × 5 ml ampoules.

Further information The arrest of bleeding (haemostasis) is a complex physiochemical process which depends on two main factors: 1) clotting of the blood: 2) capillary retraction.

Tachostyptan acts in the same way as thromboplastin (thrombokinase) by shortening the clotting time. This action, however, is exercised only at the point of haemorrhage. It does not lead to thrombosis in the intravascular system. At the same time, it appears to have a local action on the capillaries by retracting them and reducing their permeability.

Product licence number 0183/5029.

UROMIDE* DRAGEES

Presentation A specifically synthesised sulphonamide for urinary tract infections. With an anaesthetic for the relief of pain. Each dragee of Uromide contains:

Sulphacarbamide	500 mg
Phenazopyridine hydrochloride	50 mg

Uses Infections of the descending urinary tract accompanied by pain, urethral burning or micturition difficulties (urethritis, cystitis, cystopyelitis). Infection prophylaxis in cases of instrumentation (catheterisation, cystoscopy). Follow-up treatment after urological operations.

Dosage and administration *Adults and teenagers:* 2 dragees (tablets) three times daily.

Children: 1 dragee (tablet) three times daily.

Infants: ½ dragee three times daily.

The unique shaped dragee is placed in the mouth and swallowed with a little water.

Contra-indications, warnings, etc The phenazopyridine hydrochloride content of the product demands that a daily dose of ten dragees should not be exceeded. Sulphonamide sensitivity. (Side effects common to all sulphonamides, i.e. nausea, depression, headaches, skin-rash.)

Pharmaceutical precautions None.

Overdosage: Wash out stomach. Maintain high fluid intake for four days, and give potassium citrate.

Legal category POM.

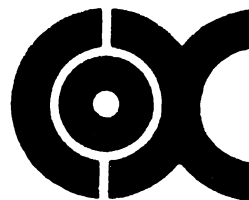
Package quantities 25 and 200 dragees.

Further information The rapid resorption and high renal clearance figure (approx. 84-96 ccm/min) of sulfanylcabamide sulphacarbamide) account for the fact that about half the quantity resorbed will be present in the urine after periods of less than two to three hours. Due to its exceptionally good solubility in any pH range, crystallisation in the lower urinary tract is avoided, and increased intake of liquid or pH adjustment are unnecessary. The product is extremely well tolerated and no adverse conditions have been reported.

Product licence number 0183/5012.

**Trade Mark*

Cox Continental Limited
Whiddon Valley
Barnstaple
North Devon EX32 8NS



ANTOIN*

Presentation White, uncoated, dispersible, aspirin compound tablets, impressed one side 'Antoin' and a division line on the reverse, each tablet containing:

Codeine Phosphate BP	5 mg
Aspirin BP	400 mg
Caffeine Citrate BPC 1959	15 mg
Calcium Carbonate BP	130 mg
Anhydrous Citric Acid BP	40 mg

Uses Antoin has analgesic and anti-inflammatory actions. It is indicated for all mild to moderate pain conditions such as headache, dental pain and that resulting from dysmenorrhoea, and as an anti-inflammatory/analgesic in the treatment of rheumatic and associated conditions.

Dosage and administration *Adults:* 1-2 tablets dissolved in water, three to four times a day; maximum daily dose is 10 tablets.

Children: Not recommended for children.

Contra-indications, warnings, etc Antoin should not be given to patients with a known idiosyncrasy to aspirin or those suffering from active peptic ulceration or haemophilia.

Special precautions: There is clinical and epidemiological evidence of the safety of aspirin in pregnancy, but it may prolong labour and contribute to maternal and neonatal bleeding and is best avoided at term.

Warnings and adverse effects: Aspirin may precipitate ironchospasm, and induce attacks of asthma in susceptible subjects; it may also induce gastro-intestinal haemorrhage, occasionally major.

Aspirin may enhance the activity of coumarin anticoagulants and oral hypoglycaemic agents. The activity of methotrexate may be markedly enhanced and its toxicity increased. The toxicity of sulphonamides may also be increased. Aspirin diminishes the effects of uricosuric agents such as probenecid and sulphinpyrazone.

Overdosage: Normal procedures for overdosage with aspirin and codeine should be followed. Gastric lavage and forced alkaline diuresis should be used if appropriate.

Pharmaceutical precautions Antoin tablets should be stored in a tightly-closed container, in a cool dry place and protected from the light.

Legal category P.

Package quantities Antoin is available in containers of 20, 50 and 250.

Further information Nil.

Product licence number 1866/5001.

COBADEX*

Presentation Cobadex Cream is available in two

strengths containing Hydrocortisone BP 0.5% w/w or Hydrocortisone BP 1.0% w/w; and Dimethicone 350 BPC 20% w/w.

Uses Cobadex Cream is formulated to include volatile and skin-penetrating solvents. This enables the hydrocortisone to be carried into the skin by the organic solvent vehicle, and at the same time evaporation of water will take place from the external surface of the cream, leaving a water-repellent silicone film in contact with the air. Cobadex is indicated, therefore, in all steroid responsive dermatoses wherever water, soap, chemicals, etc. cause irritation, e.g. contact dermatitis (especially of hands and body), pruritus ani and pruritus vulvae.

Dosage and administration A thin layer of cream should be applied to the affected area two or three times daily.

Contra-indications, warnings, etc The cream should not be used on raw, weeping surfaces because it tends to hold back any exudate. The area of skin around the eye should be avoided.

Long-term continuous topical steroid therapy should be avoided in infants, since adrenal suppression may occur, even without occlusion.

Special precautions: Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Adverse reactions: Discontinue treatment should sensitisation occur.

Pharmaceutical precautions Cobadex should be stored in a cool dry place; avoid freezing.

Legal category POM.

Package quantities Both strengths of Cobadex are available in 20 g tubes.

Further information Nil.

Product licence numbers

0.5% cream	1866/5004
1% cream	1866/5005

COBADEX-NYSTATIN*

Presentation Cobadex-Nystatin is a pale yellow ointment containing Nystatin BP 100,000 i.u./g. Hydrocortisone BP 1% w/w, Dimethicone 350 BPC 20% w/w, Benzalkonium Chloride BP 0.2% w/w.

Uses Cobadex-Nystatin is indicated in all steroid responsive dermatoses, including eczema, intertrigo, seborrhoeic dermatitis, household and industrial dermatitis and pruritus ani and vulvae, and in all other skin irritations requiring steroid therapy in which *Candida albicans* is a factor.

Dosage and administration A thin layer of ointment sufficient to cover the affected area should be applied two or three times daily until the lesion is healed.

Contra-indications, warnings, etc

Contra-indications: The ointment should not be used on raw, weeping surfaces because it tends to hold back any exudate. The area of skin around the eye should be avoided.

Special precautions: Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Adverse reactions: Discontinue treatment should sensitisation occur.

Pharmaceutical precautions Cobadex-Nystatin should be stored in a cool dry place; avoid freezing.

Legal category POM.

Package quantities Tubes of 20 g.

Further information Nil.

Product licence number 1866/0005.

CO-FEROL*

Presentation Red, sugar-coated tablets each containing:

Ferrous fumarate	120 mg (40 mg elemental iron)
Folic acid	200 mcg

Uses Normal pregnancy – as a prophylactic throughout the pregnancy. Co-ferol is not intended for the treatment of megaloblastic anaemia, though it is adequate for the treatment of mild degrees of iron-deficiency anaemia.

Dosage and administration One tablet twice daily.

Contra-indications, warnings, etc Contra-indicated in megaloblastic anaemia due to B₁₂ deficiency.

Special precautions: Keep away from children.

Co-ferol does not obviate the need for routine blood examination in late pregnancy. Co-ferol should not be continued after pregnancy has ended.

Adverse reactions: Very occasional gastro-intestinal upset.

Overdosage: Emesis should be induced, followed by intra-muscular injection of 2 g desferrioxamine mesylate in 2–3 ml water for injections. Gastric lavage is also required. Milk or 5% sodium bicarbonate may be given in the meantime. A solution of 5 g desferrioxamine mesylate in 50–100 ml water may be left in the stomach or 300 ml of 1–5% sodium bicarbonate if desferrioxamine is unavailable. Fluid maintenance is essential.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities 100 and 1,000 packs, also 5,000 hospital pack.

Further information Nil.

Product licence number 1866/5006.

COSALGESIC* ▼

Presentation Oval shaped tablets of approximate length 14 mm and breadth 8.5 mm containing dextro-

propoxyphene hydrochloride BP 32.5 mg, and paracetamol BP 325 mg. The tablets bear the letters CC impressed on one surface and COX on the other surface. The tablets are white film-coated.

Uses Analgesic. For the relief of mild to moderate pain.

Dosage and administration Two tablets, three or four times daily. (*Adults only*).

Contra-indications, warnings, etc

Contra-indications: Hyper-sensitivity to dextropropoxyphene or paracetamol.

Precautions: The safety of dextropropoxyphene has not been established in pregnancy.

Warnings and adverse effects: Because Cosalgescic is an analgesic with CNS depressing properties, it should be used with great caution in patients taking other CNS depressants, including alcohol.

The patient should be advised that alcohol should be avoided when taking Cosalgescic.

Care should be exercised in prescribing Cosalgescic for patients with a personality or other psychological disorder.

An overdosage of paracetamol can cause hepatic necrosis.

Dextropropoxyphene may impair the mental and/or the physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery.

Tolerance: Psychological and physical dependence may occur rarely.

Side-effects: Dizziness, drowsiness, headache, nausea and vomiting are all possible side-effects and appear to be more likely to occur in ambulatory than in non-ambulatory patients therefore alleviation of these side-effects can be sometimes produced by lying down after taking the tablets.

Other reported side-effects are constipation, abdominal pain, skin rashes, euphoria, lightheadedness and minor visual disturbances.

Overdosage: A chronic ingestion of dextropropoxyphene in doses exceeding 720 mg as base (equivalent to 780 mg as hydrochloride) per day has caused toxic psychoses and convulsions.

The symptoms of acute toxicity may be rapid in onset with the danger of respiratory arrest. Symptoms exhibited are similar to those experienced with morphine and other narcotics. These are respiratory depression, (a decrease in respiratory rate and/or tidal volume) Cheyne-Stokes respiration, cyanosis, extreme somnolence (progressing to stupor or coma), constriction of pupil, circulatory collapse and other characteristic symptoms of narcotic poisoning. Cardiac arrhythmias and pulmonary oedema have been reported.

Fatalities due to apnoea and cardiac arrest have occurred on rare occasions.

Treatment of overdosage: Firstly, adequate respiratory exchange should be re-established by provision of an adequate airway and assisted or controlled ventilation. The narcotic antagonist naloxone is a specific antidote against the respiratory depression produced by dextropropoxyphene. An appropriate dose of this antagonist should be administered, preferably by the intra-venous route, simultaneously with efforts at respiratory resuscitation. Repeated doses of the antagonist may be necessary over a prolonged period due to the slow elimination of dextropropoxyphene.

In addition to the use of a narcotic antagonist, the

patient may require careful titration with an anti-convulsant to control seizures. Analeptic drugs (e.g. caffeine or amphetamines) should not be used because of their tendency to precipitate convulsions.

Early assessment of the severity of paracetamol poisoning by measurement of plasma paracetamol levels is essential if treatment, which should be instituted within ten hours of ingestion, is to be effective. Present evidence suggests that cysteamine, methionine or N-acetylcysteine given within this period are effective in greatly reducing the toxic effects of paracetamol. Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated.

Gastric lavage may be helpful. Activated charcoal can absorb a significant amount of ingested dextropropoxyphene.

Pharmaceutical precautions No special requirements. Advisable to store in airtight containers and in a cool, dry place.

Legal category POM.

Package quantities Cartons of 100 tablets containing 10 blisters of 10 tablets. Special Hospital Pack containing 20 bottles of 50 tablets.

Further information Nil.

Product licence number 1866/0007.

CYCLOGEST*

Presentation White suppositories, suitable for vaginal or rectal insertion. Each 1.85 g suppository contains either 200 mg or 400 mg Progesterone.

Uses Treatment of Premenstrual Syndrome, including Premenstrual tension and depression, Premenstrual Eclampsia, Premenstrual Migraine and Premenstrual Asthma. Treatment of Puerperal depression.

Relief of Toxaemic symptoms in pregnancy.

Dosage and administration 200 mg daily to 400 mg twice a day, by vaginal or rectal insertion. For Premenstrual Syndrome commence treatment on day 14 of menstrual cycle and continue treatment until onset of menstruation. If symptoms are present at ovulation commence treatment on day 12.

Contra-indications, warnings, etc There are no known contra-indications.

Menstruation may occur earlier than expected, or more rarely, menstruation may be delayed. There is a wide margin of safety with Cyclogest Suppositories, but overdosage may produce euphoria or dysmenorrhoea.

Pharmaceutical precautions Store in a cool, dry place.

Legal category POM.

Package quantities

Packs of 12 Suppositories 200 mg

Packs of 12 Suppositories 400 mg

Further information Nil.

Product licence numbers

Cyclogest Suppositories 200 mg 2343/0001

Cyclogest Suppositories 400 mg 2343/0002

Product Licence Holder: L. D. Collins & Co Ltd.
Unray House, 9 Plantagenet Road, New Barnet, Herts.
N5 5JG.

G500* TABLETS

Presentation Orange coloured, enteric film coated, circular, biconvex tablets with a characteristic odour. Each tablet contains:

Hexamine Mandelate (Methanamine Mandelate USP)	250 mg
dl Methionine USP	250 mg

Uses *Mode of action:* Hexamine mandelate is a bacteriostatic compound, active against those Gram-negative and Gram-positive bacteria which most usually cause urinary tract infections. In the acidic urine produced by the methionine contained in G500 tablets, the hexamine mandelate dissociates to hexamine and mandelic acid. Mandelic acid is a bacteriostatic agent active against a range of urinary tract pathogens. Hexamine is subsequently hydrolysed to the bactericide formaldehyde in acidic conditions.

Hexamine mandelate is well absorbed from the gastrointestinal tract and side effects rarely develop. The enteric coated tablet protects the hexamine mandelate from premature hydrolysis in the gastric fluid by releasing the drug only in the alkaline environment of the intestine.

G500 tablets are indicated in the treatment and prophylaxis of urinary tract infections due to *Escherichia coli*, *Pseudomonas aeruginosa*, *Aerobacter aerogenes*, *Klebsiella pneumoniae*, and some *Staphylococcus* and *Streptococcus* species. It may also be effective against some protozoal infections. After acute infection successfully treated with antibiotics, G500 tablets may be used to prevent re-infection.

Chronic urinary infections and recurrent cystitis: G500 tablets may be used for long term therapy in chronic urinary tract infections and recurrent cystitis. The development of resistant organisms has not been reported.

Asymptomatic bacteriuria: may be treated with G500 tablets.

Prophylaxis and suppression of infection: G500 tablets may be used to suppress infection. Given prophylactically, G500 tablets may prevent the establishment of urinary tract infection due to instrumental procedures.

G500 tablets are particularly useful in long term treatment as bacterial resistance does not appear to develop.

G500 tablets are NOT recommended for the treatment of acute urinary tract infections which should be treated with an appropriate antibiotic, except where resistance to other antimicrobial agents is found.

Dosage and administration

Adults and children over 12 years: Treatment should commence with two tablets four times daily for one week. Urinary pH should be tested by means of a suitable test paper or reagent, and the dosage adjusted until the urine reaches pH 5. The test is best carried out on early morning urine. The maximum dose should not exceed sixteen tablets daily in four divided doses.

Children 6-12 years: One to four tablets daily (normally 14 mg hexamine mandelate per kg body weight). Check the urinary pH daily and adjust the dosage as necessary to give a urinary pH of about 5.

Children under 6 years: Because G500 tablets should not be broken or crushed, they are not recommended for children under 6 years.

As with most enteric coated preparations, G500 tablets are best given with or after food, and should be SWALLOWED WHOLE, NOT CHEWED OR CRUSHED,

in order to obtain the full therapeutic effect. Simultaneous administration of ANTACIDS SHOULD BE AVOIDED in order to prevent premature release of the active ingredients.

Where urea splitting bacteria are present in the urine, additional acidification may be necessary. Up to 2 g of ascorbic acid, *as the free acid*, may be given daily for this purpose, which must be done under medical supervision, in accordance with confirmation of acidification by laboratory tests. If the urine cannot be acidified, treatment must be discontinued.

Contra-indications, warnings, etc

Side effects: Occasionally skin rashes may occur. Pyuria is commonly observed. The urinary concentration of formaldehyde produced may give rise to painful and frequent micturition, haematuria and irritation of the bladder. The side effects are reversible when G500 tablets are withdrawn. (See Overdosage below).

Contra indications: G500 tablets should not be given to patients with hepatic insufficiency, severe dehydration, metabolic acidosis or renal impairment.

G500 tablets should not be given concurrently with sulphonamides (including Co-Trimoxazole) as crystalluria may occur. A suitable gap in treatment should occur if administering G500 tablets after a long acting sulphonamide such as sulfametopyrazine or sulphamethoxy-pyridazine. G500 should not be given with alkalinizing agents, potassium citrate, sodium bicarbonate, antacids etc.

G500 tablets are contra-indicated in patients receiving mono-amine oxidase inhibitors as the methionine content may cause symptoms of intoxication.

Overdosage: Vomiting and haematuria may occur. Bladder irritation caused by the production of acidic urine may be treated by the administration of copious amounts of water and a suitable alkalinizing agent e.g. potassium citrate, sodium bicarbonate. Because the product is enteric coated, this may lead to prolonged effect on urinary pH. It is therefore advisable to monitor urinary pH for a reasonable period.

Pharmaceutical precautions G500 tablets should be stored in a well-closed container.

Legal category P.

Package quantities 500 tablets.

Further information Methionine is a sulphur containing amino acid, which is an essential dietary constituent.

G500 tablets normally have the characteristic odour of methionine.

Administration of G500 tablets may interfere with tests to determine 17-hydroxy-corticosteroids, oestrogens or catecholamines in the urine.

Administration of G500 tablets may cause an increase in urinary ammonium, calcium, magnesium and phosphate.

Product licence number 1511/5900.

Product Licence Holder: Secretary of State for Social Services, Department of Health and Social Security, Scientific and Technical Branch 4A.

KLOREF[®]

Presentation White, effervescent, flavoured tablets equivalent to 500 mg potassium chloride (6.7 mmol K⁺ and 6.7 mmol Cl⁻). Each tablet contains:

Betaine Hydrochloride BPC 1949	740 mg
Potassium Bicarbonate BPC	455 mg
Potassium Chloride BP	140 mg
Potassium Benzoate	50 mg

Uses Kloref is indicated in all cases of potassium depletion resulting from intensive or prolonged diuretic therapy. Corticosteroid therapy. Use of carbenoxolone sodium. Patients at special risk are those on a low-salt diet and those receiving digitalis. A lack of cellular potassium in the latter can increase the toxic effect of digitalis.

Potassium deficiency resulting from an inadequate potassium dietary intake – here the elderly population are a special risk. Other indications are advanced hepatic cirrhosis, chronic renal disease, Cushing's syndrome, diabetic ketosis and in conditions requiring potassium supplementation due to prolonged or chronic diarrhoea or vomiting.

Dosage and administration In most cases 1–2 tablets three times daily (20–40 mmol K⁺ and Cl⁻). A few patients may need considerably bigger doses. Each tablet should be fully dissolved in at least 100 ml of cold or refrigerated water before drinking.

The tablets themselves should not be swallowed.

Contra-indications, warnings, etc Contra-indicated in hyperchloraemia; renal tubular or metabolic acidosis.

Special precautions: Cautious administration required in cases of chronic renal disease.

Overdosage: Hyperkalaemia. Poisoning is usually minimal below 6.5 mmol/l, moderate between 6.5 and 8 mmol/l and severe above that level. The absolute toxicity is governed by both pH and associated sodium levels. Hyperkalaemic symptoms and particularly the ECG effects may be transiently controlled by calcium gluconate, administration of glucose or glucose and insulin, sodium bicarbonate or hypertonic sodium infusions, cation exchange resins or by haemodialysis and peritoneal dialysis. Caution should be exercised in patients who are digitalised and who may experience acute digitalis intoxication in the course of potassium removal.

Pharmaceutical precautions Kloref Tablets should be stored in a cool dry place. Avoid storing at temperatures in excess of 25°C.

Legal category P.

Package quantities Kloref is available in packs of 100, also available in containers of 1,000 for supply to hospitals only.

Further information The addition of water to each tablet brings about a reaction between the betaine hydrochloride and potassium bicarbonate which with the additional potassium chloride will provide the equivalent of 500 mg potassium chloride (6.7 mmol K⁺ and 6.7 mmol Cl⁻) in solution. Effervescence results from the liberation of carbon dioxide.

Betaine is a naturally occurring substance found in beet, and is metabolised by the body.

Product licence number 1866/5009.

KLOREF-S[®]

Presentation Kloref-S is presented as effervescent granules, packed in individual sachets to contain the

equivalent of 1.50 g potassium chloride. Each sachet contains:

Betaine Hydrochloride BPC 1949	2.07 g
Potassium Bicarbonate BPC	1.35 g
Potassium Chloride BP	0.5 g

Uses Kloref-S is indicated in all cases of potassium depletion resulting from intensive or prolonged diuretic therapy. Corticosteroid therapy. Use of carbenoxolone sodium. Patients at special risk are those on a low salt diet and those receiving digitalis. A lack of cellular potassium in the latter can increase the toxic effect of digitalis.

Potassium deficiency resulting from an inadequate potassium dietary intake; here the elderly population are a special risk. Other indications are advanced hepatic cirrhosis, chronic renal disease, Cushing's syndrome, diabetic ketosis and in conditions requiring potassium supplementation due to prolonged or chronic diarrhoea or vomiting.

Dosage and administration In most cases 1 or 2 sachets daily (20–40 mmol K⁺ and Cl⁻) preferably after meals. A few patients may need considerably bigger doses. Each sachet should be dissolved in at least 200 ml of cold water.

Contra-indications, warnings, etc Contra-indicated in hyperchloraemia, renal tubular or metabolic acidosis.

Special precautions: Cautious administration required in cases of chronic renal disease.

Overdosage: Hyperkalaemia. Poisoning is usually minimal below 6.5 mmol/l, moderate between 6.5 and 8 mmol/l and severe above that level. The absolute toxicity is governed by both pH and associated sodium levels. Hyperkalaemic symptoms and particularly the ECG effects, may be transiently controlled by calcium gluconate, administration of glucose or glucose and insulin, sodium bicarbonate or hypertonic sodium infusions, cation exchange resins or by haemodialysis and peritoneal dialysis. Caution should be exercised in patients who are digitalised and who may experience acute digitalis intoxication in the course of potassium removal.

Pharmaceutical precautions Kloref-S Sachets should be stored in a cool dry place. Avoid storing at temperatures in excess of 25°C.

Legal category P.

Package quantities Kloref-S is available in boxes of 30 sachets.

Further information The addition of water to each sachet brings about a reaction between the betaine hydrochloride and potassium bicarbonate which with the additional potassium chloride will provide the equivalent of 1.5 g potassium chloride (20 mmol K⁺ and 20 mmol Cl⁻) in solution. Effervescence results from the liberation of carbon dioxide.

Betaine is a naturally occurring substance found in beet, and is metabolised by the body.

Product licence number 1866/0001.

MYOLGIN*

Presentation White, uncoated, dispersible, aspirin, paracetamol and codeine tablets impressed one side

'Myolgin' and a division line on the reverse, each tablet containing:

Codeine Phosphate BP	5 mg
Aspirin BP	200 mg
Paracetamol BP	200 mg
Citric Acid BP	15 mg
Calcium Carbonate BP	60 mg
Caffeine Citrate BPC 1954	15 mg

Uses Myolgin has analgesic and anti-inflammatory actions. It is indicated for all mild to moderate pain conditions such as headache, dental pain and that resulting from dysmenorrhoea and as an anti-inflammatory/analgesic in the treatment of rheumatic and associated conditions.

Dosage and administration One or two tablets dissolved in water, three to four times a day; maximum daily dose is 16 tablets. Myolgin should not be given to children.

Contra-indications, warnings, etc Myolgin should not be given to patients with a known idiosyncrasy to either aspirin or paracetamol; or those suffering from active peptic ulceration or haemophilia.

Special precautions: There is clinical and epidemiological evidence of the safety of aspirin in pregnancy, but it may prolong labour and contribute to maternal and neonatal bleeding, and is best avoided at term.

Warnings and adverse effects: Aspirin may precipitate bronchospasm, and induce attacks of asthma in susceptible subjects; it may also induce gastro-intestinal haemorrhage, occasionally major.

Aspirin may enhance the activity of coumarin anticoagulants and oral hypoglycaemic agents. The activity of methotrexate may be markedly enhanced and its toxicity increased. The toxicity of sulphonamides may also be increased.

Aspirin diminishes the effect of uricosuric agents such as probenecid and sulphinpyrazone. An overdose can cause hepatic necrosis.

Overdosage: Normal procedures for overdosage with aspirin, paracetamol and codeine should be followed. Gastric lavage may be helpful. Early assessment of the severity of paracetamol poisoning by measurement of plasma paracetamol levels is essential if treatment, which should be instituted within ten hours of ingestion, is to be effective. Present evidence suggests that cysteamine, methionine or N-acetylcysteine given within this period are effective in greatly reducing the toxic effects of paracetamol. Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated.

Pharmaceutical precautions Myolgin tablets should be stored in a tightly-closed container, in a cool dry place and protected from the light.

Legal category P.

Package quantities Myolgin is available in packs of 20 and 250.

Further information Nil.

Product licence number 1866/5010.

*Trade Mark

The Crookes Laboratories Limited

Basingstoke

Hampshire



KAODENE*

Presentation Kaodene is an aqueous suspension containing Codeine Phosphate BP 10 mg and Light Kaolin BP 3 g in each 10 ml. It is an off-white liquid with the odour and flavour of aniseed.

Uses Kaodene is indicated for the treatment of simple diarrhoea.

Dosage and administration *Adults and Children over 12 years:* 20 ml three or four times daily.

Children from 5 to 12 years: 10 ml three or four times daily.

Contra-indications, warnings, etc Codeine phosphate is a narcotic analgesic and, given in large doses, may induce tolerance and psychological and physical dependence. At the recommended dosage, however, it is unlikely that such effects would be encountered with Kaodene.

Whilst there is no adequate evidence of safety in

human pregnancy, codeine has been widely used without apparent ill-effect for many years and studies in animals have not demonstrated any hazard.

Treatment of overdosage: Gastric lavage and symptomatic treatment as for codeine phosphate.

Pharmaceutical precautions *Recommended storage conditions:* 5°–20°C.

Legal category P.

Package quantities Bottle of 250 ml.

Further information The effect of Kaodene is to reduce gut motility, soothe the inflamed mucosa of the bowel and consolidate loose, watery faeces into normal stools. The preparation has a pleasant taste and is suitable for both adults and children.

Product licence number 0096/0045.

***Trade Mark**

Davis + Geck
(A Division of Cyanamid of Great
Britain Limited)
Fareham Road
Gosport, Hampshire PO13 0AS

DG
DAVIS + GECK

DEXON® 'S'

Presentation Dexon 'S' sutures are Synthetic Absorbable Sutures USP made of polyglycolic acid. They are supplied in a range of sizes from 8/0 (0.4 metric) to 2 (5 metric) in sealed, direct-dispense envelopes either as non-needled pre-cut lengths or with an extensive range of needles attached. Dexon 'S' is coloured green to enhance visibility in tissue or is also available undyed, with a natural beige colour.

Uses Dexon 'S' may be used for suturing surgical and traumatic wounds and for ligating blood vessels.

Dexon 'S', polyglycolic acid, is a synthetic absorbable material which provokes minimal tissue reaction and may therefore be used where an absorbable suture is indicated.

Absorption studies in rabbits revealed minimal absorption at 7 to 15 days, significant absorption at 30 days and essentially complete absorption in 60-90 days.

Dosage and administration As indicated in the surgical procedure.

Contra-indications, warnings, etc Dexon 'S' is contra-indicated where a non-absorbable suture is needed to provide prolonged wound support. The safe use of Dexon 'S' in neural tissue and in cardiovascular surgery has not been established. When tying Dexon 'S' special care is needed in placing the first knot.

Adverse reactions Although there have been a few reports of foreign body giant cell reactions these are not considered to be specific to Dexon 'S'. As with all suture materials inflammation at the site of absorption can occur although its incidence is less than with catgut.

Pharmaceutical precautions Discard opened, unused sutures. Do not re-sterilise.

Package quantities Sealed envelopes containing sterile sutures in sizes 8/0 (0.4 metric) to 2 (5 metric) either as non-needled pre-cut lengths or swaged to Atraumatic® steel needles of varying types and sizes. This envelope is sealed within a clear peel-apart secondary envelope. The interspace is sterile. The sales unit is boxes of 1 dozen or 3 dozen sutures.

Legal category P.

Further information Nil.

Product licence numbers 0095/0023
0095/5092

HISTOACRYL®

Presentation The tissue adhesive Histoacryl is a butyl 2-cyanoacrylate monomer, which is supplied as a sterile liquid in sealed plastic vials. Histoacryl contains a blue

dye to indicate clearly the thickness of the adhesive film applied. The plastic vials are packed in cylindrical plastic tubes.

Uses Histoacryl is a tissue adhesive for wound closure when established techniques, e.g. sutures, are inconvenient or inappropriate. Histoacryl may be used to bond tissue without sutures in surgical and traumatic wounds or in combination with sutures to provide additional security and to seal off the suture tracks.

Dosage and administration Histoacryl tissue adhesive must always be applied as a very thin film as otherwise its adhesive quality will be greatly impaired. Before Histoacryl is applied the tissue must be swabbed dry as much as possible. If larger surfaces have to be joined together Histoacryl must be applied to small patches of the total area only. After accurate adaptation the tissue surfaces to be bonded must be pressed together for one minute, however, caution must be taken to adapt the tissue exactly, because polymerization time is only 10 seconds and mistakes cannot be corrected later.

Contra-indications, warnings, etc As is the case with all cyanoacrylates, Histoacryl is contra-indicated where direct contact to nerve tissue takes place, e.g. for use on brain surface or parts of the central nervous system, since cell necrosis and scar tissue formation can be a consequence.

Contact of Histoacryl with parts of the major vascular system is contra-indicated. Blood in contact with Histoacryl polymers form thrombi. Histoacryl must not come into contact with the conjunctival sac since conglutination may occur.

It must be pointed out that the polymerisation of Histoacryl produces heat. This is insignificant as long as Histoacryl is applied as a very thin film only. An injuring degree of heat on the surrounding tissue does not occur if the adhesive is applied in such a thin layer.

Pharmaceutical precautions The adhesive should be stored in the refrigerator or freezer, and must be protected from the light if removed from the packing for any length of time.

Care must be taken that no instruments, cloths, swabs or gloves come in contact with the adhesive. In that case they stick to the tissue. Instruments which have been contaminated with adhesive can be cleaned with dimethyl formamide or acetone.

Opened vials must be discarded. Histoacryl must not be resterilised.

Legal category P.

Package quantities 1 Box of Histoacryl contains 5 vials. Each vial contains 0.5 g of monomer.

Further information Nil.

Product licence number 3551/0001.

KIEL BONE GRAFT

Presentation Kiel Bone Graft, prepared by the method of Maatz and Bauermeister, is a mineral and collagenous matrix specially processed from calf bone, purified and γ -sterilised. According to the nature of the materials selected, Kiel Bone Graft consists of spongy or cortical tissue or a combination of both in various proportions. The grafts are packed in sterile double plastic bags in an outer box.

Uses The usual indications for Kiel Bone Graft are replacement of bone cysts, intervertebral locking, reparation of bone surface defects and the use as osteotomy wedges.

Dosage and administration As indicated in the surgical procedure.

Contra-indications, warnings, etc Kiel Bone Graft should not be implanted into a potentially infected host site. If the nature of the implant bed precludes the resorption process and the ingrowth of new bone, Kiel Bone Graft should not be used.

Pharmaceutical precautions Store in a dry place at room temperature. Opened and unused packages should be discarded and Kiel Bone Graft should not be resterilised.

Legal category P.

Package quantities Kiel Bone Graft is available in various sizes and types. Boxes contain 1 to 33 packages.

Further information Nil.

Product licence number 3551/5900.

LYODURA*

Presentation Lyodura is a sterile transplant material consisting of a mesh-like texture of collagenous fibres, which is developed from homologous human dura mater cerebri by special processing, lyophilised and gamma-ray sterilised. Lyodura is supplied in sterile double peel pouches in several sizes.

Uses Lyodura is a patch material which is substituted after implantation by connective tissue. Lyodura is used in the repair of defects, lesions and as a reinforcement of body tissue, e.g. for covering and sealing defects and for sheathing and securing sutures, in neuro-thoracic and general surgery.

Dosage and administration As indicated in the surgical procedure. Lyodura must be rehydrated before use.

Contra-indications, warnings, etc The use of Lyodura in an infected operating region is contra-indicated since the healing-in of Lyodura cannot be expected in such a case. The use of Lyodura as a replacement for parts of the arterial system of the heart wall must be considered as being contra-indicated.

Degenerative changes in scarred wall replacement can cause aneurisms and calcification.

Pharmaceutical precautions Store in dry place at room temperature. Opened and unused packages should be discarded and material must not be resterilised.

Legal category P.

Package quantities Lyodura is available in the following dimensions:

1. 6 × 14 cm package containing 1 piece	Cat. No.
	106 002
2. 4 × 10 cm package containing 1 piece	106 004
3. 2 × 10 cm package containing 2 pieces	106 008
4. 4 × 5 cm package containing 2 pieces	106 006
5. 1.5 × 3 cm package containing 5 pieces	106 010
6. 1.5 × 3 cm package containing 5 pcs., perforated	106 011
7. Patches 9 and 14 mm packages with 3 pcs. each	106 015

Further information Nil.

Product licence number 3551/0004.

SOFTGUT* (SOFT-CATGUT-BRAUN)

Presentation

1. *Plain*: Uniform, firmly twisted strand of collagen prepared from healthy mammals, purified, softened, dry packed and sterilised. Available in sizes 6/0 to 3 (i.e. 1 to 7 metric).
2. *Chromic*: Uniform, firmly twisted strands of collagen from healthy mammals, purified, treated with chromicising agent, softened, dry packed and sterilised. Available in sizes from 6/0 to 3 (i.e. 1 to 7 metric).

Uses Soft-Catgut-Braun is Sterile Surgical Catgut BP which may be used for suturing surgical and traumatic wounds and for ligating blood vessels. It may be used in practically all tissues. Soft-Catgut-Braun Plain is relatively rapidly absorbed and should therefore be used only where short term wound support is required. It is generally considered advisable to use Soft-Catgut-Braun Chromic where somewhat more prolonged wound support is desired.

Dosage and administration As indicated in the surgical procedure.

Contra-indications, warnings, etc Soft-Catgut-Braun is contra-indicated where a non-absorbable suture is needed to provide prolonged wound support.

Opened and unused sutures should be discarded and material must not be resterilised. Adverse reactions may include tissue reaction or inflammation.

Pharmaceutical precautions Store in a dry place at room temperature. Discard opened unused sutures.

Package quantities Sutures are available in varying sizes from 6/0 to 3 (i.e. 1 to 7 metric) in non-needed precut lengths or swaged to non-traumatic stainless steel needles of varying types and sizes. Outer boxes contain either precuts or needle thread combinations.

Legal category P.

Further information Nil.

Product licence numbers Plain 3551/0007
Chromic 3551/0008

STERILISED SURGICAL CATGUT

Presentation 1. *Plain*: Uniform, firmly twisted strands of collagen prepared from healthy mammals, purified and

sterilised. Available in sizes of 5/0 to 3 (i.e. 1.5 to 7 metric).

2. *Mild Chromic*: Black, uniform, firmly twisted strands of collagen (treated with chromicising agent) from healthy mammals, purified and sterilised. Available in sizes 7/0 to 4/0 (i.e. 0.7 to 2 metric).

3. *Chromic*: Uniform, firmly twisted strands of collagen (treated with chromicising agent) from healthy mammals, purified and sterilised. Available in sizes 4/0 to 3 (i.e. 2 to 7 metric).

Uses Sterilised Surgical Catgut may be used for suturing surgical and traumatic wounds and for ligating blood vessels. It may be used in practically all tissues. Catgut is relatively rapidly absorbed and should therefore be used only where short-term wound support is required. It is generally considered advisable to use Chromic Catgut where somewhat more prolonged wound support is desired.

Dosage and administration As indicated in the surgical procedure.

Contra-indications, warnings, etc Sterilised Surgical Catgut is contra-indicated where a non-absorbable suture is needed to provide prolonged wound support.

Opened and unused sutures should be discarded and material must not be re-sterilised. Adverse reactions may include tissue reaction or inflammation. Wound dehiscence and bleeding may occasionally occur.

Pharmaceutical precautions Store in a cool dry place. Discard opened unused sutures.

Legal category P.

Package quantities Sutures are available in varying sizes (Plain 5/0 to 3; Mild Chromic 7/0 to 4/0; and Chromic 4/0 to 3) in non-needed pre-cut lengths or swaged to Atraumatic® steel needles of varying types and sizes in three dozen packages (N.B. certain ophthalmic sutures are available in one dozen packages).

Further information Nil.

Product licence numbers

Sterilised Surgical Catgut (Plain)	0095/5090
Sterilised Surgical Catgut (Mild Chromic)	0095/5091
Sterilised Surgical Catgut (Chromic)	0095/5091

* *Trade Mark*

Delandale Laboratories Limited

Delandale House

37 Old Dover Road

Canterbury, Kent, CT1 3JB



DICYNENE*

Presentation *Dicynene Tablets 500 mg.* Each oval white, bi-convex tablet, engraved 'DICYNENE' one side, '500' on the other, contains 500 mg ethamsylate.

Dicynene Tablets 250 mg: Each circular, white bi-convex tablet, engraved 'DICYNENE' on one side, contains 250 mg of ethamsylate.

Dicynene 1000 Injection: Each clear glass 2 ml Snapule printed 'DICYNENE 1000' contains 1 g ethamsylate.

Dicynene Injection: Each clear glass 2 ml Snapule printed 'DICYNENE' contains 250 mg ethamsylate.

Uses Dicynene is a synthetic non-hormonal agent, which is used either orally or parenterally to reduce excessive capillary blood loss. Dicynene acts principally by maintaining capillary integrity probably by promoting polymerisation of mucopolysaccharide in vessel walls.

Following systemic administration of Dicynene, the mean bleeding time is significantly reduced without any effect on cell counts, fibrinolysis, plasma protein levels, prothrombin time and clotting time. Dicynene does not produce a vasoconstricting action nor does it have any effect on hepatic or renal function.

Dicynene is used clinically for the prophylaxis and treatment of small-vessel haemorrhage. Clinical reports show the value of Dicynene in the following indications.

Gynaecology: Non hormonal control of menorrhagia and control of bleeding during gynaecological surgery.

Paediatrics: Limiting or preventing periventricular haemorrhage in low birth weight babies.

Urology: Control of haemorrhage during and after prostatectomy. Symptomatic control of urinary tract haemorrhage of unknown aetiology.

Oral and dental surgery: Control of haemorrhage following oral surgery and dental extractions.

Ophthalmology: Control of surgical haemorrhage and retinal bleeding.

ENT: Epistaxis and control of surgical haemorrhage (e.g. tonsillectomy, adenoidectomy, middle ear surgery).

General surgery: Control of haemorrhage occurring during or after surgery.

General medicine: The prophylaxis and treatment of small vessel haemorrhage occurring in the gastro-intestinal or respiratory tract; the control of haemorrhage during anticoagulant therapy.

Dosage and administration *Adult dosage: Menorrhagia:* One 500 mg tablet four times a day from the start of bleeding until menstruation ceases.

Pre-surgical prophylaxis: 1 g from Dicynene 1000 Injection (or Dicynene Injection) either intramuscularly with the premedication or intravenously at induction of anaesthesia.

Haemorrhagic emergency: 1 g from Dicynene 1000

Injection intravenously. When used in conjunction with high molecular weight plasma volume expanders Dicynene is more effective if given prior to these agents.

Maintenance therapy: 500 mg intravenously, intramuscularly or orally every four to six hours.

Paediatric dosage: 500–750 mg parenterally for the control of haemorrhage; 250 mg orally or parenterally every four to six hours for maintenance therapy.

Neonatal dosage: 12.5 mg/kg intravenously or intramuscularly six hourly.

Contra-indications, warnings, etc There are no known contra-indications. Dicynene is well tolerated even in high dosage or during prolonged treatment. To date there has been no evidence of thrombogenic effect with Dicynene except in one series where six out of 23 Dicynene treated patients gave positive results postoperatively with the ¹²⁵I-labelled fibrogen technique, compared with 0 out of 19 in the placebo group. Only one of the Dicynene treated patients had a clinically apparent deep vein thrombosis.

Dicynene has been used without ill effect in patients with a history of thrombosis. Following intravenous injection a transient fall in blood pressure of the order of 30 mm Hg, lasting four to five minutes, has been reported. No major side-effects have been reported. Occasional headaches and skin rashes have been reported which usually disappear on reduced dosage. Nausea may occur in a small number of patients; however, this can be overcome by administering the dose after food.

Pharmaceutical precautions *Tablets:* Protect from light and moisture.

Ampoules: Protect from light. Discard if solution coloured.

Legal category POM.

Package quantities

Tablets 500 mg:	Securitainers of 100
Tablets 250 mg:	Securitainers of 100
Injection:	10 × 2 ml 'Snapules'
1000 Injection:	10 × 2 ml 'Snapules'

Further information Ethamsylate is a white crystalline powder, odourless with a slight saline taste and is readily soluble in water (62.8% at 18°C), producing a near neutral solution (pH 6.5).

Pharmacological effects appear within one to five minutes of parenteral administration and within one hour of oral administration. Dicynene is excreted unchanged via the urinary, biliary and intestinal routes and after one hour only 6.5–11.5% remains in the blood. Dicynene was found to have no teratogenic effects when studied in experimental animals over three generations.

Product licence numbers

Tablets 500 mg	0357/5003
Tablets 250 mg	0357/5002
Dicyclic Injection	0357/5001
Dicyclic 1000 Injection	0357/0013

ETOPHYLATE*

Presentation *Adult formulations: Etophylate Forte Tablets:* White, circular, bi-convex tablets engraved 'ETOPHYLATE FORTE' one side, scored on the other, each containing 500 mg acepifylline.

Etophylate Forte Syrup: Clear tangerine, citrus-flavoured syrup containing 500 mg acepifylline per 5 ml.

Etophylate Suppositories: White, wax, torpedo-shaped and preformed in white plastic in strips of six. Each suppository contains 500 mg of acepifylline.

Etophylate Ampoules: Clear glass, printed 2 ml 'snap-ules'. Each ampoule contains 500 mg acepifylline.

Paediatric formulations: Etophylate Tablets: White, circular, bi-convex tablets engraved 'ETOPHYLATE' on one side, each containing 250 mg acepifylline.

Etophylate Syrup for Children: Clear yellow, citrus-flavoured syrup containing 125 mg acepifylline per 5 ml.

Etophylate Paediatric Suppositories: White, waxy, torpedo-shaped and preformed in white plastic in strips of six. Each suppository contains 100 mg acepifylline.

Uses Etophylate is used clinically for: relief of bronchospasm in bronchitis and asthma; emergency relief of status asthmaticus; cor pulmonale; pulmonary manifestations of left ventricular failure.

Dosage and administration *Adult dosage: Etophylate Forte Tablets:* 1-2 tablets three times daily.

Etophylate Forte Syrup: 5-10 ml three times daily.

Etophylate Suppositories: 1-3 suppositories in 24 hours, 2 may be inserted at bedtime in severe cases of nocturnal dyspnoea.

Etophylate Ampoules: Intravenous: 1-2 ampoules as required.

Intramuscular: 1-4 ampoules daily.

Paediatric dosage: Etophylate Syrup for Children: Under 1 year: 2.5 ml three or four times daily.

1-5 years: 5 ml three or four times daily.

5-12 years: 10 ml three or four times daily.

Etophylate Tablets: 5-12 years: 1 tablet three or four times daily.

Etophylate Paediatric Suppositories: Under 1 year: 1 daily.

1-5 years: 2 daily.

5-12 years: 3 daily.

Contra-indications, warnings, etc

Contra-indications: None known.

No major side-effects have been reported. Gastric irritation has not been reported following the use of the oral formulations; proctitis has been reported on one occasion only following the use of the suppositories.

Intramuscular injections are pain-free, however, the intravenous injection should be given slowly over a period of approximately one minute to reduce the risk of headaches and giddiness arising from a possible fall in blood pressure.

Etophylate Forte Syrup is not recommended for use in children under 12 years of age.

Treatment of overdosage should be as for theophylline. If overdosage occurs with symptoms of nausea, vomiting, fall in blood pressure, tachycardia or collapse, treatment should be supportive and include the use of i.v. pressor drugs.

Pharmaceutical precautions The only special precautions are:

1. Suppositories must be stored in a cool place.
2. Etophylate Forte Syrup should be shaken before use as a slight sediment may appear on storage especially in cold conditions. The sediment readily re-dissolves on shaking.
3. If dilution of either syrup is considered necessary, it may be diluted with Syrup BP or Syrup BP preserved with para-hydroxy-benzoic acid esters only.

Legal category Tablets P.

Syrup P.

Suppositories P.

Ampoules POM.

Package quantities *Etophylate Forte Tablets:* Securainers of 100, 250.

Etophylate Forte Syrup: 200 ml glass bottles.

Etophylate Suppositories: Boxes of 12.

Etophylate Ampoules: Non-crushable plastic boxes of 10.

Etophylate Tablets: Securainers of 100, 500.

Etophylate Syrup: 200 ml glass bottles.

Etophylate Paediatric Suppositories: Boxes of 12.

Further information Nil.

Product licence numbers

Forte Tablets	0357/5009
Forte Syrup	0357/0011
Suppositories	0357/5005
Ampoules	0357/5004
Tablets	0357/5008
Syrup	0357/5007
Paediatric Suppositories	0357/5006

KIDITARD*

Presentation Hard gelatin capsules, size 0, with clear light blue and clear dark blue shell. Each capsule contains 250 mg quinidine bisulphate (equivalent to 200 mg quinidine sulphate) in the form of sustained release micro-pellets.

Uses Sustained release quinidine therapy. The active ingredient is absorbed from the gastro-intestinal tract over a 12 hour period. An even pattern of release of the drug is established which prevents excessively high initial blood levels and therefore limits undesirable side effects. The sustained release capsules permit a twice daily dosage regime and prevent wide fluctuation in plasma quinidine levels.

Kiditard capsules are used clinically for: Extra-systoles; Paroxysmal atrial tachycardia; Nodal tachycardia; Atrial fibrillation; Atrial flutter; Paroxysmal ventricular tachycardia; Maintenance of sinus rhythm following restoration by electro-conversion.

Dosage and administration Kiditard dosage should be individually adapted to each patient. As a rule, treatment should commence with two sustained release capsules every 10-12 hours, after a test dose of 1 capsule to test for patient sensitivity.

Kiditard capsules are not recommended for use in children.

Contra-indications, warnings, etc Acute infections, atrio-ventricular block and idiosyncrasy to quinidine form absolute contra-indications to Kiditard therapy. Special care must be taken with heavily digitalised patients and in patients with congestive heart failure, hypotension or ventricular tachycardia due to possible overdosage with quinidine. Special care is also needed in patients on prolonged anti-coagulant treatment since cases of quinidine-induced hypoprothrombinaemic haemorrhage have been recorded. Patients should be carefully observed for their reactions to the first dose of the drug since idiosyncrasy is a possible response to quinidine. The following allergic reactions to quinidine have been reported: urticaria, purpura, asthma, thrombocytopenia. Gastro-intestinal upset, commonly associated with quinidine therapy, is largely avoided through the use of Kiditard. There are reports of hepatitis due to quinidine; none has been fatal and signs and symptoms disappear on withdrawal. Cardiotoxic side-effects (ventricular extra systole, A-V block, increased QRS complex above 50%, ventricular tachycardia) may occur; repeated high doses may lead to cinchonism.

If overdosage occurs treatment should be as for quinidine. Gastric lavage and a saline purgative should be employed. Promote excretion by acidifying urine with ammonium chloride. Maintain fluid balance and blood pressure. Assist respiration and monitor cardiac rhythm.

Pharmaceutical precautions Protect from light and moisture.

Legal category POM.

Package quantities Aluminium cans containing 100 capsules.

Further information Nil.

Product licence number 0357/0012.

PRIADEL

Presentation Controlled release lithium carbonate tablets: white, circular, bi-convex tablets engraved PRIADEL one side, scored on the other side. Each tablet contains 400 mg Lithium Carbonate Ph Eur in a controlled release dosage form.

Uses Controlled release lithium therapy for:

1. Treatment of mania and hypomania.
2. Treatment of depression in patients who
 - (a) are suffering from recurrent bipolar affective disorder and in whom it is intended that long term lithium prophylaxis will be used or
 - (b) are suffering from recurrent depressive illness with some bipolar, endogenous or obsessional features, or a family history of bipolar illness, indicating a probable response to lithium therapy or
 - (c) have failed to respond to other antidepressive treatments.
3. Prophylactic treatment of recurrent affective disorders.

Dosage and administration A simple treatment schedule has been evolved which except for some minor variations should be followed whether using Priadel therapeutically or prophylactically. The minor variations to this schedule depend on the elements of the illness being treated and these are described later.

1. In patients of average weight (70 kg) an initial dose of 1-3 tablets (400-1,200 mg) of Priadel may be given as a single daily dose in the morning or on retiring. Alternatively, the dose may be divided and given morning and evening. When changing from other lithium preparations serum lithium levels should first be checked, then Priadel therapy commenced at a daily dose as close as possible to the dose of the other form of lithium. As bioavailability varies from product to product (particularly with regard to retard or slow release preparations) a change of product should be regarded as initiation of new treatment.

2. Four to five days after starting treatment (and never longer than one week) a blood sample should be taken for the estimation of serum lithium level.

3. The objective is to adjust the Priadel dose so as to maintain the serum lithium level permanently within the diurnal range of 0.5-1.5 mmol/l. In practice, the blood sample should be taken between 12 and 24 hours after the previous dose of Priadel. 'Target' serum lithium concentrations at 12 and 24 hours are shown in the table below.

	<i>'Target' serum lithium concentration (mmol/l)</i>	
	<i>At 12 hours</i>	<i>At 24 hours</i>
Once daily dosage	0.7-1.0	0.5-0.8
Twice daily dosage	0.5-0.8	

Serum lithium levels should be monitored weekly until stabilisation is achieved.

4. Lithium therapy should not be initiated unless adequate facilities for routine monitoring of serum concentrations are available. Following stabilisation of serum lithium levels, the period between subsequent estimations can be increased gradually but should not normally exceed three months. Additional measurements should be made following alteration of dosage, on development of intercurrent disease, during manic or depressive relapse, following significant change in sodium or fluid intake, or if signs of lithium toxicity occur.

5. Whilst a high proportion of acutely ill patients may respond within three to seven days of the commencement of Priadel therapy, Priadel should be continued through any recurrence of the affective disturbance. This is important as the full prophylactic effect may not occur for up to 12 months after the initiation of therapy.

6. In patients who show a positive response to Priadel therapy, treatment is likely to be long term. Careful clinical appraisal of the patient should be exercised throughout medication (see Precautions).

Prophylaxis against recurrent mania and hypomania, manic depressive illness, recurrent depression: It is recommended that the described treatment schedule is followed.

Treatment of acute mania, hypomania and depression: It is likely that a higher than normal Priadel intake may be necessary during an acute phase. Therefore as soon as control of mania or depression is achieved, the serum lithium level should be determined and it may be necessary, dependent on the results, to lower the dose of Priadel and re-stabilise serum lithium levels. In all other details the described treatment schedule is recommended.

Use in elderly: In elderly patients or those below 50 kg in weight, it is recommended that the starting dose be 1

tablet (400 mg). Elderly patients may be more susceptible to side effects even at lower serum levels and also may require lower doses in order to maintain normal serum lithium levels. It follows therefore that long term treatment patients often require a reduction in dosage over a period of years.

Safety in pregnancy: There is epidemiological evidence that lithium may be harmful to the foetus in human pregnancy.

<i>Total no. 'lithium babies' reported</i>	<i>Malformed infants</i>	<i>Ebstein's anomaly and other major cardiovascular malformations</i>
225	25 (11%)	18 (8%)

It is strongly recommended that lithium be discontinued before a planned pregnancy. If it is considered essential to maintain Priadel treatment during pregnancy, serum lithium levels should be closely monitored since renal function changes gradually during pregnancy and suddenly at parturition requiring dosage adjustments. It is recommended that lithium be discontinued shortly before delivery and recommenced a few days post-partum.

Babies may show signs of lithium toxicity necessitating fluid therapy in the neonatal period. Babies born with low serum lithium concentrations may have a flaccid appearance which returns to normal without any treatment. Lithium is secreted in breast milk, therefore bottle feeding is recommended.

Contra-indications, warnings, etc

Contra-indications. Renal insufficiency, cardiovascular insufficiency, Addison's disease and untreated thyroid dysfunction are all contraindications to lithium therapy.

Precautions: When considering Priadel therapy, it is necessary to ascertain whether patients are receiving lithium in any other form. If so, check serum levels before proceeding. It is important to ensure that renal function is normal – if necessary a creatinine clearance test or other renal function test should be performed. Cardiac and thyroid function should be assessed before commencing lithium treatment. Patients should be euthyroid before the initiation of lithium therapy. Renal function, cardiac function and thyroid function should be reassessed periodically.

Clear instructions regarding the symptoms of impending toxicity should be given by the doctor to all patients receiving long term lithium therapy (see Warnings and Adverse Effects). Patients should also be warned to report if polyuria or polydipsia develop. Episodes of nausea and vomiting or other conditions leading to salt/water depletion (including severe dieting) should also be reported.

Caution should be exercised to ensure that diet and fluid intake are normal thus maintaining a stable electrolyte balance. This may be of special importance in very hot weather or work environment. Infectious diseases including colds, influenza, gastro-enteritis and urinary infections may alter fluid balance and thus affect serum lithium levels. Treatment should be discontinued during any intercurrent infection and should only be re-instituted after the patient's physical health has returned to normal.

In patients undergoing surgery, lithium intoxication may result from pre-operative fluid deprivation. Lithium

should preferably be discontinued 24–48 hours before operation and recommenced only when the post-operative recovery period is safely over and normal fluid balance restored. Where interruption of lithium therapy is impractical, e.g. during a course of E.C.T., serum lithium concentration should be carefully monitored pre-operatively and fluid balance maintained. There are also reports of interaction between lithium and neuromuscular blocking agents which may result in delayed recovery from anaesthesia.

Drug interactions: Concurrent use of lithium and diuretics may cause reduced lithium clearance, leading to intoxication. If a diuretic has to be prescribed for a lithium patient, the lithium dosage should first be lowered and the patient re-stabilised with frequent monitoring. Similar precautions should be exercised on diuretic withdrawal. Other drugs affecting electrolyte balance (e.g. appetite suppressants, steroids) may alter lithium excretion and should be avoided in patients on lithium. Raised plasma levels of ADH may occur during treatment. If other psychotropic drugs are used they should be initiated at a lower dosage than usual, as their side effects may be potentiated by the use of lithium. This has been shown to be of particular importance for the concurrent use of lithium and haloperidol or flupenthixol.

There have been isolated reports of possible interactions between lithium and diazepam (resulting in hypothermia), methylgopa, propranolol, tetracyclines, phenytoin and indomethacin.

Warnings and adverse effects: *Side effects:* Side effects are usually related to serum lithium concentrations and are infrequent at levels below 1.0 mmol/l.

Mild gastrointestinal effects, nausea, vertigo, muscle weakness and a dazed feeling may occur initially, but frequently disappear after stabilisation. Fine hand tremors, polyuria and mild thirst may persist. Weight gain or oedema may present in some patients but should not be treated with diuretics.

Hypercalcaemia, hypermagnesaemia and hyperparathyroidism have been reported. Skin conditions including acne, psoriasis, generalised pustular psoriasis, rashes and leg ulcers have occasionally been reported as being aggravated by lithium treatment.

Long term treatment with lithium may be associated with disturbances of thyroid function, including goitre, hypothyroidism and thyrotoxicosis. Lithium-induced hypothyroidism may be managed successfully with concurrent thyroxine.

Nephrotoxicity: Up to one third of patients on lithium may develop polyuria with a urinary output of up to three litres per day. This is usually due to lithium blocking the effect of ADH and is reversible on lithium withdrawal. However, long term treatment with lithium may also result in permanent changes in kidney histology and impairment of renal function. High serum concentrations of lithium including episodes of acute lithium toxicity may aggravate these changes. The minimum clinically effective dose of lithium should always be used. In patients who develop polyuria or polydipsia, renal function should be monitored, e.g. with measurement of blood urea, serum creatinine and urinary protein levels in addition to routine serum lithium estimations.

Toxic effects: Such effects are indicative of impending lithium intoxication and they fall into two groups:

1. Gastro-intestinal: increasing anorexia, diarrhoea and vomiting.
2. Central nervous system: muscle weakness, lack of

co-ordination, drowsiness or lethargy progressing to giddiness with ataxia, tinnitus, blurred vision, dysarthria, coarse tremor and muscle twitching.

At blood levels about 2–3 mmol/l there may be a large output of dilute urine, with increasing disorientation, seizures, coma and death.

Patients should be instructed to stop taking their tablets and to report immediately for a serum lithium estimation if toxic symptoms occur.

Lithium intoxication: There is no specific antidote to lithium poisoning. In the event of accumulation, lithium should be stopped and serum estimations should be carried out every six hours.

Under no circumstances should a diuretic be used. Osmotic diuresis should be promoted (mannitol or urea infusion) or alkalinisation of the urine (sodium lactate or sodium bicarbonate infusion).

If the serum lithium level is over 4.0 mmol/l, if there is a deterioration in the patient's condition, or if the serum lithium concentration is not falling at a rate corresponding to a half-life of under 30 hours, peritoneal or haemodialysis should be instituted promptly. This should be

continued until there is no lithium in the serum or dialysis fluid. Serum lithium levels should be monitored for at least a further week to take account of any possible rebound in serum lithium levels as a result of delayed diffusion from body tissues.

Pharmaceutical precautions Store in a cool, dry place. Tablets should not be crushed, chewed, or taken with hot liquids nor any attempt made to dissolve them before administration: they may be halved to provide dosage increments of 200 mg.

Legal category POM.

Package quantities Securitainers of 100 and 1,000 tablets.

Further information Nil.

Product licence number 0357/5000.

**Trade Mark*

Dermal Laboratories Limited

Tatmore Place
Gosmore, Hitchin
Herts, SG4 7QR



ANHYDROL FORTE* ▼

Presentation Colourless evaporative solution containing Aluminium chloride hexahydrate 20% w/v.

Uses For the topical treatment of hyperhidrosis specifically involving axillae, hands or feet.

Directions Apply to the affected sites at night, as required, and allow to dry. Wash off in the morning.

Contra-indications, warnings, etc Care should be taken to restrict the application to the affected sites only. Keep away from the eyes. Do not bathe immediately before use and, if the axillae are treated, do not shave or use depilatories on this area within 12 hours before or after use.

Pharmaceutical precautions Store in a cool place away from flames. Always replace the cap tightly after use.

Legal category POM.

Package quantity Anhydrol Forte is packed in a 10 ml glass roll-on bottle.

Further information The formulation of Anhydrol Forte has been tested in widespread clinical practice, and has been shown to be effective when used in accordance with the recommended instructions. Should irritation occur, reduce the frequency of application and if necessary apply mild hydrocortisone cream.

References

Acta Dermato-venereologica, **55**, 241, 1975

British Medical Journal, **2**, 1447, 1976

British Medical Journal, **2**, 84, 1978

Product licence number 0173/0030.

DITHROCREAM* ▼

Presentation *Dithrocream 0.1%*: Pale yellow oil-in-water vanishing cream containing Dithranol BP 0.1% w/w. *Dithrocream 0.25%*: Pale yellow oil-in-water vanishing cream containing Dithranol BP 0.25% w/w. *Dithrocream Forte*: Pale yellow oil-in-water vanishing cream containing Dithranol BP 0.5% w/w.

Uses For the topical treatment of sub-acute and chronic psoriasis including psoriasis of the scalp.

Directions Dithrocream should be applied sparingly to the psoriatic lesions, preferably at night, and rubbed gently and carefully into the skin until absorbed. It is most important to avoid applying an excessive quantity which may cause unnecessary soiling and staining of the clothing and/or bed linen. In the morning a bath should be taken to remove any surplus cream, which will have become red/brown in colour. The margins of the lesion will gradually become stained purple/brown as treatment progresses, but this will disappear after cessation of treatment.

For use on the scalp, shampoo to remove scalar debris and any previous application. Dry the hair and, after suitably parting, rub the cream well into the lesions.

Treatment should be continued until the skin is entirely clear; i.e. when there is nothing to feel with the fingers and the texture is normal.

Contra-indications, warnings, etc A small proportion of patients are sensitive to any form of dithranol treatment. If the initial treatment produces excessive soreness or if the lesions spread (particularly when potent topical steroids have recently been used), reduce frequency of applications and in extreme cases stop treatment.

Dithrocream Forte should only be used under close and constant medical supervision by patients who have failed to respond to lower strengths of dithranol.

Not to be used for acute psoriasis.

Keep away from the eyes and always wash hands after use.

Pharmaceutical precautions Do not expose to excessive heat.

Legal category P.

Package quantities Dithrocream is supplied in collapsible tubes containing 50 grams.

Further information Dithrocream has been developed as a vanishing cream formulation of dithranol for particular convenience for home treatment and is especially suitable for the exposed surfaces and hairy regions of the body including psoriasis of the scalp.

References

British Journal of Dermatology, **100**, 475, 1979.

British Journal of Dermatology, **103**, 105, 1980.

Product licence numbers

Dithrocream 0.1% 0173/0029

Dithrocream 0.25% 0173/0028

Dithrocream Forte 0173/0027

EMULSIDERM* ▼

Presentation Pale blue/green liquid emulsion containing Benzalkonium chloride BP 0.5%, Liquid paraffin BP 25.0%, Isopropyl myristate BPC 25.0%.

Uses An aid in the treatment of dry skin conditions, especially those associated with eczema, ichthyosis or xeroderma. It permits re-hydration of the keratin by replacing lost lipids, and its antiseptic properties assist in overcoming secondary infection.

Directions Always shake bottle before use.

For use in the bath: Add 2–3 capfuls to a 6–8 inch bath of warm water. For infant bathing use 1–2 capfuls. Soak for 5–10 minutes. Pat dry.

For application to the skin: Rub a small amount of

undiluted emollient into the dry areas of skin until absorbed.

Contra-indications, warnings, etc Keep away from the eyes. Take care to avoid slipping in the bath.

Pharmaceutical precautions Store in a cool place. Always replace cap after use.

Legal category P.

Package quantity Emulsiderm is presented in a 250 ml polythene bottle with a 10 ml measuring cap.

Further information Emulsiderm contains the antiseptic Benzalkonium chloride in an emulsion system which permits rapid dispersion of its oil content in the bath water.

Product licence number 0173/0036.

EXTEROL* ▼

Presentation Viscous solution containing Urea hydrogen peroxide 5.0% w/w.

Uses An aid in the removal of hardened ear wax.

Directions Remove the protective cap, invert the pipette above the opening of the affected ear and, with the head tilted sideways, gently squeeze 5–10 drops into the ear. Retain drops in ear for several minutes by keeping head tilted or, alternatively, by gently inserting a small plug of cotton wool into the outer ear.

Repeat once or twice daily for at least 3–4 days or as directed by the physician.

Contra-indications, warnings, etc Keep away from the eyes. Do not use if eardrum is known or suspected to be perforated. Stop usage if irritation or pain occurs.

Pharmaceutical precautions Store in a cool place. After use, always replace cap and return bottle to carton.

Legal category P.

Package quantity Exterol is presented in a 12 ml amber glass bottle, incorporating a specially designed pipette enclosed in a protective cap.

Further information After insertion of the drops into the ear, the urea hydrogen peroxide liberates oxygen which acts to break up the hardened wax. Subsequently, the glycerin and urea assist in the softening of the wax in order that it may more easily be removed from the ear, either with or without syringing. Due to the release of oxygen, patients may experience a mild, temporary effervescence in the ear.

Product licence number 0173/0037.

GLUTAROL*

Presentation Colourless evaporative solution containing Glutaraldehyde 10.0% w/v.

Uses For topical use in the treatment of viral warts with the exception of warts on the face and those in the anal and perineal regions.

Directions To be applied to the wart twice daily or as directed by the physician. Pare down hard skin if it develops on and around the wart.

Contra-indications, warnings, etc Keep away from the eyes.

Pharmaceutical precautions Glutarol should be stored in a cool place away from flames.

Legal category P.

Package quantity Glutarol is packed in a 10 ml amber glass bottle fitted with a spatula for ease of application.

Further information Glutaraldehyde is virucidal^{1, 2} and thus inactivates the wart virus. On the skin, it also acts as an anhydrotic^{3, 4} drying the warts and surrounding skin, so reducing spread of lesions and making more simple the removal of persistent warts by curettage.

As the preparation stains the outer layers of the skin brown, treatment can be seen to be carried out.⁵

References

1. *Applied Microbiology*, **17**, 645, 1969.
2. *Journal of General Virology*, **13**, 415, 1971.
3. *Archives of Dermatology*, **97**, 327, 1968.
4. *Archives of Dermatology*, **100**, 564, 1969.
5. *British Journal of Clinical Practice*, **31**, 12, 1977.

Product licence number 0173/0022.

SALACTOL*

Presentation A collodion paint containing Lactic acid BP 16.7% w/w, Salicylic acid BP 16.7% w/w, Flexible collodion BP 66.6% w/w.

Uses Keratolytic and antiviral. For the treatment of warts, particularly plantar warts.

Directions for use *First day:* Paint the wart and leave to dry, taking care to prevent the paint running. Cover with a waterproof plaster and leave for 24 hours.

Subsequent days: Remove the plaster and using a pumice stone rub away the treated surface of the wart. Repeat the application covering with a fresh waterproof plaster.

Contra-indications, warnings, etc Salactol should not be used on warts near the eyes. It does not normally cause any inflammation of the skin around the wart, but should this occur, treatment should be suspended until the inflammation disappears.

Pharmaceutical precautions Salactol should be stored in a cool place away from flames.

Legal category P.

Package quantity Salactol is packed in a 10 ml amber glass bottle fitted with a spatula for ease of application.

Further information In 76 patients with plantar warts 84% were cured at 12 weeks without any side-effects.¹ Salactol may be applied successfully by the patient in his own home.²

References

1. *Practitioner*, **207**, 197, 1971.
2. *Prescribers' Journal*, **14**, 118, 1974.

Product licence number 0173/5006.

*Trade Mark

ALLEGRON®

Presentation Tablets each containing the equivalent of 25 mg nortriptyline (as the hydrochloride). The tablets are orange, scored and have a diameter of 8 mm. They are marked 'DD NN'.

Tablets each containing the equivalent of 10 mg nortriptyline (as the hydrochloride). The tablets are yellow, unscored and have a diameter of 5.5 mm. They are marked 'DN'.

Uses Allegron is indicated for the relief of symptoms of depression. It may also be used for the treatment of some cases of nocturnal enuresis.

Dosage and administration For oral administration.

Adults: The usual adult dose is 20–40 mg daily in divided doses, increasing to 100 mg daily where necessary. The usual maintenance dose is 30–75 mg/day.

The elderly: Initial dosage should be 10 mg three times a day. This may be increased with caution under close supervision. Half the normal maintenance dose may be sufficient to produce a satisfactory clinical response.

Children: (for nocturnal enuresis only)

Age (years)	Weight		Dose (mg)
	kg	lbs	
6–7	20–25	44–55	10
8–11	25–35	55–77	10–20
> 11	35–54	77–119	25–35

The dose should be administered thirty minutes before bedtime.

The maximum period of treatment should not exceed three months. A further course of treatment should not be started until a full physical examination, including an ECG, has been made.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to nortriptyline.

Recent myocardial infarction, any degree of heart block or other cardiac arrhythmias.

Severe liver disease. Mania.

Nortriptyline is contra-indicated for the nursing mother and for children under the age of six years.

Warnings: As improvement may not occur during the initial weeks of therapy, patients, especially those posing a high suicidal risk, should be closely monitored during this period.

Withdrawal symptoms, including insomnia, irritability and excessive perspiration may occur on abrupt cessation of therapy.

The use of nortriptyline in schizophrenic patients may result in an exacerbation of the psychosis or may activate latent schizophrenic symptoms. If administered to over-active or agitated patients, increased anxiety and agita-

tion may occur. In manic-depressive patients, nortriptyline may cause symptoms of the manic phase to emerge.

Cross sensitivity between nortriptyline and other tricyclic antidepressants is a possibility.

Patients with cardiovascular disease should be given nortriptyline only under close supervision because of the tendency of the drug to produce sinus tachycardia and to prolong the conduction time. Myocardial infarction, arrhythmia and strokes have occurred. Great care is required if nortriptyline is administered to hyper-thyroid patients or to those receiving thyroid medication, since cardiac arrhythmias may develop.

Nortriptyline may impair the mental and/or physical abilities required for the performance of hazardous tasks, such as operating machinery or driving a car; therefore the patient should be warned accordingly.

Drug interactions: Under no circumstances should nortriptyline be given concurrently with, or within two weeks of cessation of, therapy with monoamine oxidase inhibitors. Hyperpyretic crises, severe convulsions and fatalities have occurred when similar tricyclic antidepressants were used in such combinations.

Nortriptyline should not be given with sympathomimetic agents such as adrenaline, ephedrine, isoprenaline, noradrenaline, phenylephrine and phenylpropanolamine.

Nortriptyline may decrease the anti-hypertensive effect of guanethidine, debrisoquine, bethanidine and possibly clonidine. Concurrent administration of reserpine has been shown to produce a 'stimulating' effect in some depressed patients. It would be advisable to review all anti-hypertensive therapy during treatment with tricyclic antidepressants.

Barbiturates may increase the rate of metabolism of nortriptyline.

Usage in pregnancy: The safety of nortriptyline for use during pregnancy has not been established, nor is there evidence from animal studies that it is free from hazard; therefore the drug should not be administered to pregnant patients or women of childbearing age unless the potential benefits clearly outweigh any potential risk.

Precautions: The elderly are particularly liable to experience adverse reactions, especially agitation, confusion and postural hypotension.

Behavioural changes may occur in children receiving therapy for the treatment of nocturnal enuresis.

If possible, the use of nortriptyline should be avoided in patients with narrow angle glaucoma, symptoms suggestive of prostatic hypertrophy or a history of epilepsy.

When it is essential, nortriptyline may be administered with electroconvulsive therapy, although the hazards may be increased.

Anaesthetics given during tricyclic antidepressant therapy may increase the risk of arrhythmias and hypotension. If surgery is necessary, the drug should be

discontinued, if possible, for several days prior to the procedure, or the anaesthetist should be informed if the patient is still receiving therapy.

Tricyclic antidepressants may potentiate the CNS depressant effect of alcohol.

Both elevation and lowering of blood sugar levels have been reported.

Side-effects: Cardiac arrhythmias and severe hypotension are likely to occur with high dosage, or in patients with pre-existing heart disease taking normal dosage.

Other common side-effects include drowsiness, sweating, postural hypotension, tremor and skin rashes.

The following are seen occasionally: dizziness, confusion, restlessness, weakness, impotence and blurred vision. Side-effects rarely noted are epigastric distress, nausea and vomiting, dysgeusia, excessive weight gain, excessive weight loss, fatigue, insomnia, headache, paraesthesiae and pruritus.

The following adverse effects, although not necessarily all reported with nortriptyline, have occurred with other tricyclic antidepressants: atropine-like side-effects including dry mouth, disturbances of accommodation, tachycardia, constipation and hesitancy of micturition are common early in treatment, but usually lessen.

Serious adverse effects are rare; the following have been reported: depression of the bone marrow including agranulocytosis, cholestatic jaundice, hypomania, convulsions and peripheral neuropathy.

Adverse effects such as withdrawal symptoms, respiratory depression and agitation have been reported in neonates whose mothers had taken tricyclic antidepressants during the last trimester of pregnancy.

Overdose: Toxic overdose may result in confusion, restlessness, agitation, vomiting, hyperpyrexia, muscle rigidity, hyperactive reflexes, tachycardia, cardiac arrhythmias, ECG evidence of impaired conduction, shock, congestive heart failure, severe hypotension, stupor, coma and CNS stimulation with convulsions followed by respiratory depression. Deaths have occurred following overdose with drugs of this class.

Treatment: No specific antidote is known. General supportive measures are indicated, with gastric lavage. Activated charcoal absorbs tricyclic antidepressants very effectively. Respiratory assistance is apparently the most effective measure when indicated. The use of CNS depressants may worsen the prognosis.

Intramuscular paraldehyde or diazepam provides anticonvulsant activity with less respiratory depression than the barbiturates.

The use of digitalis and/or pyridostigmine may be considered in the event of serious cardiovascular abnormalities or cardiac failure.

The value of dialysis has not been established.

Pharmaceutical precautions Store in a cool (6°–15°C), dry place.

Legal category POM.

Package quantities

Tablets 25 mg: Bottles of 100 and 500.

Tablets 10 mg: Bottles of 100 and 500.

Further information Nil.

Product licence numbers

Tablets 25 mg 0006/5003

Tablets 10 mg 0006/5002

CAPASTAT®

Presentation Capreomycin sulphate as sterile white powder for intramuscular injection, in sealed vials each containing 1,000,000 Units (approximately equivalent to 1 g capreomycin base).

Uses For the treatment of pulmonary infections caused by capreomycin-susceptible strains of *M. tuberculosis* when the primary agents (isoniazid, rifampicin, streptomycin and para-aminosalicylic acid) have been ineffective or cannot be used because of toxicity or the presence of resistant tubercle bacilli.

Dosage and administration The usual dose is 1 g daily (not to exceed 20 mg/kg/day) given intramuscularly for 60 to 120 days, followed by 1 g intramuscularly two or three times a week. Capreomycin sulphate should be dissolved in 2 ml of 0.9% Sodium Chloride Intravenous Infusion BP or Water for Injections PhEur. Two or three minutes should be allowed for complete solution. For administration of a 1 g dose, the entire contents of the vial should be given.

Contra-indications, warnings, etc

Contra-indication: Hypersensitivity to the drug.

Warnings: The use of capreomycin in patients with renal insufficiency or pre-existing auditory impairment must be undertaken with great caution, and the risk of additional eighth cranial nerve impairment or renal injury should be weighed against the benefits to be derived from therapy.

Simultaneous administration of other antituberculous agents (e.g. streptomycin, viomycin) which also have ototoxic and nephrotoxic potential is not recommended.

Use with non-antituberculous drugs (polymyxin, colistin sulphate, gentamicin, tobramycin, vancomycin, kanamycin and neomycin) having ototoxic or nephrotoxic potential should also be undertaken only with great caution.

Usage in pregnancy: The safety of capreomycin for use during pregnancy has not been established.

The safety of capreomycin for use in infants and children has not been established.

Precautions: Audiometric measurements and assessment of vestibular function should be performed prior to initiation of therapy with capreomycin and at regular intervals during treatment.

Regular tests of renal function should be made throughout the period of treatment, and reduced dosage should be employed in patients with known or suspected renal impairment.

Since hypokalaemia may occur during capreomycin therapy, serum potassium levels should be determined frequently.

Capreomycin should be administered cautiously to patients with a history of drug allergy.

Side-effects: Kidney – Elevation of serum creatinine or serum urea and abnormal urine sediment have been observed.

Liver – A decrease in bromsulphthalein excretion without change in serum enzymes has been noted in the presence of pre-existing liver disease. Abnormal results in liver function tests have occurred in many patients receiving capreomycin in combination with other antituberculous agents which are also known to cause changes in hepatic function. Periodic determinations of liver function are recommended.

Blood – Leucocytosis and leucopenia have been observed.

Hypersensitivity – Urticaria and maculopapular skin rashes associated in some cases with febrile reactions have been reported when capreomycin and other antituberculous drugs were given concomitantly.

Ototoxicity – Clinical and subclinical auditory loss has been noted. Some audiometric changes are reversible, and others with permanent loss are not progressive following withdrawal of capreomycin. Tinnitus and vertigo have occurred.

Pain and induration at the injection sites have been observed. Excessive bleeding at the injection site has been reported. Sterile abscesses have been noted.

Pharmaceutical precautions *Dry powder:* Store in a cool (6°–15°C), dry place. *When reconstituted:* The solution should be stored in a refrigerator (0°–6°C) and be used within 14 days. At room temperature (15°–25°C) it should be used within 48 hours.

Legal category POM.

Package quantities Vials of 1,000,000 Units (1 g base approximately). Pack of 5 vials.

Further information Must be used only in conjunction with adequate doses of other antituberculous drugs. The use of Capastat alone allows the rapid development of strains resistant to it. Frequent cross-resistance occurs between capreomycin and viomycin. Varying degrees of cross-resistance between capreomycin and kanamycin or neomycin have been reported. No cross-resistance has been observed between capreomycin and isoniazid, aminosalicylic acid, cycloserine, streptomycin, ethionamide or ethambutol.

Product licence number 0006/5005.

DIREMA*

Presentation Tablets each containing the equivalent of 25 mg Hydrochlorothiazide BP. The tablets are white, blank and unscored, with a diameter of 7 mm.

Tablets each containing the equivalent of 50 mg Hydrochlorothiazide BP. The tablets are white, unscored, with a diameter of 8 mm and marked 'DD HF'.

Uses Oral diuretic. All oedematous states where a diuretic is required. Hypertension in conjunction with hypotensive drugs.

Dosage and administration For oral administration.

Oedema: From 25 mg once or twice daily to 75 mg or 100 mg twice daily, depending on the severity of the oedema and the response secured. Doses should be taken at breakfast time and shortly after lunch, so that the main diuretic action occurs during the day; the patient's sleep is then undisturbed.

Hypertension: Direma potentiates the action of hypotensive drugs, especially the ganglion blocking agents. Thus when it is used in conjunction with hypotensives, the dosage of the latter should be reduced immediately by 25–50%. The recommended starting dosage with Direma is 25–50 mg once or twice daily, with subsequent adjustments determined by the patient's response. By adopting combined therapy of this type the resultant control of blood pressure is usually smoother, with less fluctuation between doses.

Contra-indications, warnings, etc

Contra-indication: No contra-indications are known.

Side-effects and precautions: Direma rarely gives rise to

side-effects. If mild nausea is noticed doses should be taken with meals or with a short drink of milk or water. To avoid the risk of potassium depletion, it is sound practice to limit therapy to four-day periods with potassium chloride or potassium citrate being administered during the next three days at doses of 2–4 g daily. Alternatively, Direma may be given for a two-week period followed by a course of potassium during the third week. Whichever routine is adopted, the cycle is repeated as necessary – with suitable adjustments of dosage according to the patient's response.

When Direma is prescribed for patients already receiving digitalis, they should be monitored for signs of digitalis overdose as a secondary effect of potassium depletion. When there is impairment of renal function, Direma may cause some increase in blood urea. Should this occur, dosage should be reduced or the treatment completely withheld for a few days.

Warning: The safety of Direma for use during pregnancy has not been established.

Pharmaceutical precautions Store in a cool (6°–15°C), dry place.

Legal category POM.

Package quantities Tablets 25 mg: Bottles of 100. Tablets 50 mg: Bottles of 100.

Further information Nil.

Product licence numbers

Tablets 25 mg 0006/5006

Tablets 50 mg 0006/5007

DISTACLOR* ▼

Presentation Capsules (violet and white, printed Distaclor 250) containing 250 mg cefaclor.

Granules (pink) for suspension containing 125 mg cefaclor/5 ml.

Granules (pink) for suspension containing 250 mg cefaclor/5 ml.

Uses Distaclor is indicated for the treatment of the following infections due to susceptible micro-organisms:

Respiratory tract infections, including pneumonia, bronchitis, exacerbations of chronic bronchitis, pharyngitis and tonsillitis.

Otitis media.

Skin and soft tissue infections.

Urinary tract infections, including pyelonephritis and cystitis.

Distaclor has been found to be effective in both acute and chronic urinary tract infections.

Cefaclor is active against the following organisms *in vitro*:

Alpha- and beta-haemolytic streptococci

Staphylococci; including coagulase-positive, coagulase-negative and penicillinase-producing strains

Streptococcus pneumoniae

Escherichia coli

Proteus mirabilis

Klebsiella species

Haemophilus influenzae, including ampicillin-resistant strains.

Cefaclor has no activity against *Pseudomonas* species.

Cefaclor is not active against most strains of enterococci (*Str. faecalis*), *Enterobacter*, indole-positive *Proteus* and *Serratia* species. Some rare strains of staphylococci are resistant to cefaclor.

Dosage and administration Distaclor is administered orally.

Adults: The usual adult dosage is 250 mg every eight hours. For more severe infections or those caused by less susceptible organisms, doses may be doubled. Doses of 4 g per day have been administered safely to normal subjects for 28 days, but the total daily dosage should not exceed this amount.

Distaclor may be administered in the presence of impaired renal function. Under such conditions dosage is unchanged (see *Precautions*).

Patients undergoing haemodialysis: Haemodialysis shortens serum half-life by 25–30%. In patients undergoing regular haemodialysis, a loading dose of 250 mg–1 g administered prior to dialysis and a therapeutic dose of 250–500 mg every six to eight hours maintained during interdialytic periods is recommended.

Children: The usual recommended daily dosage for children is 20 mg/kg/day in divided doses every eight hours, as indicated.

Distaclor suspension

	125 mg/5 ml	250 mg/5 ml
< 1 year	2.5 ml tid	
1–5 years	5.0 ml tid	
Over 5 years		5.0 ml tid

In more serious infections, otitis media and infections caused by less susceptible organisms, 40 mg/kg/day is recommended, up to a daily maximum of 1 g.

In the treatment of beta-haemolytic streptococcal infections, therapy should be continued for at least 10 days.

Contra-indications, warnings, etc

Contra-indication: Hypersensitivity to cephalosporins.

Warnings: Cephalosporins should be given cautiously to patients with known penicillin sensitivity, as there is evidence of partial cross-allergenicity between the penicillins and cephalosporins. Severe reactions (including anaphylaxis) have been reported occasionally in patients receiving penicillins or cephalosporins.

Usage in pregnancy: The safety of cefaclor for use during pregnancy has not been established.

Precautions: If an allergic reaction to cefaclor occurs the drug should be discontinued and the patient treated with the appropriate agents.

Cefaclor should be administered with caution in the presence of markedly impaired renal function. Under such conditions, safe dosage may be lower than that usually recommended.

Prolonged use of cefaclor may result in the overgrowth of non-susceptible organisms. If superinfection occurs during therapy, appropriate measures should be taken.

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. In haematological studies or in transfusion cross-matching procedures when anti-globulin tests are performed on the minor side, or in Coombs' testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognised that a positive Coombs' test may be due to the drug.

A false-positive reaction for glucose in the urine may occur with Benedict's or Fehling's solutions or with copper sulphate test tablets, but not with Tes-Tape* (urine sugar analysis paper, Lilly).

Side-effects: Gastro-intestinal – The most frequent side-effect has been diarrhoea. It is rarely severe enough to warrant cessation of therapy. Colitis, including rare instances of pseudomembranous colitis, has been reported. Nausea and vomiting have also occurred.

Hypersensitivity – Allergic reactions, such as urticaria, morbilliform eruptions and pruritus, have been observed. These reactions usually subsided upon discontinuation of therapy. Serum sickness-like reactions, including the above skin manifestations, fever and arthralgia/arthritis, have been reported. Anaphylaxis has also occurred.

Liver – Slight elevations in AST (SGOT) and ALT (SGPT) have been reported.

Miscellaneous – Eosinophilia, positive Coombs' tests and genital pruritus and vaginitis have occurred.

Pharmaceutical precautions Store at room temperature (15–25°C). Keep containers tightly closed and protect from light. After reconstitution, the suspension should be stored in a refrigerator (0–6°C) and be used within 14 days. When dilution is unavoidable, Syrup BP should be used after the suspension has been prepared according to the manufacturer's instructions.

Legal category POM.

Package quantities

Capsules 250 mg: Bottles of 20 and 100.

Suspension 125 mg/5 ml: Bottles of 100 ml.

Suspension 250 mg/5 ml: Bottles of 100 ml.

Further information Nil.

Product licence numbers

Capsules 250 mg 0006/0118

Suspension 125 mg/5 ml 0006/0120

Suspension 250 mg/5 ml 0006/0121

DISTALGESIC*

DISTALGESIC* Soluble

Presentation Tablets each containing 32.5 mg Dextropropoxyphene Hydrochloride BP (equivalent to approximately 30 mg dextropropoxyphene base) with 325 mg Paracetamol PhEur. The tablets are white, pillow-shaped, film coated, 14 mm in length and marked 'DG'.

Soluble tablets each containing 50 mg Dextropropoxyphene Napsylate BP (equivalent to 32.5 mg dextropropoxyphene hydrochloride or 30 mg dextropropoxyphene base) with 325 mg Paracetamol PhEur. The tablets are white, octagonal, with a diameter of 12.5 mm and marked 'DGS'.

Uses Analgesic: For the management of mild to moderate pain.

Dosage and administration For oral administration to adults only.

Dosage: The usual dose is 2 tablets three or four times daily and should not normally be exceeded.

Soluble tablets should be stirred in a little water until dispersed.

Contra-indications, warnings, etc

Contra-indication: Hypersensitivity to dextropropoxyphene or paracetamol.

Warnings: Dextropropoxyphene is an analgesic with CNS depressant properties and should be used with caution in patients who are receiving other CNS

depressant drugs, as an additive effect may occur. Patients should be warned to avoid alcohol.

As with other drugs which affect the CNS, care should be taken when prescribing for patients with personality or other psychological disorders. Tolerance, psychological and physical dependence may rarely occur.

Like other centrally acting drugs, dextropropoxyphene may impair patients' mental and physical reactions in the performance of potentially hazardous tasks (e.g. driving ability, operation of machinery, etc.) to a varying extent, depending on dosage and individual susceptibility.

Overdosage of paracetamol may damage the liver, due to the accumulation of intermediate metabolites which cause hepatic necrosis.

Use in pregnancy: The safety of Distalgesic for use during pregnancy has not been established.

Side-effects: Side-effects such as dizziness, sedation, nausea and vomiting seem to be more prominent in ambulatory than in non-ambulatory patients, and some of these side-effects may be alleviated if the patient lies down.

Other reported side-effects include constipation, abdominal pain, skin rashes, lightheadedness, headache, weakness, euphoria, dysphoria and minor visual disturbances.

Overdosage: The chronic ingestion of dextropropoxyphene in doses exceeding 720 mg (as base) per day has caused toxic psychoses and convulsions.

Symptoms of acute toxicity may be rapid in onset, with the danger of respiratory arrest. Other recognised manifestations include respiratory depression, coma, circulatory collapse, pulmonary oedema, convulsions and cardiac arrhythmias.

Deterioration may be rapid, with fatal outcome.

Paracetamol overdosage is associated with nausea and vomiting and frequently with abdominal pain. Subsequent evidence of liver dysfunction may be apparent after 24 hours, and if severe, may lead to reversible hepatic necrosis and death.

Treatment: Primary attention should be given to the re-establishment of adequate respiratory exchange through provision of a patent airway and institution of assisted or controlled ventilation. The narcotic antagonist naloxone is a specific antidote against the respiratory depression produced by dextropropoxyphene. An appropriate dose of this antagonist should be administered, preferably by the intravenous route, simultaneously with efforts at respiratory resuscitation. Repeated doses of the antagonist may be necessary over a prolonged period due to the slow elimination of dextropropoxyphene.

In addition to the use of a narcotic antagonist, the patient may require careful titration with an anticonvulsant to control seizures. Analeptic drugs (for example, caffeine or amphetamine) should not be used because of their tendency to precipitate convulsions.

Early assessment of the severity of paracetamol poisoning by measurement of plasma paracetamol levels is essential if treatment, which should be instituted within 10 hours of ingestion, is to be effective. Present evidence suggests that cysteamine, methionine or N-acetylcysteine given within this period are effective in greatly reducing the toxic effects of paracetamol.

Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated.

Gastric lavage may be helpful. Activated charcoal can absorb a significant amount of ingested dextropropoxyphene.

Pharmaceutical precautions Store in a cool (6°–15°C), dry place.

Distalgesic Soluble tablets: Dispense in moisture-proof containers.

Legal category POM.

Package quantities

Distalgesic tablets: Blister packs of 100 (10 strips of 10 tablets). Bottles of 100 and 500 (available to hospitals only).

Distalgesic Soluble tablets: Bottles of 50.

Further information Nil.

Product licence numbers

Distalgesic tablets 0006/5000

Distalgesic Soluble tablets 0006/5001

DISTAMINE*

Presentation Tablets each containing 50 mg, 125 mg or 250 mg D-penicillamine base.

The 50 mg tablets are white, coated, scored and have a diameter of 5.5 mm.

The 125 mg tablets are white, coated, marked 'DS', and have a diameter of 8 mm.

The 250 mg tablets are white, coated, marked 'DM', and have a diameter of 10 mm.

Uses

1. Severe, active rheumatoid arthritis unresponsive to other treatment, including juvenile forms.

2. As a chelating agent in the treatment of Wilson's disease and lead poisoning.

3. In the treatment of cystinuria in cases where high fluid regimens are not adequate.

Dosage and administration For oral administration.

1. **Rheumatoid arthritis: Adults:** Not more than 250 mg daily for the first four weeks, increasing by the amount of the starting dose at intervals of four to eight weeks until remission of symptoms commences. Many patients respond to a daily dose within the 500–750 mg range. Some need less, and others as much as 2 g daily. The therapeutic response to Distamine is delayed for several weeks so that if unnecessarily high doses are to be avoided each increment must be allowed time for its effect to develop. Rapid increase of dose or the use of full doses from the beginning gives rise to many adverse reactions without any countervailing benefits.

If suppression of rheumatoid activity appears to have been achieved at a particular dose of Distamine this dose should be maintained for at least six months and then progressively reduced by 250 mg at intervals of two to three months. Relapse after withdrawal or at an inadequate dose level usually occurs within three months. Most patients respond to further courses of Distamine.

Paediatric Dosage

Week of therapy	Weight of child	
	Less than 20 kg	More than 20 kg
0 to 2	25 mg bd	50 mg bd
2 to 4	50 mg bd	100 mg bd
4 to 6	100 mg bd	100 mg tid
6 to 10	100 mg tid	150 mg tid
10 to 14	150 mg tid	200 mg tid

As with adult patients, the dose should be kept to the lowest effective level.

2. *Wilson's disease*: Up to 2 g daily in divided doses.
Lead poisoning: Up to 1 g daily in divided doses.

For children the dose is up to 20 mg/kg/day in divided doses. Gradual introduction of Distamine is *not* advocated in these conditions.

3. *Cystinuria*: A single 500 mg dose on retiring, following free fluids during the day, may effect stone dissolution in a functioning kidney. Otherwise 750 mg–1 g daily in divided doses is generally adequate and it should not be necessary to exceed 2 g daily.

4. *Desensitisation*: No fixed dose regimen. An initial dose of 25 mg daily is suggested, this to be gradually increased in accordance with the response of the patient.

Contra-indications, warnings, etc

Contra-indication: Hypersensitivity to penicillamine, except in a life-threatening situation.

Side-effects and adverse reactions: Most adverse reactions to Distamine are attributable to its activity as an allergen. Early symptoms of intolerance include nausea, anorexia, vomiting and fever, with or without rash, usually of morbilliform type. Thrombocytopenia and neutropenia may occur at any time and usually respond rapidly to withdrawal of Distamine, although deaths from agranulocytosis and aplastic anaemia have been recorded.

Disturbance of taste is common in the early weeks but usually resolves despite continuation of Distamine therapy. Early transient proteinuria may be observed. After about six months some 20% of patients develop more persistent proteinuria which sometimes becomes progressively heavier, or is accompanied by microscopic haematuria. Nephrotic syndrome may occur. Other disorders of later onset and attributed to Distamine are lupus erythematosus and rheumatoid-like reactions, myasthenia, stomatitis and varied lesions of the skin including pemphigus, though rarely. Goodpasture's syndrome and haemolytic anaemia have been reported.

Precautions: The frequency and severity of the adverse reactions are reduced by gradual introduction and low maintenance doses of Distamine.

White blood cell and platelet counts and tests of the urine for protein and blood are mandatory throughout treatment at not more than monthly intervals. During the first six weeks these should be weekly or fortnightly. A falling platelet or neutrophil count, even within the normal range, over three successive counts indicates withdrawal.

If Distamine is withdrawn because of thrombocytopenia (below 120,000/cumm) or neutropenia (below 2,000/cumm) recovery will be rapid and one further attempt to reinstitute Distamine may then be made. The starting dose should not exceed 250 mg daily and this should be maintained for four weeks before further gradual increases are made.

If proteinuria is detected this must be quantified in a 24-hour collection. Heavy or steadily increasing proteinuria or significant haematuria call for withdrawal of Distamine.

Allergic rash occurring early, unless severe, responds to cyproheptadine and temporary reduction of dose of Distamine.

Copper or zinc supplements are not recommended for prophylaxis or treatment of taste impairment.

Warnings: The safety of Distamine for use during pregnancy has not been established. There have been a

number of successful pregnancies in patients with Wilson's disease with no reports of adverse effects of the fetus.

Patients who have experienced reactions to gold therapy may be particularly prone to Distamine reactions; so that Distamine should be begun with a 125 mg dose which should be increased only at monthly intervals.

Because of the slowness of the response to Distamine existing treatment of rheumatoid arthritis by analgesic; anti-inflammatory drugs or steroids should be maintained and only gradually reduced later.

Distamine forms complexes with certain heavy metals including iron, therefore simultaneous oral therapy should not be given.

Treatment of overdosage: No instance of adverse reaction to an overdose of Distamine has been recorded and no specific measures are indicated.

Pharmaceutical precautions Store in a dry place below 25°C. Keep containers tightly closed.

Legal category POM.

Package quantities

Tablets 50 mg: Bottles of 100.

Tablets 125 mg: Bottles of 100.

Tablets 250 mg: Bottles of 100.

Further information Occasionally patients with rheumatoid arthritis who have responded initially to particular dose begin to relapse. Most of these will respond to a dose increase which should be gradual. Both sero-negative and sero-positive rheumatoid arthritis usually respond to Distamine.

Product licence numbers

Tablets 50 mg 0006/0105

Tablets 125 mg 0006/0090

Tablets 250 mg 0006/5008

DISTAQUAINE* V-K

Presentation Phenoxymethylpenicillin Potassium

Tablets BP: containing the equivalent of 125 mg or 250 mg phenoxymethylpenicillin. The 125 mg tablets are white, scored, 8 mm in diameter and marked 'D VK'. The 250 mg tablets are white, scored, 10.5 mm in diameter and marked 'DD KF'.

Syrup: granules for the preparation of Phenoxymethylpenicillin Elixir BPC, 125 mg/5 ml or 250 mg/5 ml. The granules are pale pink, converting to orange liquid on reconstitution.

Elixir: granules for the preparation of Phenoxymethylpenicillin Elixir BPC, 62.5 mg/5 ml. The granules are pale pink, converting to orange liquid on reconstitution.

Uses Penicillin exerts high activity *in vitro* against: staphylococci (except penicillinase-producing strains streptococci (groups A, C, G, H, L and M), pneumococci, *Corynebacterium diphtheriae*, *Bacillus anthracis*, *Actinomyces bovis*, *Streptobacillus moniliformis*, *Listeria monocytogenes*, *Neisseria gonorrhoeae*, *Treponema pallidum*, *Clostridium* species and *Leptospira*.

Phenoxymethylpenicillin and potassium phenoxymethylpenicillin are indicated in the treatment of mild to moderately severe infections associated with microorganisms whose susceptibility to penicillin is within the range of serum levels attained with these dosage forms.

The following infections will usually respond to adequate doses:

Streptococcal infections (without bacteraemia) – mild to moderate infections of the upper respiratory tract, scarlet fever and mild erysipelas.

Vote: Streptococci in groups A, C, G, H, L and M are very sensitive to penicillin. Other groups, including group D (enterococci), are resistant.

Neumococcal infections – mild to moderately severe infections of the respiratory tract.

Staphylococcal infections sensitive to penicillin – mild infections of the skin and soft tissues.

Vote: reports indicate an increasing number of strains of staphylococci resistant to penicillin G, which emphasises the need for culture and susceptibility studies when treating suspected staphylococcal infections.

Fusospirochetosis (Vincent's gingivitis and pharyngitis) – mild to moderately severe infections of the oropharynx usually respond to therapy with oral penicillin.

Prophylactic use – Prophylaxis with oral penicillin has proved effective in preventing recurrence of rheumatic fever and chorea.

Patients with a past history of rheumatic fever receiving continuous prophylaxis may harbour penicillin-resistant organisms. In these patients, the use of another prophylactic agent should be considered.

Vote: Oral penicillin should not be used as adjunctive prophylaxis for genito-urinary instrumentation or surgery, lower intestinal tract surgery, sigmoidoscopy and childbirth.

Dosage and administration For oral administration.

Adults: 125 mg or 250 mg every four to six hours depending on the severity of the condition.

Children over 5 years: The adult dose.

Children 5 years or less: 125 mg every six hours.

Infants (up to 1 year): 62.5 mg every six hours.

In all but the most serious cases, the last dose of the day may be doubled to avoid disturbing sleep. Ideally, each dose should be given half an hour before (or at least three hours after) a meal.

Diluents: For elixir and syrup, where dilution is unavoidable, Syrup BP should be used after the solution has been prepared according to the manufacturer's instructions.

Contra-indications, warnings, etc A previous hypersensitivity reaction to any penicillin is a contra-indication.

Warnings: All degrees of hypersensitivity including fatal anaphylaxis have been observed with oral penicillin. These reactions are more likely to occur in individuals with a history of sensitivity to multiple allergens, and inquiry should be made for such a history before therapy is begun. If an allergic reaction occurs, the drug should be discontinued and the patient treated with the usual agents (e.g. adrenaline and other pressor amines, antihistamines and corticosteroids).

Precautions: Penicillin should be used with caution in individuals with histories of significant allergies and/or asthma.

Oral therapy should not be relied upon in patients with severe illness, or with nausea, vomiting, gastric dilatation, aridospasm or intestinal hypermotility.

Occasionally patients do not absorb therapeutic amounts of orally administered penicillin.

Streptococcal infections should be treated for a minimum of 10 days, and post-therapy cultures should be performed to confirm the eradication of the organisms.

Prolonged use of antibiotics may promote the overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, appropriate measures should be taken.

Adverse reactions: The most common reactions to oral penicillin are nausea, vomiting, epigastric distress, diarrhoea and black, hairy tongue.

Hypersensitivity reactions observed may be skin eruptions, urticaria, reactions resembling serum sickness, chills, fever, oedema, arthralgia, prostration, laryngeal oedema and anaphylaxis. Fever and eosinophilia may frequently be the only reactions observed. Haemolytic anaemia, leucopenia, thrombocytopenia, neuropathy and nephropathy are infrequent reactions and are usually associated with high doses of parenteral penicillin.

Pharmaceutical precautions **Tablets:** Store in a cool (6°–15°C), dry place. Protect from moisture.

Syrup and Elixir: Store in a cool place (6°–15°C) and protect from moisture. Reconstituted preparations should be stored in a cool place and used within seven days.

Legal category POM.

Package quantities

Tablets 125 mg: Bottles of 100 and 500.

Tablets 250 mg: Bottles of 100, 500 and 1,000.

Syrup Granules 125 mg/5 ml: Bottles of 100 ml (when reconstituted).

Syrup Granules 250 mg/5 ml: Bottles of 100 ml (when reconstituted).

Elixir Granules 62.5 mg/5 ml: Bottles of 100 ml (when reconstituted).

Further information Nil.

Product licence numbers

Tablets 125 mg 0006/5031

Tablets 250 mg 0006/5032

Syrup 125 mg/5 ml 0006/5121

Syrup 250 mg/5 ml 0006/5122

Elixir 62.5 mg/5 ml 0006/5119

FENOPRON[®] FENOPRON D[®]

Presentation *Fenopron* – Fenopron Calcium Tablets BP, each containing fenopron calcium equivalent to 300 mg fenopron or 600 mg fenopron.

Fenopron D – Dispersible tablets each containing fenopron calcium equivalent to 300 mg fenopron.

The 300 mg tablets are orange, elliptical, 14 mm long and marked DISTA 4019.

The 600 mg tablets are orange para-capsule, scored, 20 mm long and marked DISTA 4021.

The dispersible tablets are white, biconvex, triangular/trochoid, 14 mm long and marked FND.

Uses For the treatment of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis. For the relief of mild/moderate pain.

Dosage and administration For oral administration to adults only, and not recommended for administration

to children. Stir the dispersible tablets in half a cup of water.

Dosage: 300–600 mg three or four times a day.

300 mg tablet: Recommended initial dosage is 2 tablets three times per day, then adjusted to the needs of the patient.

600 mg tablet: Recommended initial dosage is 1 tablet three times per day, plus one at night if necessitated by a more severe condition. The dosage may then be adjusted to the needs of the patient.

Dispersible tablets: Recommended initial dosage is 2 tablets three times per day, then adjusted to the needs of the patient.

The maximum daily dose should not exceed 3 g.

Gastro-intestinal intolerance can be minimised by taking Fenopron with milk or at meal times.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to the drug. Active peptic ulceration.

Warnings: Adverse effects may include gastro-intestinal intolerance and episodes of bleeding. Although fenopron has been associated with less gastro-intestinal microbleeding than aspirin, patients with a history of peptic ulcer or gastro-intestinal bleeding should be closely supervised during fenopron therapy.

Bronchospasm may be precipitated in patients suffering from, or with a previous history of, bronchial asthma or allergic disease.

Although cross-sensitivity has not been established, the drug should not be given to patients in whom salicylates induce the syndrome of asthma, rhinitis or urticaria.

Usage in pregnancy: The safety of fenopron for use during pregnancy or lactation has not been established; therefore it should not be administered to pregnant women or nursing mothers unless the potential benefits clearly outweigh any potential risk. Animal studies showed prolongation of parturition.

Precautions: Because of its affinity for albumin, fenopron may displace other drugs from their binding sites, and this may lead to drug interaction. In patients receiving coumarin-type anticoagulants, the addition of fenopron could prolong the prothrombin time. Patients receiving hydantoins or sulphonylureas should be carefully monitored.

When aspirin and fenopron are administered concurrently, plasma concentrations of fenopron are reduced. It may be advisable to discontinue the concomitant use of aspirin to maximise the beneficial effects of fenopron. However, single or intermittent doses of aspirin may be administered if they are indicated.

Since fenopron is eliminated primarily by the kidney, the drug should not be administered to patients with significantly impaired renal function.

Patients with initial low haemoglobin values who are receiving long-term therapy should be monitored, as transient reduction of haemoglobin and haematocrit values due to fenopron have been reported.

Elevation of AST (SGOT), LDH and ALP levels have been reported occasionally, and it is therefore recommended that fenopron be discontinued if any significant liver abnormalities occur.

Side-effects: *Gastro-intestinal* – These are the most commonly observed side-effects and include dyspepsia, constipation, diarrhoea, ulceration of the buccal mucosa, nausea, vomiting, anorexia and occult blood in the stool.

Cases of peptic ulceration, including some complicated by bleeding, have occurred.

Renal – Rare cases of acute renal insufficiency, in association with allergic nephritis, nephrosis or papillary necrosis, have been reported. As a general rule, these are reversible on withdrawal of the drug. Episodes of dysuria, cystitis and haematuria have occurred.

Haematological – Various syndromes involving the bone marrow have been reported rarely; thrombocytopenia, pancytopenia and aplastic anaemia have occurred.

Allergic – Pruritis, rash, urticaria, Stevens-Johnson syndrome and angio-neurotic oedema have been reported.

Neurological – Reactions reported include headache, somnolence, dizziness, tremor, confusion and insomnia.

Miscellaneous – Tinnitus, hearing decrease, amblyopia, blurred vision, palpitations, increased sweating, nervousness and peripheral oedema have been reported.

Overdosage: Information is available on two cases of intentional overdose. A patient who ingested 7.5 g fenopron developed severe lower abdominal pain, scrotal pain, burning on micturition, haematuria and proteinuria. All symptoms subsided within forty-eight hours.

A second patient who ingested 33 g fenopron over a seven-hour period developed abdominal pain followed by vomiting, and excessive perspiration. She was anuric for twenty-four hours, despite supportive therapy, and during this time developed severe headache and tinnitus. Subsequent urinalysis indicated haematuria. Symptoms gradually resolved and recovery was uneventful.

Treatment: Standard therapy to evacuate gastric contents and to support vital functions should be employed. Since fenopron is acidic and is excreted in the urine, it would seem theoretically beneficial to try forced alkaline diuresis.

Pharmaceutical precautions 300 mg and 600 mg tablets: Store in a cool (6°–15°C), dry place.

Dispersible tablets: Keep tightly closed. Store in a cool dry place. Dispense in moistureproof container.

Legal category POM.

Package quantities

Tablets 300 mg: Bottles of 100 tablets.

Tablets 600 mg: Bottles of 100 tablets.

Dispersible tablets: Bottles of 100 tablets.

Further information Nil.

Product licence numbers

Tablets 300 mg 0006/0101

Tablets 600 mg 0006/0104

Dispersible tablets 0006/0142

HAELAN*

HAELAN-X*

Presentation *Haelan*: Collapsible tubes containing 0.0125% flurandrenolone in cream or ointment base. The cream is white in colour and the ointment is translucent.

Haelan-X: Collapsible tubes containing 0.05% flurandrenolone in cream or ointment base. The cream is white in colour and the ointment is translucent.

Uses Topical steroid. For the topical management of those dermatological disorders which may be expected

to respond to corticosteroids and in the case of Haelan, those which may require prolonged application.

Dosage and administration *Cream:* For moist weeping lesions the cream should be applied gently to the affected area two or three times daily.

Ointment: For dry, scaly lesions, the ointment should be applied as a thin film to the affected area two or three times daily.

Dilution is not recommended, but if considered necessary Aqueous Cream BP may be used for the creams and White Soft Paraffin BP for the ointments.

Contra-indications, warnings, etc

Contra-indication: Not to be used in the presence of tuberculosis of the skin.

Warnings: Preparations of Haelan are not intended for ophthalmic use.

A few individuals may be sensitive to Haelan. If any reaction indicating sensitisation is observed discontinue the use of the products.

In infants, long-term continuous topical steroid therapy should be avoided. Adrenal suppression can occur even without occlusion.

Usage in pregnancy: Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of these findings to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Side-effects: Neither local nor systemic side-effects have been reported so far from the use of either Haelan Cream or Ointment. Evidence of absorption of the steroid has been observed only when a much higher concentration has been used under an occlusive dressing.

Pharmaceutical precautions No special pharmaceutical precautions. See 'Administration' for diluents.

Legal category POM.

Package quantities

Haelan Cream (0.0125% flurandrenolone): Tubes of 10 g.

Haelan Ointment (0.0125% flurandrenolone): Tubes of 10 g.

Haelan-X Cream (0.05% flurandrenolone): Tubes of 5 g.

Haelan-X Ointment (0.05% flurandrenolone): Tubes of 5 g.

Further information As with all topical steroids the activity can be enhanced by the use of occlusive dressings. Preparations of Haelan are recommended only as a supplement to, and not as a substitute for, reparations (lotions, wet dressings, etc.) used in the conventional management of skin lesions.

Product licence numbers

Haelan Cream 0006/5012

Haelan Ointment 0006/5011

Haelan-X Cream 0006/5020

Haelan-X Ointment 0006/5039

HAELAN-C*

Presentation Collapsible tubes containing 0.0125% flurandrenolone with the addition of 3% Cliquinol BP cream or ointment base. The cream is white in colour and the ointment is translucent.

Uses Topical steroid with antibacterial added. For the topical management of those dermatological disorders complicated by bacterial or fungal infection and which may be expected to respond to corticosteroids, particularly those requiring prolonged application.

Dosage and administration *Cream:* For moist weeping lesions, the cream should be applied gently to the affected area two or three times a day.

Ointment: For dry, scaly lesions, the ointment should be applied as a thin film to the affected area two or three times a day.

Dilution is not recommended, but if considered necessary Aqueous Cream BP may be used for the creams and White Soft Paraffin BP for the ointments.

Contra-indications, warnings, etc

Contra-indication: Not to be used in the presence of tuberculosis of the skin.

Side-effects and adverse reactions: Neither local nor systemic side-effects have been reported so far from the use of either Haelan-C Cream or Ointment. Evidence of absorption of the steroid has been observed only when a much higher concentration has been used under an occlusive dressing.

A few individuals may be sensitive to Haelan-C. If any reaction indicating sensitisation is observed, discontinue the use of the product.

Warnings:

1. Preparations of Haelan-C are not intended for ophthalmic use.

2. In infants, long-term continuous topical steroid therapy should be avoided. Adrenal suppression can occur even without occlusion.

3. Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of these findings to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

4. Haelan-C may cause staining of the hair, clothing and many fabrics.

Pharmaceutical precautions No special pharmaceutical precautions. See 'Administration' for diluents.

Legal category POM.

Package quantities

Haelan-C Cream (0.0125% flurandrenolone with 3% Cliquinol BP): Tubes of 30 g.

Haelan-C Ointment (0.0125% flurandrenolone with 3% Cliquinol BP): Tubes of 30 g.

Further information When secondary bacterial and fungal infection of the skin is present or suspected in an otherwise steroid responsive skin condition, Haelan-C should be used and treatment resumed with Haelan after the infection has been controlled. Such patients must be under constant medical observation.

Product licence numbers

Haelan-C Cream 0006/5018

Haelan-C Ointment 0006/5021

HAELAN* Tape

Presentation A translucent, polythene adhesive film impregnated with 4 mcg flurandrenolone per square centimetre and protected by a removable paper liner.

Uses Occlusive topical steroid. Adjunctive therapy for chronic recalcitrant dermatoses that may respond to topical corticosteroids, and particularly dry, scaling and localised lesions.

Dosage and administration For application to the skin, which should be clean, dry and shorn of hair. In most instances the tape need only remain in place for 12 out of 24 hours.

Cosmetics may be applied over the tape.

Application: The tape is cut so as to cover the lesion and a $\frac{1}{4}$ inch margin of normal skin. Corners should be rounded off. After removing the lining paper, the tape is applied to the centre of the lesion with gentle pressure and worked to the edges, avoiding excessive tension of the skin. If longer strips of tape are to be applied, the lining paper should be removed progressively.

Contra-indications, warnings, etc

Contra-indications: Chicken pox, vaccinia, tuberculosis of the skin and hypersensitivity to any of the components.

Side-effects and adverse reactions: Irritation, itching, dryness and folliculitis may be troublesome. Maceration of the skin, secondary infection, skin atrophy, striae and miliaria are more likely to occur under occlusion. In their presence the use of the tape should be discontinued. If extensive areas are treated there may be undue systemic absorption, especially in infants, where long-term continuous use should be avoided.

Warnings: Not advocated for acute and weeping dermatoses.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of these findings to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Pharmaceutical precautions Store in a dry place at room temperature, below 25°C.

Legal category POM.

Package quantities Single rolls of tape, 7.5 cm wide, 200 cm long.

Further information Nil.

Product licence number 0006/5158.

ILOSONE®

Presentation Capsules each containing the equivalent of 250 mg erythromycin base as Erythromycin Estolate BP. The capsules are ivory/red, marked 'DISTA' and are 2.1 cm long.

Tablets each containing the equivalent of 500 mg erythromycin base as Erythromycin Estolate BP. The tablets are pink, para-capsule shaped, 1.9 cm long and coded DISTA D1.

Ready-mixed suspension, each 5 ml containing the equivalent of 125 mg erythromycin base as Erythromycin Estolate BP. The suspension is orange coloured.

Ready-mixed suspension forte, each 5 ml containing the equivalent of 250 mg erythromycin base as Erythromycin Estolate BP. The suspension is orange coloured.

Uses Antibiotic. Erythromycin is indicated in the treatment of conditions associated with the following micro-organisms:

Streptococcus pyogenes (group A beta-haemolytic): Upper and lower respiratory tract, skin, and soft tissue infections of mild to moderate severity.

Alpha-haemolytic streptococci (viridans group): Short term prophylaxis against bacterial endocarditis prior to dental or other operative procedures in patients with a history of rheumatic fever or congenital heart disease who are hypersensitive to penicillin.

Staphylococcus aureus: Acute infections of skin and soft tissue which are mild to moderately severe. Resistance may develop during treatment.

Streptococcus pneumoniae: Upper and lower respiratory tract infections of mild to moderate severity.

Mycoplasma pneumoniae: Primary atypical pneumonia when due to this organism.

Bordetella pertussis: When given early after exposure to whooping cough, erythromycin may reduce the risk of development of classical symptoms.

Treponema pallidum: Erythromycin is an alternative choice of treatment for syphilis in penicillin-allergic patients.

Corynebacterium diphtheriae: As an adjunct to antitoxin, to prevent establishment of carriers, and to eradicate the organism in carriers.

Corynebacterium minutissimum: In the treatment of erythrasma.

Entamoeba histolytica: In the treatment of intestinal amoebiasis only. Extra-enteric amoebiasis requires treatment with other agents.

Listeria monocytogenes: Infections due to this organism.

Legionnaires' disease: Although no controlled clinical studies have been conducted, *in vitro* and limited preliminary clinical data suggest that erythromycin may be effective in treating Legionnaires' disease.

Dosage and administration For oral administration.

Adults: The usual dose is 250 mg every six hours. This may be increased up to 4 g or more per day according to the severity of the infection.

Children: Age, weight, and severity of the infection are important factors in determining the correct dosage. The usual range is 20–50 mg/kg/day in divided doses.

For mild to moderate infections

Body weight	Total daily dose
10 kg or less	250 mg
10–18 kg	375 mg
18–25 kg	500 mg
25–36 kg	750 mg
More than 36 kg	1000 mg (adult dose)

For more severe infections these dosages may be doubled.

If administration on a twice daily schedule is desirable one-half of the total daily dose may be given every 12 hours.

Streptococcal infections: In the treatment of group A beta-haemolytic streptococcal infections, a therapeutic dosage of erythromycin should be administered for at least 10 days. In continuous prophylaxis of streptococcal infections in persons with a history of rheumatic heart disease, the dosage is 250 mg twice daily.

When Ilosone is used prior to surgery to prevent endocarditis caused by alpha-haemolytic streptococci (viridans group) a recommended schedule for adults is:

1 g pre-operatively and 500 mg every six hours for eight doses post-operatively: for children, 30–50 mg/kg/day divided into three or four evenly spaced doses.

Pertussis: Doses of erythromycin estolate utilised in reported clinical studies were 40–50 mg/kg/day, given in divided doses for five to 14 days.

Syphilis: A regimen of 20 g of erythromycin estolate in divided doses over a period of 10 days has been shown to be effective.

Amoebic dysentery: Dosage for adults is 250 mg four times daily for 10 to 14 days; for children, 30–50 mg/kg/day in divided doses for 10 to 14 days.

Legionnaires' disease: Although optimum regimens have not been established, 1–4 g daily in divided doses has been utilised in reported clinical studies.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to erythromycin.

Patients who have previously developed jaundice or who have pre-existing liver disease or dysfunction.

Warnings: The administration of erythromycin estolate has been associated with the infrequent occurrence of reversible cholestatic hepatitis. Hepatic dysfunction with or without jaundice has occurred, chiefly in adults. It may be accompanied by malaise, nausea, vomiting, abdominal colic and fever. In some instances severe abdominal pain may simulate the pain of biliary colic, pancreatitis, perforated ulcer, or an acute abdominal surgical problem. In other instances, clinical symptoms and results of liver function tests have resembled findings in extrahepatic obstructive jaundice. Laboratory findings have been characterised by abnormal hepatic function test values, peripheral eosinophilia and leucocytosis. If he above findings occur, discontinue Ilosone promptly.

Initial symptoms have developed in some cases after a few days of treatment, but generally have followed one or two weeks of continuous therapy. Symptoms reappear promptly, usually within 48 hours, after the drug is re-administered to sensitive patients. The syndrome seems to result from a form of sensitisation, occurs chiefly in adults, and has been reversible when medication is discontinued.

Usage in pregnancy: Although laboratory and clinical studies have shown no evidence of teratogenicity, caution should be exercised when prescribing for the pregnant patient.

Precautions: The use of erythromycin in patients who are receiving concomitant high doses of theophylline may be associated with an increase in serum theophylline levels and potential theophylline toxicity. If symptoms of toxicity develop, the dose of theophylline should be reduced.

During prolonged or repeated therapy, there is a possibility of overgrowth of nonsusceptible bacteria or fungi. If such infections arise, the drug should be discontinued and appropriate therapy instituted.

Side-effects: The most frequent side-effects of erythromycin preparations are gastro-intestinal (e.g. abdominal cramping and discomfort) and are dose-related. Nausea, vomiting and diarrhoea occur infrequently with usual oral doses.

Mild allergic reactions, such as urticaria and other skin rashes, have occurred. Serious allergic reactions, including anaphylaxis, have been reported.

Overdosage: Symptoms – nausea, vomiting and diarrhoea.

Treatment: General management may consist of supportive therapy.

Pharmaceutical precautions Capsules and tablets: Keep container tightly closed and store in a cool place (6°–15°C).

Suspensions: Keep container tightly closed and protect from light. Store in a cool place. Shake well before use. For dilution, use Syrup BP, and when diluted use within 14 days.

Legal category POM.

Package quantities

Capsules 250 mg Bottles of 100 and 500

Tablets 500 mg Bottles of 12

Ready-mixed Suspension 125 mg/5 ml: Bottles of 100 ml

Ready-mixed Suspension 250 mg/5 ml: Bottles of 100 ml

Strengths expressed are base equivalent as Erythromycin Estolate BP.

Further information Nil.

Product licence numbers

Capsules 250 mg 0006/5022

Tablets 500 mg 0006/5015

Suspension 125 mg/5 ml 0006/5023

Suspension 250 mg/5 ml 0006/5024

NAPSALGESIC*

Presentation Tablets containing 50 mg Dextropropoxyphene Napsylate BP (equivalent to approximately 32.5 mg dextropropoxyphene hydrochloride or 30 mg dextropropoxyphene base) with 500 mg Aspirin PhEur. The tablets are pale yellow, pillow-shaped, marked 'DP' and are 16 mm in length.

Uses Analgesic. For the treatment of pain such as that of rheumatic conditions, especially where there is a need for additional analgesia to that provided by aspirin alone, or where high doses of aspirin have to be reduced to avoid side-effects.

Dosage and administration For oral administration to adults only.

Dosage: The usual dose is 4–6 tablets daily in divided doses, and should not normally be exceeded.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to dextropropoxyphene or aspirin, active peptic ulceration and haemophilia.

Warnings: Dextropropoxyphene is an analgesic with CNS depressant properties and should be used with caution in patients who are receiving other CNS depressant drugs, as an additive effect may occur. Patients should be warned to avoid alcohol.

As with other drugs which affect the CNS, care should be taken when prescribing for patients with personality or other psychological disorders.

Tolerance, psychological and physical dependence may rarely occur.

Like other centrally acting drugs, dextropropoxyphene may impair patients' mental and physical reactions in the performance of potentially hazardous tasks (e.g. in driving ability, operation of machinery, etc.) to a varying extent, depending on dosage and individual susceptibility.

Salicylates should be used with caution in patients with asthma or coagulation abnormalities. They may also induce gastro-intestinal haemorrhage, occasionally major.

Use in pregnancy: The safety of Napsalgesic for use during pregnancy has not been established. Aspirin may prolong labour and contribute to maternal and neonatal bleeding, and is best avoided at term.

Precautions: Aspirin may enhance the effect of anti-coagulants, inhibit the action of uricosuric agents, precipitate bronchospasm or induce attacks of asthma in susceptible individuals.

Side-effects: Side-effects such as dizziness, sedation, nausea and vomiting seem to be more prominent in ambulatory than in non-ambulatory patients, and some of these side-effects may be alleviated if the patient lies down.

Other reported side-effects include constipation, abdominal pain, skin rashes, lightheadedness, weakness, euphoria, dysphoria and minor visual disturbances.

Overdosage: The chronic ingestion of dextropropoxyphene in doses exceeding 720 mg (as base) per day has caused toxic psychoses and convulsions.

Symptoms of acute toxicity may be rapid in onset, with the danger of respiratory arrest. Other recognised manifestations include respiratory depression, coma, circulatory collapse, pulmonary oedema, convulsions and cardiac arrhythmias.

Deterioration may be rapid, with fatal outcome.

The clinical picture may be complicated by salicylism.

Treatment: Primary attention should be given to the re-

establishment of adequate respiratory exchange through provision of a patent airway and institution of assisted or controlled ventilation. The narcotic antagonist naloxone is a specific antidote against the respiratory depression produced by dextropropoxyphene. An appropriate dose of this antagonist should be administered, preferably by the intravenous route, simultaneously with efforts at respiratory resuscitation. Repeated doses of the antagonist may be necessary over a prolonged period due to the slow elimination of dextropropoxyphene. In addition to the use of a narcotic antagonist, the patient may require careful titration with an anticonvulsant to control seizures. Analeptic drugs (for example, caffeine or amphetamine) should not be used because of their tendency to precipitate convulsions.

Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated.

Gastric lavage may be helpful. Activated charcoal can absorb a significant amount of ingested dextropropoxyphene. Dialysis is of little value in poisoning by dextropropoxyphene alone. Salicylates are dialysable.

Pharmaceutical precautions Store in a cool (6°–15°C), dry place. Keep containers tightly closed.

Legal category POM.

Package quantities Bottles of 100 and 500 tablets.

Further information Nil.

Product licence number 0006/5016.

**Trade Mark*

Dome/Hollister-Stier

Division of Miles Laboratories Limited

Stoke Court, Stoke Poges
Slough SL2 4LY



ALLPYRAL* ALLERGEN EXTRACTS

Presentation *Ingredients:* An Allpyral Allergen Extract is a sterile, pyridine-extracted, alum-precipitated antigen complex in suspension, in an aqueous solution of 0.9% saline containing 0.4% phenol as a preservative. Allpyral Allergen Extracts are standardised on a protein nitrogen unit (PNU) basis.

Allpyral Allergen Extracts are prepared *either* according to the specific sensitivities of individual patients (these Extracts are designated Allpyral-Specific), *or* as standard extracts of pollens of five common grasses (these Extracts are designated Allpyral-G).

Allpyral-Specific Allergen Extracts are prepared from one or more of the following source materials (subject to conditions given in Notes 1-6):

Pollens

Grass mix (see Note 1)	<i>Ash</i>	} Tree mix (see Note 3)
Plantain	<i>Birch</i>	
Mugwort	<i>Elm</i>	
Nettle	<i>Oak</i>	
Flower mix compositae (see Note 2)	<i>Plane</i>	

Beech
Hazel
Alder
Willow
Sycamore

Other inhalants

D. pteronyssinus	Feather mix (see Note 5)
Mite Fortified house dust (see Note 4)	Rye flour
House dust	Wheat flour
Cat	Horse
Cow	Rabbit
Dog	Sheep wool

Moulds

Botrytis cinerea
Dry rot (*Merulius lacrymans*)
Phoma betae
Sporobolomyces roseus
Candida albicans
Fusarium oxysporum
Helminthosporium sativum
Mucor racemosus

<i>Alternaria tenuis</i>	} Mould mix (see Note 3)
<i>Aspergillus fumigatus</i>	
<i>Dadosporium herbarum</i>	
<i>Penicillium notatum</i>	

Pullularia pullulans
Rhizopus nigricans

Stinging insects (see Note 6)

Nasp Bee

Note 1. Grass mix contains extracts of the pollens of cocksfoot, meadow fescue, perennial rye, timothy, and Yorkshire fog.

These extracts are available *only* as constituents of Allpyral-Specific (grass mix) and *not* as individual extracts.

Note 2. Flower mix compositae contains extracts of the pollens of golden rod, Michaelmas daisy, dahlia and chrysanthemum.

These extracts are available *only* as constituents of Allpyral-Specific (flower mix) and *not* as individual extracts.

Note 3. Those individual tree pollens and moulds underlined are available *either* individually *or* as constituents of tree mix and mould mix.

Note 4. D. pteronyssinus and Mite Fortified house dust are available *only* as individual extracts and *not* mixed with any other extract.

Note 5. Feather mix contains extracts of the feathers of chicken, duck and goose. These are available *only* as constituents of Allpyral-Specific (feather mix) and *not* as individual extracts.

Note 6. The stinging-insect extracts of wasp and bee are available *either* individually *or* as a wasp/bee mixture, but *not* mixed with any other allergens.

Allpyral-G Allergen Extract contains extracts of the pollens of cocksfoot, meadow fescue, perennial rye, timothy, and Yorkshire fog. Allpyral-G is recommended for the treatment of classical hay fever and/or grass pollen asthma. (This is a standard item available immediately from stock.)

Form and appearance: The colour of Allpyral Allergen Extracts depends upon the type of allergens used and the strength of extract in each vial. Grass pollen extracts range from pale to olive green, extracts of house dust and mite fortified house dust range from grey to black, mould extracts range from clear to pale brown, epithelial extracts range from clear to milky white, tree pollen extracts range from olive to dark green, and D. pteronyssinus extracts range from clear to milky white. Allpyral Allergen Extracts are available in three types of treatment set:

1. Initial Treatment Sets consist of 3 colour-coded, graduated-strength vials.

Vial No. 1 (Green Label) contains extract of 100 PNU/ml strength.

Vial No. 2 (Blue Label) contains extract of 1,000 PNU/ml strength.

Vial No. 3 (Black Label) contains extract of 10,000 PNU/ml strength.

(D. pteronyssinus only - Vial No. 3 (Brown Label) contains extract of 4,000 PNU/ml strength).

2. Special Dilution Treatment Sets consist of 1 vial containing extract of 10 PNU/ml strength. This treatment set may be required for use *before* the Initial Treatment Set in certain cases (see 'Dosage and administration' below), and will be supplied on *request* with the Initial Treatment Set.

3. Maintenance Treatment Sets consist of 1 vial (Black Label) containing extract of 10,000 PNU/ml

strength (D. pteronyssinus only – Maintenance Sets consist of 3 × 2 ml vials (Brown Labels) containing extracts of 4,000 PNU/ml strength) (see 'Dosage and administration' below).

All treatment sets are supplied complete with sufficient sterile disposable syringes and needles for the course ordered.

Uses Indications

Allpyral-Specific: For the hyposensitisation of patients whose allergies have been determined by case history and confirmed by skin testing. (To ensure conformity between the results of skin-testing and subsequent treatment, it is recommended that Dome[®] Glycerinated Skin Testing Solutions are used. There is a Dome Glycerinated Skin Testing Solution for each of the Allpyral Allergen Extracts listed above with the exception of bee and wasp extracts; the diagnostic solutions and the treatment extracts are prepared from common source materials.)

Allpyral-G: For the hyposensitisation of patients known to suffer from classical hay fever and/or grass pollen asthma.

Dosage and administration Allpyral Allergen Extracts should be administered only by subcutaneous injection. Patients sensitive to seasonal allergens should be treated *pre-seasonally*, in order to ensure that treatment is completed before the seasonal allergen becomes airborne.

Patients sensitive only to perennial, i.e. non-seasonal, allergens may be treated at any time of the year.

Each Allpyral-Specific Treatment Set is supplied with a dosage schedule appropriate to the individual patient's requirements, together with complete instructions on administration. (Each such treatment set and its accompanying dosage instructions are prepared from the information given on the Allpyral Order Form by the prescribing physician.)

Each Allpyral-G Treatment Set is supplied with alternative dosage schedules from which the physician should select the dosage appropriate to the particular patient. Complete instructions on administration are also supplied.

SEASONAL ALLERGENS

Initial treatment: Each year's treatment with Allpyral Allergen Extracts should always commence with an Initial Treatment Set.

Initial treatment on a pre-seasonal basis consists of a course of 9 subcutaneous injections from the Allpyral-G or Allpyral-Specific Initial Treatment Set.

This course should be completed not less than three weeks before the particular allergen becomes airborne. Clinical evidence suggests that best results are obtained if the pre-seasonal course is timed to end as close as possible to the date three weeks before pollination.

It is recommended that children under 14 in the first year of treatment should be treated according to either the 'Extremely Sensitive' or the 'Very Sensitive' dosage schedules. For extremely sensitive patients a Special Dilution Treatment Set can be supplied *on request*. This should precede administration of the Initial Treatment Set.

Increasingly, clinical experience indicates that if pre-seasonal hyposensitisation is repeated for three consecutive years, long-lasting relief may be expected, rendering treatment in subsequent years unnecessary. *For each year of treatment an Initial Treatment Set will be required.* The previous year's treatment should have reduced the

patient's degree of sensitivity and, therefore, in the second and third years of treatment the dosage schedule should be adjusted accordingly (i.e. from 'Very Sensitive' to 'Moderately Sensitive', or from 'Moderately Sensitive' to 'Mildly Sensitive'), dependent upon the patient's progress.

Maintenance treatment: Maintenance treatment is advisable in cases where pre-seasonal initial treatment has been completed long before the onset of pollination, e.g. in the case of grass pollen, if the course has finished in February (the grass pollen season usually starts in late May). Treatment with an Allpyral Maintenance Set involves repeat injections of the top dose achieved on the preceding initial treatment course, given at four to six weekly intervals until three weeks before the onset of pollination.

Not more than six weeks should elapse between the last injection of the initial treatment course and the first maintenance injection, or between subsequent maintenance injections. If more than six weeks elapse, then the dosage should be reduced accordingly.

PERENNIAL ALLERGENS

Initial treatment: Treatment with Allpyral Allergen Extracts should always commence with an Initial Treatment Set.

Initial treatment consists of 9–10 subcutaneous injections from the Allpyral-Specific Initial Treatment Set. Where only perennial or 'non-seasonal' allergens are involved, treatment with Allpyral-Specific may be started at any time of the year. It is recommended that children under 14 in the first course of treatment should be treated according to either the 'Extremely Sensitive' or the 'Very Sensitive' dosage schedules. For extremely sensitive patients a Special Dilution Treatment Set can be supplied *on request*. This should precede administration of the Initial Treatment Set.

Maintenance treatment: Maintenance treatment is intended to maintain the protection afforded by the initial treatment course and should only be given where an initial treatment course has previously been completed. Maintenance treatment consists of repeat injections of the top dose achieved on the initial treatment course, given every four to six weeks.

Not more than six weeks should elapse between the final injection of the initial treatment course and the first maintenance injection, or between subsequent maintenance injections. If more than six weeks elapse, then the dosage should be reduced accordingly.

Other advice on the administration of Allpyral Allergen Extracts is as follows:

1. Observe the usual sterile techniques.
2. Do not inject intravenously.
3. Shake the vial well before withdrawing the dose.

Where two different courses are being given concurrently the two extracts must *never* be mixed within the same syringe. Injections of the two extracts may be given at the same visit, but in opposite arms.

Alternatively, the normal weekly interval between injections may be increased to two weeks, so that the two courses can be given on alternate weeks (i.e. one course on weeks 1, 3, 5, 7, etc., the other course on weeks 2, 4, 6, 8, etc.).

For recommendations concerning dilution see 'Pharmaceutical precautions' below.

Contra-indications, warnings, etc

Contra-indications: Whilst no adverse reactions have

been reported, it is not considered advisable to administer Allpyral Allergen Extracts during pregnancy.

Precautions: Patients should be detained in the surgery for 15 minutes following each injection, and should be advised not to take any strenuous exercise for some hours.

Adrenaline Injection BP should always be available when administering hyposensitisation therapy.

Overdosage: See 'Main side-effects/adverse reactions' below.

Main side-effects/adverse reactions: As with all forms of hyposensitisation therapy the possibility of reactions in very sensitive individuals cannot be ruled out. This risk is considerably reduced in the case of Allpyral Allergen Extracts, since the antigens are slowly released from the site of injection.

In the event that a constitutional or systemic reaction should occur, this will generally appear slowly and gradually in three to six hours after the injection, and may last for two to four days due to continued slow release of the antigen. Such reactions are rarely critical, and are usually readily controlled with antihistamines. However, itching and swelling could remain for several days, and the patient should be supplied with medication and information to prevent undue apprehension. The dose of antigen to be injected at the next visit should be reduced.

In the case of a moderate local reaction at the site of injection, the same dose should be repeated at the next visit and increased cautiously thereafter.

In the case of a severe local reaction, a tourniquet should be applied to the arm above the site of injection, 0.2–0.3 ml of Adrenaline Injection BP should be injected near the site of injection, and 0.2 ml into the opposite arm. The tourniquet is then gradually released. The dose at the next visit should be reduced.

A general reaction may require a subcutaneous injection of 0.5 ml of Adrenaline Injection BP, repeated as necessary. Additionally, the injection of an antihistamine or an anti-inflammatory steroid may be considered.

Pharmaceutical precautions *Storage:* Store between 2°C and 8°C. Do not freeze.

Dilution: Allpyral Allergen Extracts are supplied ready or use. It is important that, in the event of a pharmacist or physician wishing to dilute an Allpyral Allergen Extract, only diluent supplied for this purpose by Dome should be used. Failure to observe this recommendation may adversely affect the integrity of the Allpyral Allergen Extract, thereby reducing its safety.

Legal category POM.

Package quantities Initial Treatment Sets consist of three colour-coded, graduated-strength vials.

Special Dilution Courses consist of 1 vial.

Maintenance Treatment Sets consist of 1 (top-strength) vial. (D. pteronyssinus only – 3 top-strength vials.) For details of PNU strengths please see 'Presentation – Form and appearance' above.

All Allpyral Allergen Extracts are supplied complete with the appropriate dosage schedule and a sufficient quantity of sterile, disposable syringes and needles for the course.

Further information Allpyral Allergen Extracts are prepared by a process which minimises residual free allergen, and allows slow absorption from the site of

injection. Thus fewer severe reactions, both local and systemic, are experienced than with aqueous extracts, and fewer injections are required.

Treatment with Allpyral Allergen Extracts reduces the patient's hypersensitivity, thereby dealing with the cause of his allergic symptoms. Thus Allpyral Allergen Extracts provide prophylactic rather than palliative therapy.

Product licence number 0055/5001.

DTIC-DOME*

Presentation *Active ingredients:* 5-(3,3-dimethyl-1-triazeno) imidazole-4-carboxamide prepared as the citrate salt (dacarbazine).

100 mg and 200 mg vials of sterile dacarbazine.

DTIC-Dome is a colourless to ivory-coloured solid to be reconstituted with Water for Injections BP.

Uses *Actions:* Although the exact mechanism of action of dacarbazine is unknown, three hypotheses have been offered:

1. Inhibition of DNA synthesis by acting as a purine analogue.
2. Action as an alkylating agent.
3. Interaction with SH groups.

The volume of distribution of DTIC-Dome exceeds body water content, suggesting localisation in some body tissues. DTIC is only slightly (approximately 5%) protein bound. Its plasma half life after i.v. administration is approximately 35 minutes. After 6 hours in animal study, approximately 46% of radiolabelled dose was recovered from the urine. Of this 46% almost half was unchanged DTIC and a like quantity was amino-imidazole carboxamide, a metabolite. DTIC is subject to renal tubular secretion rather than glomerular filtration.

Indications: Metastatic Malignant Melanoma.

Sarcoma.

Hodgkin's Disease.

In addition, DTIC-Dome has been shown when used in combination with other cytotoxic agents, to be of value in treatment of other malignant diseases including: Carcinoma of colon, ovary, breast, lung.

Testicular teratoma.

Solid tumours in children.

Dosage and administration *Standard dose:* The following dosage schedules are recommended:

1. 2.0–4.5 mg/kg/day for 10 weeks, which may be repeated at 4 week intervals.
2. 250 mg/m²/day for 5 days, which may be repeated at 3 week intervals.
3. A further alternative is to administer the total schedule dose on the first day.

Other schedules may be used at the discretion of the prescribing physician.

Children: The dosage for children is calculated on a mg/kg or mg/m² basis as per the standard dosage.

Administration: DTIC-Dome 100 mg and 200 mg vials are reconstituted with 9.9 ml and 19.7 ml, respectively, of Water for Injections BP. The resulting solution contains an equivalent of 10 mg/ml of dacarbazine. After the solution has been prepared, the calculated dose is drawn into a syringe and injected intravenously. Injection may be completed in one or two minutes.

If desired, the reconstituted solution may be further diluted with 125–250 ml of Dextrose Injection BP 5% or

Sodium Chloride Injection BP 0.9% and administered by intravenous infusion over a period of 15 to 30 minutes.

Contra-indications, warnings, etc DTIC-Dome is contra-indicated in patients who have demonstrated a hypersensitivity to it in the past.

This product should not normally be administered to patients who are pregnant or to mothers who are breast feeding.

Studies have demonstrated this agent to have a carcinogenic and teratogenic effect when used on animals.

DTIC-Dome should be administered preferably to patients who are hospitalised and who can be observed carefully and frequently during and after therapy, with particular reference to the haemopoietic system.

Care must be taken to avoid extravasation of the drug subcutaneously during intravenous administration as this may result in tissue damage and severe pain.

Users should avoid contact of DTIC-Dome with the skin and eyes when reconstituting or administering.

It is recommended that DTIC-Dome be administered under the supervision of a physician experienced in the use of cancer chemotherapeutic agents. Since facilities for necessary laboratory studies must be available, hospitalisation is recommended.

Haemopoietic depression is the most common toxic side effect of DTIC-Dome and involves primarily the leucocytes and platelets, although mild anaemia may sometimes occur. Leucopenia and thrombocytopenia may be severe enough to cause death. The possible bone marrow depression requires careful monitoring of white blood cell, red blood cell and platelet levels. Haemopoietic toxicity may warrant temporary suspension or cessation of DTIC-Dome therapy.

Symptoms of anorexia, nausea and vomiting are the most frequently noticed side-effects. Over 90% of patients are affected with the first few doses. The vomiting lasts for 1–12 hours and may be completely but unpredictably palliated by phenobarbital and/or prochlorperazine. Rarely, DTIC-Dome causes diarrhoea. Some helpful suggestions include restricting the patient's oral intake of fluids and food for 4–6 hours prior to treatment. The rapid toleration of these symptoms suggests a central nervous system mechanism, and usually these symptoms subside after the first 1 or 2 days.

Infrequently, some patients have experienced an influenza-like syndrome of fever to 39°C, myalgias and malaise. This syndrome occurs usually after large single doses and approximately 7 days after treatment with DTIC-Dome and lasts 7–21 days, and may recur with successive treatments.

Alopecia has been noted as has facial flushing and facial paraesthesia.

Hepatic toxicity with hepatic necrosis has been extremely rare and has only been observed in patients with advanced malignancy when DTIC-Dome has been administered concomitantly with other anti-neoplastic drugs and when the drug has been used alone in the presence of already existing hepatic pathology.

Anaphylaxis can occur very rarely following administration of DTIC-Dome.

Erythematous and urticarial rashes have been observed infrequently after administration of DTIC-Dome.

Rarely photosensitivity reactions may occur.

Pharmaceutical precautions Store in a refrigerator between 2° and 8°C.

DTIC-Dome, like all triazenes is sensitive to unneces-

sary exposure to light and the reconstituted solution should be protected from light.

Use within 8 hours of reconstitution.

After reconstitution in the vial the solution may be stored, suitably protected from light, at 4°C for 72 hours or at normal room temperature for up to 8 hours.

If the reconstituted solution is further diluted in 5% Dextrose Injection BP or Sodium Chloride Injection BP 0.9% the resulting solution may be stored at 4°C for up to 24 hours.

Legal category POM.

Package quantities Vials containing 100 mg and 200 mg DTIC-Dome as sterile dacarbazine.

Further information When reconstituted each ml of solution for injection contains:

dacarbazine 10 mg, citric acid 10 mg and mannitol 5.0 mg (100 ml vial) or 3.75 mg (200 ml vial) pH 3.0–4.0.

Product licence numbers

100 mg 0055/0046

200 mg 0055/0047

MIGRAVESS*

Presentation Round, flat, white tablets, 22 mm diameter engraved with a breakline and a letter 'M' in each half of the tablet.

Each dry tablet contains:

Metoclopramide Monohydrochloride	5 mg
Aspirin BP	325 mg
Sodium Bicarbonate PhEur	1180 mg
Citric Acid PhEur	850 mg

Uses Analgesic/anti-emetic for the rapid symptomatic relief of headache and nausea associated with migraine.

Dosage and administration *Adults:* 2 tablets dissolved in water to be taken at the first symptoms of a migraine attack. If the attack persists the dose may be repeated up to a maximum of 3 doses (6 tablets) per day.

Children/young adults (10–15 years): Half the adult dose.

Migravess must be dissolved completely in half a glass of water before taking.

Contra-indications, warnings, etc True hypersensitivity to salicylates. Migravess should not be administered concomitantly with atropine, any anticholinergic drugs or concurrent with the administration of phenothiazines or butyrophenones. If vomiting persists the patient should be reassessed to exclude the possibility of an underlying disorder e.g. cerebral irritation.

Side-effects: Various extra-pyramidal reactions to metoclopramide have been reported, particularly in the young and the elderly. The incidence may be increased if daily doses in excess of those recommended are administered. The rarely occurring reactions include spasm of facial, extra ocular or cervical muscles. There may be a generalised increase in muscle tone. Any side-effects normally disappear within 24 hours of withdrawal of the drug.

Should treatment be required an anti-Parkinson drug of the anticholinergic type may be used to counteract these reactions.

In common with most anti-emetic drugs, metoclopramide may cause drowsiness but this is less common than with antihistamines.

Although studies in several mammalian species have

demonstrated no teratogenic effects with metoclopramide the use of Migravess is not recommended during the first trimester of pregnancy.

Each tablet contains 14 m Eq Na⁺.

Overdosage: Treat with gastric lavage and supportive therapy. Atropine 2 mg i.m. should be given for dystonic reactions in adults.

Pharmaceutical precautions Store at room temperature in a dry place and do not remove tablets from the foil until required.

Legal category POM.

Package quantities Migravess is available in cartons of 30 tablets (15 strips of 2 tablets). The tablets are packed in moisture proof aluminium foil laminate.

Further information Migravess presents aspirin and metoclopramide in effervescent form intended to hasten gastric emptying and therefore absorption, with freedom from the side-effects often associated with ergotamine containing preparations.

Product licence number 0055/0050.

NYSTAFORM[®]-HC OINTMENT NYSTAFORM[®]-HC CREAM

Presentation *Nystaform-HC ointment: Active ingredients:* Nystatin BP 100,000 units/g; Chlorhexidine acetate BP 1.0% w/w; Hydrocortisone PhEur 1.0% w/w.

Form and appearance: Nystaform-HC ointment is a yellow ointment containing the active ingredients in a water-repellent base.

Nystaform-HC cream: Active ingredients: Nystatin BP 100,000 units/g; Chlorhexidine hydrochloride BP 1.0% w/w; Hydrocortisone PhEur 0.5% w/w.

Form and appearance: Nystaform-HC cream is a light yellow cream containing the active ingredients in a water miscible base.

Uses *Actions:* Nystatin is a fungistatic and fungicidal antibiotic primarily effective against *Candida albicans*. Chlorhexidine has activity against a wide range of bacteria. Hydrocortisone exercises a vasoconstrictive effect, thus reducing inflammation and oedema and also has an antipruritic effect.

Indications: Nystaform-HC preparations are indicated in infected dermatoses where fungal (particularly monilial) and/or bacterial infection is present. The choice of cream or ointment presentations will depend upon the severity, physical characteristics and site of the condition, and upon the physician's preference.

Dosage and administration For topical application only. Apply liberally to infected areas 2-3 times daily. Continue application for one week after lesions have healed. This dosage is recommended for both children and adults.

Contra-indications, warnings, etc

Contra-indications: Tuberculous lesions of the skin. Known sensitivity to any of the ingredients.

Precautions: For external use only. Keep out of eyes. In infants, long term continuous topical steroid therapy should be avoided. Adrenal suppression can occur even without occlusions. As with other topical corticosteroids, systemic absorption may occur when extensive areas are treated, particularly under occlusion.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to humans has not been established. However, topical steroids should not be used extensively in the first trimester of pregnancy, i.e. in large amounts or for prolonged periods. However, the unproven theoretical teratogenic hazard must be placed in perspective against the need to maintain the health of the patient.

Overdosage: Not applicable.

Main side-effects/adverse reactions: None reported.

Pharmaceutical precautions *Storage:* Store in a cool place.

Legal category POM.

Package quantities Nystaform-HC cream and ointment 15 g and 30 g tubes.

Further information If sensitivity occurs, or if new infection appears, discontinue use and institute appropriate therapy.

The micronisation and microdispersion of the hydrocortisone in Nystaform-HC preparations ensure that the dispersal of this active ingredient over the affected area is as uniform as possible.

The water miscible base of Nystaform-HC cream is particularly easy to apply to inflamed and tender skin. It is pleasant to use and does not leave the skin feeling greasy. The water repellent base of Nystaform-HC ointment spreads easily and helps to protect against urine when used in the nappy rash area.

Product licence numbers

Nystaform-HC ointment 0055/0059

Nystaform-HC cream 0055/0060

NYSTAFORM[®] OINTMENT NYSTAFORM[®] CREAM

Presentation *Nystaform ointment: Active ingredients:* Nystatin BP 100,000 units/g; Chlorhexidine acetate BP 1.0% w/w.

Form and appearance: Nystaform ointment is a yellow ointment containing the active ingredients in a water-repellent base.

Nystaform cream: Active ingredients: Nystatin BP 100,000 units/g Chlorhexidine hydrochloride BP 1.0% w/w.

Form and appearance: Nystaform cream is a light yellow cream containing the active ingredients in a water miscible base.

Uses *Actions:* Nystatin is a fungistatic and fungicidal antibiotic primarily effective against *Candida albicans*. Chlorhexidine has activity against a wide range of bacteria.

Indications: For the treatment of infected skin conditions where fungal (particularly monilial) and/or bacterial infections are present.

Dosage and administration For topical application only. Apply liberally to infected area 2-3 times daily. Continue application for one week after lesions have healed.

This dosage is recommended for both children and adults.

The patient should be advised that if the condition is not better within seven days, to return to the surgery for a further consultation. In any event the duration of this treatment should not normally exceed fourteen days.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to any of the ingredients.

Precautions: For external use only. Keep out of eyes.

Overdosage: Not applicable.

Main side-effects/adverse reactions: None reported.

Pharmaceutical precautions *Storage:* Store in a cool place.

Legal category POM.

Package quantities 30 g tubes.

Further information If sensitivity occurs, or if new infection appears, discontinue use and institute appropriate therapy.

The water miscible base of Nystaform cream is particularly easy to apply to inflamed and tender skin. It is pleasant to use and does not leave the skin feeling greasy. The water repellent base of Nystaform ointment spreads easily and helps to protect against urine when used in the nappy rash area.

Product licence numbers

Nystaform ointment 0055/0058

Nystaform cream 0055/0057

**Trade Mark*

Duncan, Flockhart & Co. Limited

700 Oldfield Lane North
Greenford, Middlesex UB6 0HD



AIRBRON*

Presentation Airbron is a clear, colourless, sterile aqueous solution of 20% w/v *N*-acetylcysteine (*N*-acetyl-3-mercapto-alanine) adjusted to pH 7.0 with sodium hydroxide.

Uses Acetylcysteine, a derivative of the naturally occurring amino acid L-cysteine, is neither an enzyme nor a detergent.

Airbron dramatically reduces the viscosity and tenacity of sputum, its liquefying action being due to the presence in acetylcysteine of a free sulphhydryl group which opens up disulphide bonds present in mucus. The high viscosity of secretions in various pulmonary conditions is dependent primarily on their content of mucoprotein and, when an acute infection is involved, of deoxyribonucleic acid. The mucolytic activity of acetylcysteine is unaffected by the presence of deoxyribonucleic acid and it is, therefore, equally effective against purulent and non-purulent mucus.

Airbron facilitates the removal of mucus in broncho-pulmonary diseases:

In general medicine: Chronic bronchitis with or without emphysema, Bronchiectasis, Lung abscesses.

In anaesthetics: During general anaesthesia. Post-operative care. Pulmonary complications of heart or lung surgery. Intensive care (including routine cleansing of tracheostomies).

Dosage and administration Airbron is administered topically by nebulisation, direct instillation or, occasionally, by percutaneous intratracheal catheter. Apparatus should be of plastic or glass. Metals (particularly iron, copper and nickel) and rubber should be avoided as they react with the drug. Airbron is rapidly inactivated by high concentrations of oxygen.

By nebulisation: 1–10 ml Airbron may be given into a face mask, mouth piece, tracheostomy tube or opening every two to six hours. Usually 2–5 ml three or four times a day are sufficient for most cases.

If given into a tent, sufficient Airbron should be used to maintain a heavy mist for the duration of the treatment period and up to 250 ml may be administered.

By direct instillation: 1–2 ml Airbron may be given every one to four hours.

Contra-indications, warnings, etc Studies in various animal species have shown that acetylcysteine is virtually non-toxic and no contra-indications have been reported.

Precautions: As Airbron loosens large volumes of mucus, patients who cannot cough it up may require mechanical suction to maintain an open airway.

Care should be exercised in administering Airbron to asthmatic patients, as cases of bronchospasm have been reported. If bronchospasm occurs, Airbron should be replaced by a sympathomimetic agent, such as salbutamol, in aerosol form.

Side-effects: Side-effects due to Airbron are slight and infrequent. Stomatitis, nausea and vomiting, coughing and irritation have occasionally been reported. During nebulisation the patient may at first notice a slightly disagreeable odour, but this usually disappears. With a face mask, there may be stickiness on the face which can easily be removed by washing with warm water.

Pharmaceutical precautions Airbron should be stored in a cool place. If only a portion of a vial is used, the remainder should be stored in a refrigerator and used within 96 hours.

Legal category POM.

Package quantities Airbron is supplied in ampoules of 2 ml in containers of 25, and in multidose vials of 10 ml in containers of 3.

Further information Airbron is not suitable for use with an ordinary hand nebuliser as pressure of between 6 and 10 lbs per square inch should be used to produce a particle size of 10 microns or less.

Product licence number 0021/5026.

ANCOLOXIN* TABLETS

Presentation White tablets engraved DF/AR, each tablet containing:

Meclozine Hydrochloride BP	25 mg
Pyridoxine Hydrochloride BP	50 mg

Uses Meclozine hydrochloride is an anti-histamine of the piperazine group with marked anti-emetic properties and a duration of action of 12–24 hours. Its toxicity is low and it has been widely investigated for possible teratogenic effects in man. Pyridoxine hydrochloride (vitamin B₆) complements the action of meclozine. It forms, with other vitamins of the B group, part of an enzyme system concerned with the metabolism of amino acids. Severe vomiting is sometimes associated with a specific deficiency of pyridoxine and administration of this vitamin is of value in the treatment of such cases. Ancoloxin is indicated for the prevention and treatment of most forms of nausea and vomiting.

Dosage and administration *Radiation sickness:* 1 or 2 tablets two or three times a day.

Post-operative vomiting: 2 tablets not less than four hours before surgery.

Severe nausea and vomiting of pregnancy: 2 tablets at night; an additional tablet may be taken in the morning.

Nausea and vomiting in other conditions: 1 or 2 tablets two or three times daily, according to the severity of the symptoms.

Ancoloxin is not recommended for children.

Contra-indications, warnings, etc There are no contra-indications.

Precautions: Whilst drug therapy is undesirable during the first trimester of pregnancy the administration of Ancoloxin may be warranted if vomiting is severe.

Side-effects: Like other antihistamines, Ancoloxin occasionally gives rise to drowsiness. Patients should be advised not to drive a car or operate machinery if they feel sleepy and warned that drowsiness is more likely to occur if alcohol is taken.

Overdosage: Gastric aspiration and lavage with 1% sodium bicarbonate solution and general supportive measures.

Pharmaceutical precautions Ancoloxin Tablets should be stored in well closed containers.

Legal category POM.

Package quantities Ancoloxin Tablets are available in containers of 50 and 250.

Further information Nil.

Product licence number 0021/5060.

BETA-CARDONE*

Presentation *Beta-Cardone Tablets 200 mg:* White, circular, scored tablets engraved DF/BC20, each containing sotalol hydrochloride 200 mg.

80 mg: Red, circular, scored tablets engraved DF/BC8, each containing sotalol hydrochloride 80 mg.

40 mg: Green, circular, scored tablets engraved DF/BC4, each containing sotalol hydrochloride 40 mg.

Beta-Cardone Injection: 5 ml ampoules containing sotalol hydrochloride 10 mg in each 5 ml of solution.

Uses Beta-Cardone is a β -adrenoceptor blocking agent which is devoid of intrinsic sympathomimetic and local anaesthetic activity. Its major therapeutic effect is to protect the heart from undesirable sympathetic activity. Beta-Cardone reduces the rate and force of contraction of the heart; cardiac work and oxygen consumption are diminished.

In angina pectoris: Beta-Cardone reduces the frequency and severity of anginal attacks and increases exercise tolerance.

In hypertension: Beta-Cardone reduces blood pressure without the side-effects usually associated with peripherally acting hypotensive drugs.

In cardiac arrhythmias: Beta-Cardone is used to restore normal rate and rhythm or to reduce the rate of ventricular contraction, particularly in arrhythmias of supraventricular origin. It is also indicated for the control and prevention of arrhythmias after recent myocardial infarction.

In thyrotoxicosis: Beta-Cardone is recommended for short-term symptomatic relief of sympathetic over-activity as an adjunct to specific anti-thyroid therapy.

Dosage and administration *Oral administration in adults:*

General instructions: When administering Beta-Cardone to a patient for the first time, it is desirable to start with a low dose and gradually increase the dose until the desired response is obtained; as a general rule the heart rate should not be reduced to less than 55 beats per minute.

No special precautions, other than the observance of

the contra-indications listed below, are required when transferring patients to Beta-Cardone from other β -blockers. Beta-Cardone can be administered in conjunction with diuretic agents, digitalis, lignocaine and specific anti-thyroid drugs such as carbimazole. The following are guide lines for oral administration.

Dosage in angina pectoris: The optimum dosage is usually found to be between 200 mg and 600 mg per day in a single or divided dose.

Treatment should be initiated with 80 mg twice daily for the first 7 to 10 days. The patient may then be given 200 mg once daily, preferably on rising in the morning. Further increments of 200 mg may thereafter be given, if necessary, at intervals of two or more weeks but, in angina pectoris, it is rarely found necessary to administer more than 400 mg per day.

Dosage in hypertension: The optimum dosage is usually found to be between 200 mg and 600 mg per day in a single or divided dose.

Again treatment should be initiated with 80 mg twice daily for the first 7 to 10 days. The patient may then be given 200 mg once daily, preferably on rising in the morning. Further increments of 200 mg may thereafter be given, if necessary, at intervals of two or more weeks and, in hypertension, there have been occasional reports of up to 4,000 mg being administered daily in divided doses.

Dosage in cardiac arrhythmia: The optimum dosage is usually found to be between 120 mg and 240 mg per day in a single or divided dose.

Dosage in Thyrotoxicosis: In most cases it has been found that a dosage of between 120 mg and 240 mg per day, in a single or divided dose, will reduce sympathetic overactivity.

In cardiac arrhythmia and thyrotoxicosis, treatment should be commenced with a dose of 40 mg, three times daily for the first 7 to 10 days. Once the maintenance phase is reached a single dose of 200 mg daily, preferably on rising in the morning, may be adequate.

Intravenous administration in adults:

Dosage in acute cardiac arrhythmias: In acute cardiac arrhythmias, especially those following myocardial infarction, 10–20mg of Beta-Cardone (i.e. 5–10 ml of Beta-Cardone injection) should be given slowly by the intravenous route; similar doses may be repeated if required.

Contra-indications, warnings, etc

Heart block and bronchospasm: Beta-Cardone should not be given to patients suffering from heart block or who have a history of bronchospasm.

In patients with poor cardiac reserve β -blockade can precipitate heart failure; in such cases, Beta-Cardone therapy should not be commenced until the patient has been controlled by cardiac glycosides and, if necessary, diuretic therapy.

Warning: There have been reports of skin rashes and/or dry eyes associated with the use of β -adrenoceptor-blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when the treatment was withdrawn. Discontinuation of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a β -blocker should be gradual.

Diabetic keto-acidosis and metabolic acidosis: Beta-Cardone should not be given to patients suffering from diabetic keto-acidosis or metabolic acidosis; therapy

with Beta-Cardone can be commenced or resumed when the metabolic condition has been corrected.

Treated diabetes: Beta-Cardone, like other β -blocking agents, may reduce or mask the usual pre-hypoglycaemic warning signs.

General anaesthesia: If desired, Beta-Cardone may be stopped four days prior to surgery. However, where sudden withdrawal might expose the patient to severe angina or arrhythmias, anaesthesia can proceed provided that the following precautions are taken.

1. Vagal dominance is counteracted by premedication with atropine sulphate (0.25–2.0 mg) administered intravenously.

2. Ether, chloroform, cyclopropane and trichlorethylene are not used.

Pregnancy: Animal studies with sotalol hydrochloride have shown no evidence of teratogenicity or other harmful effects to the fetus, nevertheless its use throughout pregnancy should be avoided unless it is absolutely necessary. It crosses the placenta and may cause fetal bradycardia.

Breast milk: Infants should not be fed with breast milk from mothers being treated with Beta-Cardone.

Alcoholism: Beta-adrenoceptor blocking drugs may precipitate cardiac failure in alcoholic patients.

Renal insufficiency: Since Beta-Cardone is mainly excreted unchanged in the urine, accumulation may be avoided by reduction in dosage.

Upper respiratory infections: In these conditions patients without a history of airways obstruction may suffer bronchospasm from β -blockade.

Side-effects: Beta-Cardone is usually well tolerated. Bronchoconstriction has been reported in a few sensitive individuals; it may be controlled by the intravenous administration of atropine sulphate (0.25–2.0 mg) and/or by inhalation of a selective β -adrenoceptor stimulant such as salbutamol.

Interactions: In combined therapy clonidine should not be discontinued until several days after withdrawal of Beta-Cardone.

Overdosage: Overdosage causes excessive bradycardia and hypotension; to counteract this atropine sulphate (0.25–2.0 mg) should be administered intravenously and, if need be, isoprenaline (about 5 mcg per minute) by slow intravenous injection.

Pharmaceutical precautions Beta-Cardone Tablets and Injection should be protected from light.

Legal category POM.

Package quantities Beta-Cardone Tablets 200 mg are available in containers of 30 tablets.

Beta-Cardone Tablets 80 mg are available in containers of 100 and 500 tablets.

Beta-Cardone Tablets 40 mg are available in containers of 100 and 500 tablets.

Beta-Cardone Injection is available in ampoules of 5 ml in boxes of 10 ampoules.

Further information Beta-Cardone is not metabolised and, in the main, is excreted in the urine. After oral administration the plasma half life has been shown to be 17 hours; the lipid solubility is very low.

Product licence numbers

Beta-Cardone Tablets 200 mg 0021/0056

Beta-Cardone Tablets 80 mg 0021/0055

Beta-Cardone Tablets 40 mg 0021/0054

Beta-Cardone Injection 0021/0057

DF 118

Presentation DF 118 Tablets: White tablets engraved DF 118. Each tablet contains Dihydrocodeine Tartrate BP 30 mg.

Elixir DF 118: A brown syrup. Each 5 ml contains Dihydrocodeine Tartrate BP 10 mg.

DF 118 Injection: A colourless solution. Each ampoule contains in 1 ml Dihydrocodeine Tartrate BP 50 mg.

Uses Relief of moderate to severe pain. The action of dihydrocodeine tartrate is almost purely analgesic – it is virtually free from sedative or hypnotic effects. 30 mg given parenterally has been shown to have an analgesic potency equivalent to that of 10 mg of morphine; in a study of oral analgesics for the relief of chronic pain, the same dose was found to be equivalent to 100 mg of pethidine. In both these trials dihydrocodeine was found to have a lower incidence of side-effects than either morphine or pethidine.

It is fully active when administered orally and, in the recommended doses, causes little or no respiratory depression; in addition to being a potent analgesic the compound also exhibits well-defined antitussive activity.

DF 118 is indicated in all painful conditions where an alert patient is desired, viz. sciatica, osteoarthritis, chronic rheumatoid arthritis, arthritis of the spine, peripheral vascular disease, post-herpetic neuralgia, Paget's disease, malignant disease, post-operative pain.

Because DF 118, in the recommended doses, causes little or no respiratory depression, its use in the treatment of post-operative pain may reduce the risk of chest complications.

Dosage and administration *General information:* As DF 118 is fully active when administered orally this route is to be preferred whenever possible. The analgesic effect of DF 118 is not materially enhanced by increasing the dose above that recommended below; in severe cases the interval between doses should be reduced to obtain the requisite analgesic cover.

DF 118 is best administered with or after food. It is not recommended for administration to children under 4 years.

Elixir DF 118 is a pleasant tasting liquid suitable for administration to patients who may have difficulty swallowing the tablets.

Dosage – Analgesia.

Adults: DF 118 Tablets: 1 tablet (30 mg) every four to six hours or at the discretion of the physician.

Elixir DF 118: One to three 5 ml spoonfuls (10–30 mg) every four to six hours or at the discretion of the physician.

DF 118 Injection: Patients who, for one reason or another are unable to be treated with the tablets or elixir may be given up to 50 mg by intramuscular or deep subcutaneous injection.

Children aged 4 to 12 years: 0.5 to 1 mg/kg body weight every 4 to 6 hours.

Dosage – Antitussive.

Adults: Elixir DF 118: One 5 ml spoonful (10 mg) every four to six hours or at the discretion of the physician.

Children aged 4 to 12 years: 200 mcg/kg body weight every 4 to 6 hours.

Contra-indications, warnings, etc Respiratory depression; obstructive airways disease.

Precautions: As dihydrocodeine may bring about histamine-release, DF 118 should not be given during an attack of asthma and it should be administered with due care to persons liable to such attacks.

Dosage should be reduced in the elderly, in hypothyroidism and in chronic hepatic disease. Alcohol should be avoided whilst under treatment with DF 118.

There is no, or inadequate evidence of safety in human pregnancy but the drug has been used for many years without apparent ill consequence.

Side-effects: Constipation, nausea, vomiting, headache and vertigo occur and are relatively more common when the dose is increased above 30 mg. If constipation occurs it can be treated with a gentle laxative.

Overdosage: Conservative management is recommended; gastric lavage should be carried out. Severe respiratory depression can be treated with naloxone hydrochloride 0.4 mg subcutaneously, repeated as required at 2 or 3 minute intervals.

Pharmaceutical precautions The recommended diluent of the Elixir is Unpreserved Syrup BP, or syrup preserved with *p*-hydroxybenzoic acid. The resulting dilution will keep for 14 days at room temperature.

DF 118 preparations should be protected from light.

Legal category DF 118 Tablets POM.

Elixir DF 118 POM.

DF 118 Injection POM: MDA.

Package quantities DF 118 Tablets are available in packs of 100 and 500.

Elixir DF 118 is available in bottles of 150 ml and 1 litre.

DF 118 Injection is available in boxes of 5 ampoules of 1.1 ml.

Further information In patients already habituated to a drug such as pethidine, the substitution of dihydrocodeine in equi-analgesic doses has led to the appearance of abstinence symptoms. This suggests that dihydrocodeine, despite its effectiveness as an analgesic, has a very low addiction potential and can be safely administered more frequently than the more potent narcotic drugs and for longer periods.

Product licence numbers

DF 118 Tablets 0021/5063R

Elixir DF 118 0021/0053R

DF 118 Injection 0021/5028R

DINDEVAN* TABLETS

Presentation *Dindevan Tablets 10 mg:* White tablets engraved DF/D10, each tablet containing Phenindione BP 10 mg.

Dindevan Tablets 25 mg: Green tablets engraved DF/D25, each tablet containing Phenindione BP 25 mg.

Dindevan Tablets 50 mg: White tablets engraved DF/D50, each tablet containing Phenindione BP 50 mg.

Uses Dindevan (Phenindione BP) is a synthetic anticoagulant which acts by interfering with the formation of certain clotting factors. It produces its effect in 36–48 hours after the initial dose; the effect wanes over a period of 48–72 hours after Dindevan is stopped.

Coronary occlusion; deep vein thrombosis; pulmonary embolism; peripheral vascular thromboembolic states;

mesenteric and retinal thromboembolism. In emergencies, such as the conditions listed above, anticoagulant therapy should be initiated with heparin and Dindevan together. Where there is less urgency, as in patients at special risk of thromboembolism, anticoagulant therapy may be initiated with Dindevan alone.

Appropriate indications include predisposition to thromboembolism following surgery, during pregnancy and the puerperium, and chronic embolic pulmonary hypertensive disease.

Dosage and administration *Initial loading dose:* Usually 200 mg, followed on the second day with a dose of 100 mg.

Maintenance therapy: Dosage must be adjusted, from the third day, in accordance with the results of appropriate coagulation tests. Concomitant heparin therapy affects the results of control tests and should be discontinued at least six hours before the first test is carried out.

Control tests must be made at regular intervals and the dosage further adjusted according to the results obtained. As a general guide, a maintenance dosage of between 50–150 mg per day will prove satisfactory in most cases. Occasionally, a resistant patient may need 200 mg or more per day; on the other hand a sensitive patient may need less than 50 mg per day.

Contra-indications, warnings, etc

Contra-indications: Dindevan should not be given in the presence of severe hepatic or renal disease, actual or potential haemorrhagic conditions, or to patients with uncontrolled hypertension. Its use within 24 hours following surgery or labour should be undertaken with caution, if at all.

Precautions: The following factors may exaggerate the effects of Dindevan and necessitate a reduction in dosage; loss of weight; elderly subject; acute illness; deficient renal function; decreased dietary intake of vitamin K; administration of a number of drugs, including salicylates, quinidine, broad-spectrum antibiotics, phenformin, tolbutamide, phenylbutazone, indomethacin, cimetidine, azapropazone, clofibrate, ACTH and corticosteroids and all potentially hepato-toxic drugs.

Factors which may call for an increase in maintenance dosage include weight gain, gastro-intestinal upset, increased intake of vitamin K, fats and oils, and administration of drugs (e.g. phenobarbitone) that increase liver enzyme activity.

Oral anticoagulants should not be used in pregnancy unless there are firm indications. In particular, because of possible teratogenicity, they should not be used for the remainder of the first trimester following diagnosis. In addition the risk of foetal haemorrhage is increased when they are used near term. It is therefore suggested that heparin (which does not cross the placenta) be used during the first trimester and after 37 weeks' gestation. However, the use of heparin in pregnancy is not absolutely safe and specialist guidance is advisable for those who are pregnant and who need anti-coagulant therapy. Women of child-bearing age who are receiving treatment with Dindevan should be cautioned about the possible complications of pregnancy. Infants should not be fed with breast milk from mothers being treated with Dindevan.

Side-effects: The following effects have been reported: skin rashes of various kinds, skin necrosis, fever, leucopenia and agranulocytosis, diarrhoea, hepatitis and renal damage with tubular necrosis. If any of these are

observed administration of Dindevan should stop immediately and full investigations of blood and of liver and kidney function should be carried out. Possible sensitivity to other drugs should be considered. Other anticoagulants, such as Marevan[®], are usually tolerated by patients sensitive to Dindevan. If therapy is controlled as recommended then bleeding due to overdosage of anticoagulant is rare. An episode of bleeding occurring during anticoagulant therapy must, therefore, be investigated fully and not regarded automatically as a manifestation of overdosage.

N.B. The metabolites of Dindevan often colour the urine pink or orange. This may be distinguished from discoloration caused by haemoglobin by the addition of a few drops of dilute acetic acid to the urine. If the colour is due to Dindevan it will disappear immediately.

Overdosage: If haemorrhage occurs or a potential bleeding state arises, excessive depression of the coagulation activity can be corrected by temporary withdrawal of Dindevan accompanied, if necessary, by administration of vitamin K₁, in oral doses of 2–20 mg; rarely it may be necessary to give vitamin K₁ intravenously, or to infuse fresh whole blood.

Pharmaceutical precautions No special requirements or precautions.

Legal category POM.

Package quantities Dindevan Tablets 10 mg. Dindevan Tablets 25 mg and Dindevan Tablets 50 mg are each available in containers of 100 and 500 tablets.

Further information Nil.

Product licence numbers

Dindevan Tablets 10 mg	0021/5064
Dindevan Tablets 25 mg	0021/5065
Dindevan Tablets 50 mg	0021/5066

ADSORBED DIPHTHERIA AND TETANUS VACCINE BP (PTAH) (DT/Vac/Ads)

Presentation Adsorbed Diphtheria and Tetanus Vaccine is a mixture of diphtheria formol toxoid and tetanus formol toxoid adsorbed on aluminium hydroxide; each 0.5 ml dose contains not less than 30 i.u. of diphtheria toxoid and not less than 40 i.u. of tetanus toxoid.

Uses Active immunisation against diphtheria and tetanus in infants and children. Reinforcement of immunity to diphtheria and tetanus in children under the age of 10 years.

Dosage and administration *Children under 10 years:* Adsorbed Diphtheria and Tetanus Vaccine (0.5 ml) should be administered by intramuscular injection; the container should be shaken before withdrawing the prescribed dose.

Basic course: The course consists of three doses with an interval of 6–8 weeks between the first and second dose and 4–6 months between the second and third dose.

Reinforcing doses: Children under the age of 10 years immunised in infancy with diphtheria and tetanus adsorbed vaccine or diphtheria, tetanus and pertussis vaccine should receive a reinforcing dose of diphtheria and tetanus vaccine at 5 years of age.

Contra-indications, warnings, etc

Contra-indications: Presence of acute infectious disease.

Warnings: A sterile syringe and Adrenaline Injection BP should be ready for use in case the need arises for emergency treatment of an allergic reaction.

Not for intradermal use.

Adverse effects: Acute allergic reactions, pallor and dyspnoea are rarely reported. Transient pyrexia, headaches, malaise, local swelling, redness and tenderness may occur. A small painless nodule may form at the injection site.

Pharmaceutical precautions Protect from light. Store between 2°C and 8°C (36°F and 46°F). Do not freeze.

Partly used multidose containers should be discarded within three hours of withdrawal of the first dose.

Legal category POM.

Package quantities Single-dose ampoules containing 0.5 ml and multidose vials containing 5 ml.

Further information Nil.

Product licence number 0021/0061.

ADSORBED DIPHTHERIA, TETANUS AND PERTUSSIS VACCINE BP (PTAH) (DTPer/Vac/Ads)

Presentation Adsorbed Diphtheria, Tetanus and Pertussis Vaccine is a mixture of diphtheria formol toxoid, tetanus formol toxoid and killed *Bordetella pertussis* organisms.

Each 0.5 ml dose contains not less than 30 i.u. diphtheria toxoid, 60 i.u. tetanus toxoid (estimated by mouse test) and 4 i.u. *B. pertussis* adsorbed on aluminium hydroxide; the pertussis component contains the currently known immunogenic serotypes of *B. pertussis*.

Uses Active immunisation against diphtheria, tetanus and whooping cough in children under the age of five years.

Dosage and administration Adsorbed Diphtheria, Tetanus and Pertussis Vaccine should be administered by intramuscular injection. The container should be shaken before withdrawing the prescribed dose.

The routine course of immunisation consists of 3 doses, each of 0.5 ml, beginning after the age of three months. The Department of Health and Social Security recommends the first dose should preferably be given at three months of age, the second after an interval of six to eight weeks and the third four to six months later.

In the event of a whooping cough epidemic three doses may be given at monthly intervals, starting at the age of three months. In this case a booster dose of DT/Vac/Ads should be given between the ages of 12 and 18 months.

Contra-indications, warnings, etc

Contra-indications: Adsorbed Diphtheria, Tetanus and Pertussis Vaccine should **not** be given to adults or children over the age of three years.

It is advisable to postpone vaccination if the child is suffering from any acute febrile illness, particularly respiratory, until fully recovered. (Minor infections without fever or systemic upset are not regarded as a contra-indication.)

Vaccination should not be carried out in children who have:

- (a) a history of any severe local or general reaction (including a neurological reaction) to a preceding dose;
- (b) a history of cerebral irritation or damage in the neonatal period, or who have suffered from fits or convulsions.

Even when pertussis vaccine is contra-indicated an infant should still be considered for immunisation against diphtheria and tetanus.

Precautions: There are certain groups of children in whom whooping cough vaccination is not absolutely contra-indicated but who require special consideration as to its advisability. These groups are:

- (a) children whose parents or siblings have a history of idiopathic epilepsy;
- (b) children with developmental delay thought to be due to a neurological defect;
- (c) children with neurological disease.

For these groups the risk of vaccination may be higher than in normal children but the effects of whooping cough may be more severe, so that the benefits of vaccination would also be greater. The balance of risk and benefit should be assessed with special care in each individual case.

A personal or family history of allergy has in the past been regarded as a contra-indication to vaccination but there is now a substantial body of medical opinion which no longer considers this to be so. Doctors should, however, use their own discretion in the individual case.

Side-effects: Local oedema and redness sometimes occur, particularly if the vaccine has been administered by subcutaneous rather than intramuscular injection; superficial injections may also give rise to a local nodule at the site of injection.

Encephalitis has been reported after the administration of Pertussis Vaccine with incidence variously reported between 1 in 1,000 to 1 in 10,000 cases.

Warnings: A sterile syringe and Adrenaline Injection BP should be ready for use, in case the need arises for emergency treatment of an allergic reaction.

Not for intradermal use.

Pharmaceutical precautions Protect from light. Store in a refrigerator between 2°C and 8°C (36°F and 46°F). Do not freeze.

Partly used multi-dose containers should be discarded within three hours of withdrawal of the first dose.

Legal category POM.

Package quantities Single-dose ampoules containing 0.5 ml and multidose vials containing 5 ml.

Further information Nil.

Product licence number 0021/0062.

EXTIL* COMPOUND LINCTUS

Presentation A reddish-pink, translucent linctus, each 10 ml dose containing:

Noscapine BP	25 mg
Pseudoephedrine (equivalent to 60 mg Pseudoephedrine Hydrochloride BPC)	49.2 mg
Carbinoxamine maleate	6 mg

Uses The antitussive activity of noscapine, an isoquinoline derivative, is comparable to that of codeine. Unlike codeine, noscapine has no narcotic or analgesic

effect, does not depress the respiratory centre and, in normal dosage, does not cause constipation.

Pseudoephedrine has decongestant and bronchodilator properties similar to those of ephedrine, but is relatively less toxic and less active as a cardiac and CNS stimulant.

The antihistamine, carbinoxamine maleate, complements the effect of pseudoephedrine and is valuable in conditions where an allergic component is present.

Extil Compound Linctus is indicated in troublesome cough, especially cough accompanied by bronchospasm or congestion of the upper respiratory tract. Also in cough associated with the common cold; in such conditions it not only relieves the cough but reduces both nasal and bronchial congestion.

Dosage and administration *Adults and children over 12:* One 10 ml dose three or four times a day as required.

Children over 2 years and up to 12: Half to one 5 ml dose three or four times a day as required.

Contra-indications, warnings, etc

Contra-indications: Should not be given to patients suffering from advanced hypertension or heart failure, or undergoing treatment with monoamine oxidase inhibitors.

Precautions: Carbinoxamine only rarely gives rise to drowsiness, but as alcohol potentiates the action of antihistamines, patients should be warned that drowsiness may well occur if alcohol is taken.

Notice should be taken of current views that any drug should be prescribed with caution during pregnancy.

Side-effects: Pseudoephedrine in clinical doses has very little pressor activity in normotensive individuals, but minor side-effects, similar to those encountered with ephedrine, may occur if the recommended dosage is exceeded.

Overdosage: Gastric lavage and general supportive measures.

Pharmaceutical precautions Extil Compound Linctus must not be shaken or diluted.

Legal category POM.

Package quantities Extil Compound Linctus is available in bottles of 500 ml.

Further information Noscapine does not produce addiction: It has been recommended by the World Health Organisation as a substitute for codeine for suppression of cough.

Product licence number 0021/5004.

FAZADON*

Presentation A clear yellow solution containing fazadinium bromide equivalent to 15 mg of fazadinium per ml. Each 5 ml ampoule contains the equivalent of 75 mg of fazadinium base made isotonic by the inclusion of 0.6% w/v of sodium chloride and stabilised with 0.3% w/v of α -thioglycerol – the latter gives the solution a characteristic smell of sulphides.

Uses Fazadon is a neuromuscular blocking agent for *intravenous administration*; it acts by competitive (non-depolarising) blockade of the acetylcholine receptors in the motor-end plates.

Fazadon produces profound muscular relaxation within 60 seconds and, at the recommended dosage,

this profound relaxation is maintained for about 40 minutes. It is indicated in surgical and obstetric procedures which call for endotracheal intubation and subsequent muscle relaxation.

Its action is reversed promptly and permanently by the administration of an anticholinesterase drug.

Dosage and administration For adults, the dose, given intravenously, should be calculated on the basis of 0.75 mg to 1 mg per kilogram body weight. At this dosage sufficient laryngeal relaxation for intubation may be expected in between 30 and 60 seconds.

At present there is insufficient evidence to recommend a dosage regimen for routine use in children under 10 years of age.

Increments: Increments of up to 1 ml according to body weight and clinical circumstances (i.e. approximately 25% of the initial dose) should provide relaxation for a further period of between 10 to 20 minutes.

Reversal: The action of Fazadon is completely and permanently reversed by 2.5 to 5 mg of neostigmine methylsulphate administered intravenously; the bradycardia following the intravenous administration of neostigmine may be avoided by the prior intravenous administration of 1.0 mg atropine sulphate.

Contra-indications, warnings, etc Whenever Fazadon is used, respiration must be assisted and facilities must be available for controlled ventilation.

Fazadon is a competitive inhibitor of neuromuscular transmission; it should NOT be used simultaneously with a depolarising agent.

The following anaesthetics increase the neuromuscular blocking effect of Fazadon: ether, halothane, cyclopropane, Althesin*. The following drugs may also prolong the duration of action: diazepam, pentobarbitone, clindamycin, colistin, kanamycin, neomycin, polymyxins, streptomycin, tobramycin, framycetin, amikacin, gentamicin and other amino-glycoside antibiotics.

Fazadon, with a pH of 3.2 to 4.3, must not be mixed in the same syringe with alkaline anaesthetic agents, e.g. thiopentone. Fazadon may potentiate halothane-induced hypotension.

Fazadon is mainly excreted unchanged in the urine; care should therefore be taken in patients with renal insufficiency and dosage should be reduced according to the severity of the condition.

In patients with myasthenia gravis or myasthenic syndrome Fazadon should be administered in very small doses and with extreme caution; a reduction in dosage is also advisable in cases of gross obesity, myopathy or after poliomyelitis.

It should be noted that in operations requiring hypothermia the neuromuscular blockade of non-depolarising drugs is decreased, but increases again when the patient's body temperature returns to normal.

Although animal studies have not shown any teratogenic or other harmful effects on the fetus the use of Fazadon in the first trimester of pregnancy should be avoided unless absolutely necessary.

Side-effects: A transient, moderate tachycardia often accompanies the use of Fazadon. In most patients it serves to counter an adverse effect of anaesthesia and in a few it may be more marked.

In a few cases minor local inflammatory reactions have been noticed at the site of injection.

Neither bronchospasm nor increased whole blood histamine has been reported.

Overdosage: In case of accidental overdosage the patient should remain on assisted respiration and oxygen, and should be given atropine sulphate 1 mg intravenously, followed by an adequate intravenous dose of neostigmine methylsulphate (2.5 mg to 5 mg).

Pharmaceutical precautions Store, protected from light, at a temperature not exceeding 20°C. Stored under these conditions, Fazadon is stable for two years.

Legal category POM.

Package quantities 5 ml ampoules, in boxes of 10.

Further information Fazadon crosses the placental barrier only in very small amounts, and has been shown to have no adverse effect on fetal movement; it has been used successfully in Caesarean section.

After the administration of Fazadon there is no significant change in plasma potassium or whole blood histamine levels.

Fazadon does not raise intragastric or intraocular pressure.

Product licence number 0021/0064.

FLUVIRIN* ▼

Presentation Fluvirin is Inactivated Influenza Vaccine (Surface Antigen) BP containing highly purified haemagglutinin and neuraminidase antigens prepared from those strains of influenza virus currently recommended.

Uses *Protection against influenza* especially in those cases deemed to be at special risk, viz.

Chronic pulmonary disease, e.g. chronic bronchitis and emphysema, asthma, bronchiectasis, pulmonary tuberculosis and fibrosis.

Chronic heart disease, e.g. valvular and hypertensive heart disease.

Chronic renal disease, e.g. chronic nephritis; patients with renal disease on immunosuppressive drugs.

Diabetes and possibly other less common endocrine disorders.

Patients who are being actively considered for immunosuppressive therapy.

Immunisation against influenza is also recommended in:

School children over four years of age and in elderly persons living in residential establishments, in which rapid spread is likely to follow the introduction of infection.

Doctors, nurses, ambulance men, and others at special risk of infection by reason of their contacts with persons suffering from influenza.

Dosage and administration *Adults and children over 13 years:* Single dose of 0.5 ml by deep subcutaneous or intramuscular injection.

Children aged 4 to 13 years: 2 doses of 0.5 ml, one month apart.

If the vaccine has been stored in a refrigerator it must be allowed to reach room temperature before use: the container should be well shaken immediately before making the injection. Unused contents of multidose vials should be discarded within three hours of first use.

Contra-indications, warnings, etc

Contra-indications: Fluvirin is contra-indicated in persons sensitive to egg, chicken or influenzal viral protein. Immunisation should be delayed if there is active or suspected infection.

Warnings: Because the vaccine contains highly purified haemagglutinin and neuraminidase antigens the total viral content of the vaccine has been reduced to about one tenth of that of whole virus vaccines. Even so, a sterile syringe and Adrenaline Injection BP should be ready for use, in case the need arises for emergency treatment of an allergic reaction.

Spirit should not be allowed to come in contact with the vaccine.

Side-effects: Local effects such as redness and soreness at the site of injection may occur.

Systemic effects, such as headache, pyrexia and a feeling of malaise may occur.

Both local and systemic side effects are less frequent with Fluvirin than with Inactivated Influenza Vaccine BP.

Overdosage: Not applicable.

Pharmaceutical precautions Fluvirin should be protected from light and stored at between 2°C and 8°C (36°F and 46°F). Do not freeze. Though limited exposure to light and higher temperatures has no adverse effect on the vaccine, temperatures above 20°C (68°F) should be avoided.

Legal category POM.

Package quantities Fluvirin is available in 0.5 ml disposable syringe packs, in 5 ml multidose vials and 25 ml multidose vials for hospital or industrial use with the Port-O-Jet or other suitable jet injector.

Further information Studies with surface antigen influenza vaccine have shown that the purified haemagglutinin and neuraminidase antigens contained in a single dose of Fluvirin will produce a protective antibody response in up to 90% of patients.

Product licence number 0021/0096.

JEXIN*

Presentation Jexin is Tubocurarine Injection BP and is a clear colourless, or faintly colourless sterile solution containing Tubocurarine Chloride BP 10 mg per ml.

Uses Jexin produces paralysis of voluntary muscle by interfering with transmission across the neuromuscular junction. It acts by competitive blockade of motor endplates. Paralysis appears in the muscles of the face and neck, of the limbs and of the abdomen, in that order, the intercostal muscles and diaphragm being affected last. The paralysis reaches its maximum two to five minutes after intravenous injection and lasts for about 30 minutes. There is, however, a residual action lasting for as long as 24 hours, and during this time smaller doses are required to reproduce the effect of the initial dose.

Jexin is mainly indicated as an adjunct to anaesthesia to secure muscular relaxation in surgery and obstetrics. It can also be used in tetanus.

Dosage and administration *Adults:* Dosage should be based on the response to an initial intravenous injection of 10–15 mg. A test dose of 5 mg in the unanaesthetised patient may be administered before

giving the full initial dose. Supplementary doses of 5 mg are adequate, if required for lengthy operations. A total of 40 mg for a single operation should not be exceeded.

Children: The initial dose is of the order of 0.32 mg per kg of body weight.

Contra-indications, warnings, etc

Contra-indications: Jexin is contra-indicated in patients with respiratory insufficiency or in the presence of renal or hepatic impairment.

Precautions: In patients with myasthenia gravis or myasthenic syndrome, Jexin should be administered in very small doses and with extreme caution; a reduction in dosage is also advisable in cases of gross obesity, myopathy and after poliomyelitis. Patients with asthma or those susceptible to bronchospasm require especial care as Jexin is known to cause the release of histamine. In such patients the prophylactic administration of an anti-histamine may be advisable.

Care is necessary if Jexin has to be given to a patient on two occasions within 24 hours. Administration of Jexin either with or before a depolarising relaxant, such as suxamethonium, may cause a muscle relaxation which is irreversible by neostigmine. The effects of Jexin are enhanced by ether; the hypotension produced by halothane anaesthesia is increased by Jexin and a reduced dose of Jexin should be used.

Jexin may be potentiated by diazepam and by clindamycin, colistin, kanamycin, neomycin, polymyxins, streptomycin, tobramycin, framycetin, amikacin, gentamicin and other amino-glycoside antibiotics and by quindine.

Side-effects: The dosage recommended produces few side-effects; a transient fall in blood pressure may sometimes occur.

Overdosage: Intravenous neostigmine with atropine sulphate. Oxygen and assisted respiration may be required.

Pharmaceutical precautions No special requirements or precautions.

Legal category POM.

Package quantities Jexin is supplied in 1.5 ml ampoules in boxes of 5.

Further information Although Jexin should not normally be mixed with thiopentone, this can be done if prepared immediately prior to injection and used only if the solution remains perfectly clear.

Product licence number 0021/5025.

LOCAN* CREAM

Presentation Locan Cream, a smooth, white cream, contains:

Amylocaine	1%
Amethocaine	0.8%
Cinchocaine BPC	0.4%

in a non-greasy base which does not soil or stain the clothing.

Uses The combination of the lipid-soluble free bases of amethocaine, amylocaine and cinchocaine provides rapid, yet sustained, relief from pruritic and painful conditions.

Locan Cream is of particular value in the treatment of pruritus ani, pruritus vulvae, external haemorrhoids and anal fissure; it should also be found useful in relieving the pain of cracked or sore nipples, minor burns,

chilblains and athlete's foot. The analgesic effect may also be found useful in alleviating localised muscular pain arising from conditions which do not need prolonged treatment.

Administration A thin layer of Locan Cream should be applied over the affected area and massaged in gently until absorption is complete. The application may be renewed as required.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to local anaesthetics.

Precautions: Sensitisation may occur to the local anaesthetics contained in Locan Cream. This should be suspected, and application stopped, if increased irritation or reddening occurs.

Side-effects: No other side-effects are likely to be encountered.

Overdosage: Not applicable.

Pharmaceutical precautions No special requirements or precautions.

Legal category P.

Package quantities Locan Cream is available in tubes of 30 g.

Further information Nil.

Product licence number 0021/5010.

MARCAIN* PLAIN

Presentation Marcain Plain is Bupivacaine Hydrochloride Injection BP and is a clear, colourless, aqueous sterile solution in three strengths:

Marcain Plain 0.25%, containing Bupivacaine Hydrochloride BP 0.25% w/v.

Marcain Plain 0.5%, containing Bupivacaine Hydrochloride BP 0.5% w/v.

Marcain Plain 0.75% containing Bupivacaine Hydrochloride BP 0.75% w/v.

Uses The principal action of Marcain is to inhibit impulse transmission in nerve fibres with which it comes in contact. In a mixed nerve, sensory fibres are blocked before motor fibres; and among the different types of sensory fibres, those carrying the sensation of pain are affected before those carrying sensations of cold, heat, touch and deep pressure.

The local analgesic effect of Marcain is similar in rate of onset and depth to that of lignocaine and mepivacaine, but is of much greater duration; clinical evidence indicates that the quality of sensory blockade and interference with motor function provided by Marcain compares favourably with alternative agents. Marcain is approximately four times as potent as lignocaine or mepivacaine; hence a 0.5% solution of Marcain is equivalent in nerve-blocking activity to a 2% solution of lignocaine. Marcain is indicated primarily for specialist use in situations where prolonged analgesia is required. A list of suggested indications and the dose of solution appropriate for each are shown in the adjacent table.

Dosage and administration In nerve blocks the maximum recommended dose of Marcain in any four-hour period is 2 mg/kg, representing 25 to 30 ml of 0.5% Marcain for an adult weighing 65 to 70 kg.

In intravenous regional analgesia the method of use is to place a tourniquet cuff over padding on the upper arm. A number 21 or 23 gauge indwelling needle is placed in a suitable vein, preferably on the dorsum of the hand,

Marcain Plain				
Surgical procedure	Concentration (%)	Dose		
		(ml)	(mg)	
Brachial plexus (axillary) block	0.25	20-40	50-100	
	0.5	15-30	75-150	
Lumbar extradural block	0.25	15-20	37.5-50	
	0.5	15-20	75-100	
	0.75	10-18	75-135	
Caudal extradural block	0.25	15-40	37.5-100	
	0.5	15-25	75-125	
Continuous extradural analgesia	0.25	The dose depends on the number of segments to be rendered analgesic and the patient's age (1-3 ml per segment)		
	0.5			
	0.75			
Intercostal block	0.25	4-8	10-20	
	0.5	3-5	15-25	
Digital block (each digit)	0.25	2-10	5-25	
	0.5	2-6	10-30	
Stellate ganglion block	0.25	10-20	25-50	
Lumbar sympathetic block	0.25	10-20	25-50	
Intravenous regional analgesia	0.5	0.3 ml/kg	1.5 mg/kg	(suitably diluted - see dosage section)
	OR: 0.25	0.6 ml/kg	1.5 mg/kg	(undiluted - see dosage section)
Herniorrhaphy	0.25	30-60	75-150	
Obstetrical procedure				
Lumbar extradural block	1st stage	0.25	6-15	15-37.5 depending on site of catheter tip
	2nd stage	0.25	12-20	30-50
		0.5	8-14	40-70
Caudal extradural block	1st stage	0.25	15-30	37.5-75
	2nd stage	0.25	15-30	37.5-75
(intermittent)		0.5	10-20	50-100
Bilateral pudendal block		0.25	50-60	125-150

and the limb is exsanguinated either by simple gravity drainage or by the use of Esmarch's bandage. The cuff is then inflated to 50 mm Hg above the patient's systolic blood pressure and the injection of diluted Marcain (i.e. 0.2%) is made through the indwelling needle.

For intravenous regional analgesia Marcain Plain 0.5% may be used in a dose of 0.3 ml/kg body weight (1.5 mg/kg). The 0.5% solution should be mixed with an appropriate volume of Sodium Chloride Injection BP to reduce the concentration to 0.2% before administration by intravenous injection to the cuffed patient. Each 10 ml of 0.5% Marcain Plain will require 15 ml of Sodium Chloride Injection BP to achieve the recommended reduction in concentration to 0.2%.

Alternatively, Marcain Plain 0.25% may be used undiluted in the cuffed patient in a dose of 0.6 ml/kg body weight (1.5 mg/kg).

Satisfactory analgesia and muscle relaxation may be expected to follow in about four minutes. Following the

surgical procedure, the cuff is deflated (without subsequent reinflation) and recovery to normal sensation and tone may be expected in about eight minutes.

For herniorrhaphy Marcain 0.25% with adrenaline 1 in 400,000 is used. Usually 30 to 40 ml is sufficient for the operation; up to 60 ml may be used but the dosage should not exceed 2 mg/kg. Some operators prefer to use Marcain Plain as this aids identification of the bleeding points.

In epidural analgesia for surgical purposes, Marcain Plain 0.75% is recommended because of the increased depth of motor block obtained with this concentration.

Contra-indications, warnings, etc Known hypersensitivity.

Precautions: As with all local analgesic solutions, every care should be taken to avoid accidental intravascular injection.

Marcain Plain can be administered intravenously under controlled conditions (i.e. in the cuffed patient) as described under intravenous regional analgesia in the section 'Dosage and administration'. Care should be taken to ensure that the cuff used does not leak.

Side-effects: Hypotension after extradural or autonomic block may occur commensurate with such procedures. Other side-effects include tremor, tachycardia, bradycardia, malaise, vomiting and, rarely, convulsions or coma.

Overdosage: The occurrence of adverse effects is related directly to the concentration of the drug in the blood, which in turn depends on the dose and the site of administration. Supportive measures to maintain vital functions such as maintenance of the airway, oxygenation with or without assisted ventilation, maintenance of blood pressure, etc., are essential.

Severe convulsions may be treated cautiously with thiopentone or a short-acting neuromuscular blocking agent such as suxamethonium chloride.

Pharmaceutical precautions No special requirements or precautions.

Legal category POM.

Package quantities Marcain Plain 0.25%, Marcain Plain 0.5% and Marcain Plain 0.75% are each available in ampoules of 10 ml in boxes of 10 ampoules.

Further information Investigations in animals and man show Marcain in clinically used concentrations to be exceptionally well tolerated by all tissues with which it comes in contact. Electroneurographic studies after ulnar nerve blockade in volunteers indicate Marcain to have, if anything, less after-effect on both motor and sensory functions than equipotent concentrations of lignocaine and mepivacaine.

Product licence numbers

Marcain Plain 0.25% 0021/5020
Marcain Plain 0.5% 0021/5021
Marcain Plain 0.75% 0021/0108

MARCAIN* WITH ADRENALINE

Presentation Marcain with Adrenaline is Bupivacaine and Adrenaline Injection BP and is a clear, colourless, aqueous sterile solution in two strengths:

Marcain 0.25% with Adrenaline 1 in 400,000, containing:

Bupivacaine Hydrochloride BP 0.25% w/v
Adrenaline BP 1 in 400,000

Marcain 0.5% with Adrenaline 1 in 200,000, containing:

Bupivacaine Hydrochloride BP 0.5% w/v
Adrenaline BP 1 in 200,000

Uses The principal action of Marcain is to inhibit impulse transmission in nerve fibres with which it comes in contact. In a mixed nerve, sensory fibres are blocked before motor fibres, and among the different types of sensory fibres, those carrying the sensation of pain are affected before those carrying sensations of cold, heat, touch and deep pressure.

The local analgesic effect of Marcain is similar in rate of onset and depth to that of lignocaine and mepivacaine, but is of much greater duration; clinical evidence indicates that the quality of sensory blockade and interference with motor function provided by Marcain compares favourably with alternative agents. The addition of adrenaline in low concentration has been shown to increase both the speed of onset and the duration of analgesia. Marcain is approximately four times as potent as lignocaine or mepivacaine; hence a 0.5% solution of Marcain is equivalent in nerve-blocking activity to a 2% solution of lignocaine. Marcain is indicated primarily for specialist use in situations where prolonged analgesia is required. A list of suggested indications and the dose of solution appropriate for each are shown in the table below.

Marcain with Adrenaline				
Surgical procedure		Concentration (%)	Dose	
			(ml)	(mg)
Brachial plexus (axillary) block	0.25	20-40	50-100	
	0.5	15-30	75-150	
Lumbar extradural block	0.25	15-20	37.5-50	
	0.5	15-20	75-100	
Caudal extradural block	0.25	15-40	37.5-100	
	0.5	15-25	75-125	
Continuous extradural analgesia	0.25	The dose depends on the number of segments to be rendered analgesic and the patient's age (1-3 ml per segment)		
	0.5			
Intercostal block	0.25	4-8	10-20	
	0.5	3-5	15-25	
		for each nerve		
Stellate ganglion block	0.25	10-20	25-50	
Lumbar sympathetic block	0.25	10-20	25-50	
Herniorrhaphy	0.25	30-60	75-150	
Obstetrical procedure				
Lumbar extradural block	1st stage	0.25	6-15	15-37.5
		depending on site of catheter tip		
	2nd stage	0.25	12-20	30-50
0.5		8-14	40-70	
Caudal extradural block (intermittent)	1st stage	0.25	15-30	37.5-75
		2nd stage	0.25	15-30
	0.5		10-20	50-100
Bilateral pudendal block	0.25	50-60	125-150	

Dosage The maximum recommended dose of Marcain in any four-hour period is 2 mg/kg, representing 25–30 ml of 0.5% solution for a 65–70 kg adult.

For herniorrhaphy Marcain 0.25% with adrenaline 1 in 400,000 is used. Usually 30 to 40 ml is sufficient for the operation; up to 60 ml may be used but the dosage should not exceed 2 mg/kg. Some operators prefer to use Marcain Plain as this aids identification of the bleeding points.

Contra-indications, warnings, etc

Contra-indications: Known hypersensitivity. Solutions of Marcain with Adrenaline should not be used in digital block or for intravenous regional analgesia because of the adrenaline content; Marcain Plain solutions should be used for these purposes.

Precautions: As with all local analgesic solutions, every care must be taken to avoid intravascular injection.

Side-effects: Hypotension after extradural or autonomic block may occur commensurate with such procedures. Other side-effects include tremor, tachycardia, bradycardia, malaise, vomiting, similar to other local analgesics.

Overdosage: The occurrence of adverse effects is related directly to the concentration of the drug in the blood, which in turn depends on the dose and the site of administration. Supportive measures to maintain vital functions such as maintenance of the airway, oxygenation with or without assisted ventilation, maintenance of blood pressure, etc. are essential.

Severe convulsions may be treated cautiously with thiopentone or a short-acting neuromuscular blocking agent such as suxamethonium chloride.

Pharmaceutical precautions Store in a cool place. Avoid freezing. Protect from light.

Legal category POM.

Package quantities Marcain 0.25% with Adrenaline 1 in 400,000 and Marcain 0.5% with Adrenaline 1 in 200,000 are each available in ampoules of 10 ml in boxes of 10 ampoules.

Further information Investigations in animals and man show Marcain in clinically used concentrations to be exceptionally well tolerated by all tissues with which it comes into contact. Electroneurographic studies after ulnar nerve blockade in volunteers indicate Marcain to have, if anything, less after-effect on both motor and sensory functions than equipotent concentrations of ignocaine and mepivacaine.

Product licence numbers

Marcain 0.25% with Adrenaline 1 in 400,000	0021/5022
Marcain 0.5% with Adrenaline 1 in 200,000	0021/5023

WAREVAN* TABLETS

Presentation Marevan Tablets are Warfarin Tablets BP.

Marevan Tablets 1 mg: Brown tablets engraved DF/M1, each tablet containing Warfarin Sodium BP 1 mg.

Marevan Tablets 3 mg: Blue tablets engraved DF/M3, each tablet containing Warfarin Sodium BP 3 mg.

Marevan Tablets 5 mg: Pink tablets engraved DF/M5, each tablet containing Warfarin Sodium BP 5 mg.

Jses Marevan is a synthetic anticoagulant of the coumarin series and acts by inhibiting the formation of

certain clotting factors. An effect on prothrombin time is produced in 24–36 hours after the initial dose. This reaches a maximum in 36–48 hours and is maintained for 48 hours or more after administration is stopped.

Coronary occlusion; deep vein thrombosis; pulmonary embolism; peripheral vascular thromboembolic states; mesenteric and retinal thromboembolism.

In emergencies, such as the conditions listed above, anticoagulant therapy should be initiated with heparin and Marevan together. Where there is less urgency, as in patients disposed to or at special risk of thromboembolism, anticoagulant therapy may be initiated with Marevan alone. Appropriate indications include predisposition to thromboembolism following surgery, during pregnancy and the puerperium and chronic embolic pulmonary hypertensive disease.

Dosage and administration 10–15 mg daily, according to age and body weight, and adjusted with relation to the results of daily control tests until the desired level of anticoagulant activity is achieved – usually three to six days after the initiation of treatment.

Concomitant heparin therapy affects the results of control tests and should be discontinued at least six hours before the first test is carried out.

Control tests should be made at regular intervals and Marevan maintenance dosage further adjusted according to the results obtained.

Contra-indications, warnings, etc

Contra-indications: Marevan should not be given in the presence of severe hepatic or renal disease, actual or potential haemorrhagic conditions, or to patients with uncontrolled hypertension. Its use within 24 hours following surgery or labour should be undertaken with caution if at all.

Precautions: The following factors may exaggerate the effects of Marevan and necessitate a reduction in dosage: loss of weight; elderly patient; acute illness; deficient renal function; decreased dietary intake of vitamin K; administration of a number of drugs, including salicylates, indomethacin, cimetidine, azapropazone, quinidine, broad spectrum antibiotics, phenformin, tolbutamide, phenylbutazone, clofibrate, ACTH and corticosteroids and all potentially hepatotoxic drugs. Factors which may call for an increase in maintenance dosage include weight gain, gastro-intestinal upset, increased intake of vitamin K, fats and oils, and administration of drugs (e.g. phenobarbitone) that increase liver enzyme activity.

Oral anticoagulants should not be used in pregnancy unless there are firm indications. In particular, because of possible teratogenicity, they should not be used for the remainder of the first trimester following diagnosis. In addition the risk of foetal haemorrhage is increased when they are used near term. It is therefore suggested that heparin (which does not cross the placenta) be used during the first trimester and after 37 weeks' gestation. However, the use of heparin in pregnancy is not absolutely safe and specialist guidance is advisable for those who are pregnant and who need anticoagulant therapy. Women of child-bearing age who are receiving treatment with Marevan should be cautioned about the possible complications of pregnancy.

Side-effects: Side-effects from Marevan are uncommon. A few instances of alopecia, skin rashes of various kinds, diarrhoea and an unexplained drop in haematocrit have been reported, and a 'purple toes' syndrome has been described. If any of these are observed administration of

Marevan should cease and a change be made to another anticoagulant. It may be advisable to avoid other coumarin preparations when a suitable alternative could be Dindevan*.

Skin necrosis within a few days of starting treatment has been infrequently reported. Most subjects are obese, elderly women. The first sign is an erythematous swollen patch. Administration of vitamin K₁ at this stage may prevent the development of ecchymosis and infarction.

Possible sensitivity to other drugs used should be considered. Bleeding due to anticoagulant overdosage is uncommon and unlikely to occur if the recommended method and degree of control is practised and the patient is maintained stable within the therapeutic range. An episode of bleeding occurring during anticoagulant therapy must, therefore, be investigated fully and not regarded simply as a manifestation of overdosage.

Overdosage: If haemorrhage occurs or a potential bleeding state arises, excessive depression of the coagulation activity can be corrected by temporary withdrawal of Marevan accompanied, if necessary, by administration of vitamin K₁ in oral doses of 2–20 mg; rarely it may be necessary to give vitamin K₁ intravenously, or to infuse fresh whole blood.

Pharmaceutical precautions Replace cap securely and protect from light.

Legal category POM.

Package quantities Marevan Tablets 1 mg are available in containers of 100 and 500.

Marevan Tablets 3 mg are available in containers of 100 and 500.

Marevan Tablets 5 mg are available in containers of 100 and 500.

Further information Nil.

Product licence numbers

Marevan Tablets 1 mg	0021/5071
Marevan Tablets 3 mg	0021/5072
Marevan Tablets 5 mg	0021/5073

MEVILIN[®]-L

Measles Vaccine (Live Attenuated) BP (Schwarz strain) Meas/Vac (Live)

Presentation Mevilin-L is a freeze-dried preparation of living attenuated virus of the Schwarz strain. It must be reconstituted with Water for Injections BP immediately prior to injection; the reconstituted vaccine may vary in colour from pale straw to pink – this variation is not indicative of deterioration.

Uses General prophylaxis against measles and within 3 days of exposure to measles.

Dosage and administration One dose by intramuscular or subcutaneous injection (contains not less than 1,000 TCID₅₀ of measles virus). Mevilin-L should be administered to infants at about 12 months of age. There is no upper age limit for measles vaccination.

To reconstitute Mevilin-L inject the required amount of Water for Injections BP (0.5 ml for the single-dose vial) into the vial containing the freeze-dried vaccine, allow to stand for about a minute then mix the suspension by withdrawing it into the syringe and expelling it back into the vial. The use of a 2 ml disposable syringe is recommended. The dose of the reconstituted vaccine is 0.5 ml.

Contra-indications, warnings, etc

Contra-indications: Mevilin-L should not be given to children below the age of one year unless at special risk. If this is the case, a second dose should be given at a later date as interference from maternally derived antibody may cause a failure to respond.

Any active or suspected infection is reason for delaying vaccination.

Mevilin-L should not be given to children suffering from leukaemia, Hodgkin's disease or other malignant conditions or hypogammaglobulinaemia. Also those with impaired immune responsiveness, whether occurring naturally or as a result of treatment with steroids, radiotherapy, cytotoxic drugs or other agents.

Pregnancy is a contra-indication. Also hypersensitivity to hen's egg, neomycin and polymyxin.

Children with the following conditions should not be given measles vaccine, unless with the simultaneous administration of normal immunoglobulin (0.6 mg/lb (1.3 mg/kg) body weight)† with a specific content of measles antibody:

1. History of convulsions.
2. Parental history of epilepsy (non traumatic).
3. Chronic disease of the heart or lungs.
4. Seriously underdeveloped.

If there is a history of convulsions or a history or family history of epilepsy, consideration should be given to delaying immunisation until after the second birthday.

Human Normal Immunoglobulin with a specific content of measles antibody is used to reduce the potential for adverse reactions where constitutional disturbance may be avoided in administering measles vaccine. A separate syringe should be used for injecting the immunoglobulin into the contralateral arm. It is important not to exceed the dose as overdosage can prevent the development of immunity.

Precautions: Attenuated measles vaccine is quickly killed by ether, alcohol and detergents: these agents should not be used for sterilising syringes prior to immunisation. Liquids used for cleansing the skin prior to injection should be allowed to dry before the vaccine is given.

Warnings: A sterile syringe and Adrenaline Injection BP should be ready for use, in case the need arises for emergency treatment of an allergic reaction.

Mevilin-L must not be given intravenously and should not normally be given within 3 months of a transfusion of blood or human plasma or treatment with Human Immunoglobulin except as previously specified. If any of these substances have been used near to the time of vaccination a test for the presence of measles antibody should be made at a later date.

The vaccine should not normally be given less than 2 weeks before or after immunisation with other live virus vaccines.

Measles vaccine may depress tuberculin skin sensitivity for 4 weeks or longer.

Adverse effects: When adverse reactions occur they

† Human Normal Immunoglobulin for use with Measles Vaccine is issued in ampoules, each containing 4–8 i.u. measles antibody in 15 mg protein in 0.5 ml solution. (See CMO letter CMO 5/68, CMO 18/71 and CMO (77) 3.) Supplies are available from Area Health Authorities in England and from Blood Transfusion Centres in Scotland.

usually appear about the eighth day. The symptoms are usually mild and may include malaise, cough, coryza, rash, pharyngitis, pyrexia and headache. Convulsions may accompany the fever.

Severe reactions are uncommon, but encephalitis has been reported – the incidence is considered to be approximately 1 in 1,000,000 vaccinees.

Pharmaceutical precautions Mevlin-L should be protected from light and stored in a refrigerator at between 2°C and 8°C (36°F to 46°F). Do not freeze.

The reconstituted vaccine should be used as soon as possible and certainly within one hour.

Neomycin and polymyxin are used in the tissue culture medium employed during manufacture and traces of these antibiotics may be present in the final vaccine.

Legal category POM.

Package quantities Single dose vial with 0.5 ml ampoule of Water for Injections BP.

Further information It is important to recognise that children in residential or day care over the age of one year are at special risk.

Product licence number 0021/0059.

MULTIVITE* PELLETS

Presentation A dark brown, sugar-coated pellet. Each Multivite Pellet contains:

Vitamin A	2,500 i.u.
Vitamin B ₁	0.5 mg
Vitamin C	12.5 mg
Vitamin D	250 i.u.

Uses Vitamins A, B₁, C and D are essential to health and vitality. Although these vitamins occur naturally in various foods, adequate nutrition is not always attainable or all. Even if balanced diets are achieved the vitamin content may be reduced or even completely destroyed by cooking. Patients with diminished appetites, restricted diets or inadequate meals, especially during childhood, pregnancy, illness and old age, often develop vitamin deficiencies. Multivite will help to correct a vitamin deficiency, and to build resistance against infection.

Dosage and administration *Adults:* 2 Multivite daily.

Children: 1 Multivite daily.

Multivite Pellets are pleasant tasting and may be chewed or swallowed whole, according to preference.

Contra-indications, warnings, etc There are no contra-indications.

Precautions: Excessive prolonged dosage of vitamins A and D may lead to hypervitaminosis.

Side-effects: None in the absence of overdosage.

Overdosage: No emergency treatment is necessary.

Pharmaceutical precautions To be stored in a cool place and protected from light.

Legal category P.

Package quantities Multivite Pellets are available in containers of 50, 150 and 500.

Further information Nil.

Product licence number 0021/5081.

NEO-NACLEX*

Presentation Small white tablets engraved Neo-NaClex on one side and scored on the reverse. Each tablet contains 5 mg bendroflumazide and complies with the specification for Bendroflumazide Tablets BP, BNF.

Uses *Oedema:* Neo-NaClex inhibits the renal tubular absorption of salt and water. Sodium and chloride ions are excreted in equivalent proportions, and there is little or no disturbance of the acid/base equilibrium. There is no important effect upon carbonic anhydrase. Neo-NaClex causes a steady diuresis lasting for about 12 hours. It is indicated in the treatment of oedema associated with conditions such as: congestive heart failure, nephrotic syndrome, cirrhosis of the liver, and pre-menstrual tension.

Suppression of unwanted lactation: Neo-NaClex can inhibit lactation as effectively as the oestrogens, but without early engorgement of the breast or other hormonal effects.

Essential hypertension: The mechanism whereby the thiazides exert their antihypertensive effect has not been clearly established. In non-oedematous patients there may be little noticeable diuretic effect. Neo-NaClex may be used as the sole antihypertensive agent, or as an adjunct to other drugs whose action it potentiates.

Dosage and administration *Oedema:* In adults 5 mg given orally once daily in the morning usually produces the desired effect, but this dose can be increased to 10 mg if required. During the first few days of treatment there is usually a large increase in urinary volume, which diminishes as treatment continues.

Maintenance: many patients will respond adequately to a daily dose of 2.5 mg or 5 mg on only two or three days in the week: sometimes a single dose once a week may be sufficient. The intervals allow opportunity for replenishment of any potassium loss. Appropriately smaller doses should be used for children.

Essential hypertension: 2.5–10 mg once daily, alone or in conjunction with other antihypertensive agents.

Pre-menstrual tension: 2.5 mg taken each morning for seven days before the period is due is usually adequate.

Suppression of lactation: A suitable dosage is 5 mg (or 10 mg) on rising in the morning and 5 mg about noon. A course of five days' treatment is usually adequate.

Contra-indications, warnings, etc

Contra-indications: Severe renal insufficiency, hypercalcaemia. Neo-NaClex should not be administered concurrently with lithium carbonate.

Precautions: Neo-NaClex may impair control of diabetes in patients receiving sulphonylureas.

Thiazide diuretics are secreted in mothers' milk, hence breast feeding should be avoided.

When treatment with Neo-NaClex is intensive or continuous, some loss of potassium may occur, and in these circumstances potassium chloride supplements are recommended. If the patient is vomiting, has diarrhoea or is suffering from an acute febrile or chronic illness (especially cirrhosis of the liver or heart failure) supplementary potassium may be particularly important. Supplementary potassium is strongly recommended if patients receiving digitalis require prolonged diuretic treatment. Concurrent therapy with carbenoxolone may also necessitate potassium supplements.

Potassium depletion may cause polyuria, malaise, muscle weakness or cramp, decreased tendon reflexes,

anorexia, dizziness, nausea or vomiting. Also, sensitivity to digitalis may increase and signs of over-dosage appear. Prolonged potassium deficiency may induce chronic pyelonephritis. Potassium supplements should not be given in renal insufficiency complicated by hyperkalaemia.

Side-effects: Impotence may occur and is usually reversible within a few weeks of stopping Neo-NaClex therapy. Mild anorexia or indigestion may occur occasionally, but it can be avoided or reduced by taking the dose during or immediately after a meal.

Skin reactions have been reported in a few patients and blood dyscrasias have occurred rarely. Expectant mothers who receive thiazide diuretics may be at increased risk from acute haemorrhagic pancreatitis; thrombocytopenia has been reported in newborn infants following antepartum use of thiazides. Such cases are very rare, and should not prevent the use of thiazide diuretics when indicated in pregnancy. Thiazides may aggravate existing diabetes mellitus, and cause symptoms in patients with latent disease. Serum uric acid levels may be raised, with or without gout, in some patients.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Bottles of 100 and 500 tablets.

Further information Nil.

Product licence number 0021/5906.

NEO-NACLEX[®]-K

Presentation Neo-NaClex-K is a film-coated, two-layer tablet containing bendrofluzide in the white layer and potassium chloride in the pink layer. The white side is engraved Neo-NaClex-K. The potassium chloride is in a special matrix which provides gradual release of the electrolytes, so minimising gastro-intestinal irritation. Each tablet contains 2.5 mg bendrofluzide and 630 mg potassium chloride, providing 330 mg elemental potassium (8.4 mEq).

Uses *Essential hypertension:* The mechanism whereby the thiazides exert their antihypertensive effect has not been clearly established. In non-oedematous patients there may be little noticeable diuretic effect. Neo-NaClex-K may be used as the sole antihypertensive agent, or as an adjunct to other drugs whose action it potentiates. When Neo-NaClex-K is used alone in hypertension, the fall in diastolic blood pressure is often between 10 and 20 mm Hg.

When Neo-NaClex-K is added to other antihypertensive drugs, the dosage of the latter can usually be reduced gradually as the Neo-NaClex-K takes effect.

The potassium chloride contained in Neo-NaClex-K provides a useful supplement to offset the potassium-losing effect of bendrofluzide.

Oedema: Neo-NaClex-K is particularly suitable for the treatment of chronic oedema.

Dosage and administration *Essential hypertension: Adults:* 1-4 tablets once daily, alone or in conjunction with other antihypertensive agents.

Oedema: *In adults:* 2 tablets given orally once daily in the morning usually produce the desired effect, but this dose can be increased to 4 tablets if required. During the

first few days of treatment there is usually a large increase in urinary volume, which diminishes as treatment continues.

Maintenance: Many patients will respond adequately to a daily dose of 1 or 2 tablets on only two or three days in the week, sometimes a single dose once a week may be sufficient.

Appropriately smaller doses should be used for oedema in children.

Contra-indications, warnings, etc

Contra-indications: Gross impairment of renal function hypercalcaemia. Neo-NaClex-K should not be administered concurrently with lithium carbonate.

Precautions: Thiazide diuretics are secreted in mother's milk, hence breast feeding should be avoided.

When treatment is prolonged and intensive, potassium depletion can develop insidiously particularly in the presence of diarrhoea or vomiting. Neo-NaClex-K Tablets usually provide sufficient potassium to maintain the serum concentration in hypertension, but in oedema it is sometimes advisable to give potassium chloride in addition to that contained in Neo-NaClex-K. Potassium deficiency increases the activity of digitalis and signs of overdosage may appear.

Neo-NaClex-K may impair control of diabetes in patients receiving sulphonylureas.

Side-effects: Impotence may occur and is usually reversible within a few weeks of stopping Neo-NaClex-K therapy. Mild anorexia or indigestion may occur occasionally, but it can be avoided or reduced by taking the dose during or immediately after a meal. If abdominal pain, distension, nausea, vomiting or gastro-intestinal bleeding occur during the administration of tablets containing potassium salts, administration should be discontinued immediately. Small bowel lesions are usually associated with enteric-coated tablets, and are less likely to occur with Neo-NaClex-K.

Skin reactions have been reported in a few patients and blood dyscrasias have occurred rarely. Expectant mothers who receive thiazide diuretics may be at increased risk from acute haemorrhagic pancreatitis; thrombocytopenia has been reported in newborn infants following ante-partum use of thiazides. Such cases are very rare and should not prevent the use of thiazide diuretics when indicated in pregnancy. Thiazides may aggravate existing diabetes mellitus, and cause symptoms in patients with latent disease. Serum uric acid levels may be raised, with or without gout, in some patients.

Pharmaceutical precautions None.

Legal category POM.

Package quantities Bottles of 100 and 500 tablets.

Further information Nil.

Product licence number 0021/5907.

ONADOX[®]-118 TABLETS

Presentation Soluble white tablets engraved DF/C each tablet containing:

Acetylsalicylic Acid BP (as soluble salt)	300 mg
Dihydrocodeine Tartrate BP	10 mg

Uses Aspirin in soluble form as calcium aspirin has been shown to reduce the risk of gastric intolerance and bleeding. Dihydrocodeine tartrate has been widely used

for a number of years as a powerful analgesic: 30 mg of dihydrocodeine has been reported to have analgesic potency equal to 60–120 mg codeine. In addition the compound exhibits well-defined anti-tussive activity.

There is evidence that aspirin and centrally acting analgesics (such as dihydrocodeine) probably act by different mechanisms, and their actions should, therefore, complement each other. Onadox-118 thus provides an effective combination of drugs for the long-term treatment of rheumatic conditions, where adequate relief of pain is not obtained with aspirin alone, and, more generally, where relief of mild to moderate pain is required.

Dosage and administration Onadox-118 should be dissolved in water and taken during or after a meal.

Adults: 1–3 tablets, three or four times a day, as required. Onadox-118 Tablets are not recommended for administration to children.

Contra-indications, warnings, etc

Contra-indications: Onadox-118 should not be administered to patients with peptic ulceration, respiratory depression, obstructive airways disease, haemophilia or a sensitivity to aspirin; nor should it be prescribed concurrently with oral anticoagulants.

Precautions: Additive CNS depression may occur with alcohol.

Onadox-118 should be given with caution to patients with allergic disorders and should not be given during an attack of asthma.

Dosage should be reduced in the elderly, in hypothyroidism and in chronic hepatic disease.

Aspirin may induce asthma, precipitate bronchospasm and inhibit action of uricosurics. There is no, or inadequate evidence of safety in human pregnancy but the drug has been used for many years without apparent ill consequence. It may prolong labour and contribute to maternal and neonatal bleeding and is best avoided at term.

Side-effects: Constipation, if it occurs, is readily treated with a mild laxative. Nausea, headache, vertigo and gastro-intestinal haemorrhage, occasionally major, may occur in a few patients.

Overdosage: Gastric aspiration, lavage and general supportive measures should be carried out. Severe respiratory depression can be treated with naloxone hydrochloride 0.4 mg subcutaneously, repeated as required at 2 or 3 minute intervals.

Pharmaceutical precautions No special requirements or precautions.

Legal category POM.

Package quantities Onadox-118 Tablets are available in cartons of 100, strip packed in protective foil.

Further information Nil.

Product licence number 0021/5055R.

PARAMOL*-118 TABLETS

Presentation A white tablet engraved DF/P, each tablet containing:

Paracetamol BP	500 mg
Dihydrocodeine Tartrate BP	10 mg

Uses Paracetamol is an effective analgesic possessing a remarkably low level of side-effects. Its broad clinical utility has been extensively reported, and it now largely

replaces aspirin for routine use. Paracetamol is well tolerated; having a bland effect on gastric mucosa, unlike aspirin, it neither exacerbates symptoms of peptic ulcer nor precipitates bleeding. Dihydrocodeine tartrate has been widely used for a number of years as a powerful analgesic; 30 mg of dihydrocodeine has been reported to have analgesic potency equal to 60–120 mg codeine.

In addition the compound exhibits well-defined anti-tussive activity.

By fortifying paracetamol with 10 mg dihydrocodeine, Paramol-118 provides an effective combination of drugs for the treatment of mild to moderate pain and as an anti-pyretic.

Dosage and administration Paramol-118 Tablets should, if possible, be taken during or after meals.

Adults and children over 12 years: Analgesia: 1 tablet every four hours. This may be increased to 2 tablets four times a day if necessary.

Antitussive: 1 tablet every four hours.

Paramol-118 is not recommended for children under 12.

Contra-indications, warnings, etc Respiratory depression, obstructive airways disease.

Precautions: Additive CNS depression may occur with alcohol.

Paramol-118 should be given with caution to patients with allergic disorders and should not be given during an attack of asthma. Caution should also be observed if there is marked impairment of liver function or advanced kidney disease.

Dosage should be reduced in the elderly, in hypothyroidism and in chronic hepatic disease. An overdose can cause hepatic necrosis.

There is no, or inadequate evidence of safety in human pregnancy but the drug has been used for many years without apparent ill consequence.

Side-effects: Constipation, if it occurs, is readily treated with a mild laxative. Nausea, headache, vertigo and giddiness may occur in a few patients.

Overdosage: Conservative management is recommended; gastric lavage should be carried out. Severe respiratory depression can be treated with naloxone hydrochloride 0.4 mg subcutaneously, repeated as required at 2 or 3 minute intervals. Treatment for paracetamol overdosage should be commenced as soon as possible after ingestion using preferably N-acetylcysteine or cysteamine or methionine.

Pharmaceutical precautions No special requirements or precautions.

Legal category POM.

Package quantities Paramol-118 Tablets are available in packs of 100 and 500.

Further information Nil.

Product licence number 0021/5056.

PARVOLEX* ▼

Presentation Parvolex is a clear, colourless, sterile, pyrogen-free, aqueous solution of 20% w/v N-acetylcysteine (N-acetyl-3-mercaptoproline) adjusted to pH 7.0 with sodium hydroxide. Parvolex contains 200 mg N-acetylcysteine in each ml.

Uses N-acetylcysteine is a derivative of the naturally-occurring amino acid L-cysteine.

In paracetamol overdosage the observed hepatotoxicity is due to the formation of a toxic metabolite which is thought to cause liver cell damage and necrosis. Hepatic-reduced glutathione inactivates the toxic metabolite by conjugation but glutathione stores are rapidly depleted with hepatotoxic doses of paracetamol. N-acetylcysteine, being a sulphhydryl (SH) group donor, protects the liver possibly by restoring depleted hepatic-reduced glutathione or by acting as an alternative substrate for the toxic paracetamol metabolite.

Indications: Paracetamol overdosage.

Dosage and administration An initial dose of 150 mg/kg body weight of N-acetylcysteine is infused in 200 ml of 5% dextrose intravenously over 15 minutes, followed by an intravenous infusion of 50 mg/kg body weight in 500 ml of 5% dextrose over the next four hours, and 100 mg/kg body weight in 1 litre of 5% dextrose over the next 16 hours. (This gives a total dose of 300 mg/kg body weight of N-acetylcysteine in 20 hours.)

Children: The quantity of intravenous fluid used in children should be modified to take into account age and weight.

Critical times: Parvolex is very effective when administered up to eight hours after paracetamol overdosage. The protective effect falls off slowly between 8 and 10 hours, more rapidly after 10 hours and increasingly between 12 and 15 hours. Parvolex is ineffective after 15 hours and its use after this time may be associated with harmful effects.

Contra-indications, warnings, etc No contra-indications have been reported.

Precautions: N-acetylcysteine is not compatible with rubber and metals, particularly, iron, copper and nickel. Silicone rubber and plastic are satisfactory for use with Parvolex.

Side-effects: Rash and anaphylaxis have been reported.

Hypokalaemia and ECG changes have been noted in patients with paracetamol poisoning irrespective of the treatment given. Monitoring of plasma potassium concentration is therefore recommended. The safety of Parvolex in pregnancy has not been established.

Overdosage: There is a theoretical risk of hepatic encephalopathy. There is no specific treatment and general supportive measures should be carried out.

Pharmaceutical precautions Parvolex should be stored in a cool place.

Legal category POM.

Package quantities Parvolex is supplied in ampoules of 10 ml. 10 × 10 ml ampoules are packed in printed cartons.

Further information Nil.

Product licence number 0021/0086.

PERNIVIT* TABLETS

Presentation Salmon-pink, sugar-coated tablets, each tablet containing:

Acetomenaphthone BP	7 mg
Nicotinic Acid BP	25 mg

Uses The action of Pernivit is based principally on the vasodilating effect of nicotinic acid while aceto-

menaphthone (vitamin K analogue) is to alleviate symptoms. A combination of these substances, Pernivit has long been recognised as a useful preparation for the prophylaxis of chilblains.

Dosage and administration *Adults:* 2-times a day after meals.

Children: 1-2 tablets three times a day a prophylactic treatment half the recom should be taken.

Patients with advanced atherosclerosis the maximum benefit from Pernivit.

Contra-indications, warnings, etc

Contra-indications: Patients who are on a coagulant therapy.

Precautions: Pernivit should be given to patients with a history of peptic ulceration receiving antihypertensive agents.

Allergic reactions to Pernivit have been rare occasions and treatment should be sought if they appear.

Notice should be taken of current view: should be prescribed with caution during

Side-effects: A flushing of the face associated with the tablets, but this is not

Overdosage: The toxic effects normally seen with treatment.

Pharmaceutical precautions There are no special requirements or precautions.

Legal category P.

Package quantities Pernivit Tablets are supplied in containers of 100.

Further information Nil.

Product licence number 0021/5083.

PROSPAROL* EMULSION

Presentation A white emulsion containing Arachis Oil BP in water and providing 4.5 (1.9 MJ per 100 ml).

Uses The special homogenising process used in the manufacture of Prosparol produces extremely small particles of approximately 1-2 microns in diameter which have little tendency to separate out. The emulsion is palatable and better tolerated than other oil emulsions.

In radiology (cholecystography): Prosparol is an essential part of a satisfactory gall-bladder examination - quick absorption, reliable visual examination.

In dietetics: Prosparol is indicated in traumatic and ketogenic diet in the management of convalescence, whenever a high calorie diet is required to minimise tissue destruction and favour repair. It is also indicated following trauma, or in preparation for surgery should provide an adequate margin of safety. It is a requirement to correct possible deficits: for total nourishment and 2,000 calories would permit steady weight gain.

Dosage and administration *Cholecystography:* 60 ml.

Dietetics: Up to 500 ml (2,250 calories

generally be administered without any digestive disturbance. It is best given in frequent small doses 20–40 ml at a time.

Prosparol may be taken neat, or diluted with milk or fruit juice; some patients prefer it chilled. It can be given orally or by nasogastric tube. 1 oz (28.3 g) Prosparol mixed with 1 oz sugar in $\frac{1}{2}$ pint (284 ml) water can be used as a non-protein milk substitute in tea, coffee or made into custard or instant whip.

Easily prepared supplemental and total diets containing Prosparol have been recommended in conjunction with milk, lactose and finely divided protein e.g. Casilan* (Farley), with the addition of electrolytes as needed.

Infants with sugar intolerance can be fed initially with a low-fat preparation and then, when they begin to thrive, to increase the fat intake gradually by adding Prosparol to the feeds. Prosparol is a valuable calorific supplement to Aminogran* (Allen & Hanburys), and other amino-acid preparations used in the management of phenylketonuria.

For the dietetic treatment of patients with anorexia nervosa, a liquid diet has been suggested containing Prosparol, Complian* (Farley) and glucose suitably flavoured with instant coffee or cocoa.

Contra-indications, warnings, etc There are no contra-indications.

Precautions: Prosparol should only be given to diabetic patients as part of their diet.

Patients with liver or gall-bladder disorders are unlikely to tolerate appreciable quantities of Prosparol.

Side-effects: Occasional fat intolerance may be encountered.

Overdosage: An overdosage will produce intolerance and no special treatment is necessary.

Pharmaceutical precautions Prosparol should be stored in a cool place but must not be frozen.

Legal category P.

Package quantities Prosparol is available in containers of 1 litre.

Further information Fat contains considerably less bulk per calorie than does protein or carbohydrate and here is over 90% absorption.

Unlike protein, fat is not wasted by 'spill-over' through the kidneys and the small rise in blood sugar following at ingestion causes less interference to appetite than do carbohydrates.

Prosparol contains 0.1% w/v Sodium Benzoate (6.9 milliequivalents of sodium per litre); it does not contain potassium.

Product licence number 0021/5009.

SCOLINE*

Presentation A clear colourless, sterile solution containing Suxamethonium Chloride (succinylcholine chloride) BP 50 mg per ml. This is equivalent to 36.5 mg of active cation.

Uses Scoline is a depolarising, short-acting neuromuscular blocking agent for intravenous administration. It is suitable for brief procedures in which profound muscular relaxation is required such as tracheal intubation, short operations, orthopaedic manipulations, electroconvul-

sive therapy and closure of the peritoneum. Prolonged muscular relaxation in surgery can be attained by means of repeated injections of the drug or by continuous intravenous drip.

Dosage and administration Scoline must not be administered to the conscious patient. It is given intravenously after anaesthesia has been induced and should be accompanied by assisted respiration. The dosage for children and adults depends on body weight and the degree of muscular relaxation required. It ranges from 20 mg (0.4 ml) to 100 mg (2 ml) according to the body weight of the patient and the degree of muscular relaxation required. In adults the dosage for intubation is from 50 mg (1 ml) to 80 mg (1.6 ml), for electroconvulsive therapy 40 mg (0.8 ml) to 75 mg (1.5 ml) and for manipulation 80 mg (1.6 ml). For administration by continuous intravenous drip, a 0.1% solution may be prepared by mixing 10 ml injection of Scoline with 500 ml of 5% glucose or isotonic sodium chloride. The adult dose ranges from 2–5 mg per minute.

Contra-indications, warnings, etc

Contra-indications: Scoline should not be used in patients known to have atypical serum pseudocholinesterase or low serum levels of pseudocholinesterase. Deficiency of this serum enzyme may occur as a very rare inherited characteristic or result from liver disease, severe anaemia, malnutrition or poisoning with an organo-phosphorus insecticide.

Patients with myasthenia gravis are resistant to Scoline and a state of dual block may develop rapidly.

Patients with the myasthenic (Eaton-Lambert) syndrome are relatively sensitive to Scoline and the dose should be reduced.

If eye drops containing long-acting cholinesterase inhibitor drugs, such as ecothiopate iodide (Phospholine iodide* Ayerst Laboratories Ltd) or demecarium bromide (Tosmilen* Astra Chemicals), are used within a period of one month prior to an operation, then decreased plasma cholinesterase levels may preclude the use of Scoline.

Scoline should not be used in ophthalmic cases when the anterior chamber of the eye is open. Nor must it be used in cases of hyperkalaemia.

Precautions: Neostigmine and other anticholinesterase drugs are not antidotes to Scoline but would normally have the effect of intensifying the depolarisation effect. However, in some cases of prolonged apnoea following Scoline, a state of 'dual block' may be responsible. In dual block the muscle relaxation is due to non-depolarising blockade and is reversible with neostigmine. To investigate this possibility the short-acting anticholinesterase drug, edrophonium, should be given and a transitory return of muscle power confirms the presence of dual block, which can then be reversed with neostigmine. In seriously burnt children Scoline can precipitate gross cardiac arrhythmias and cardiac arrest. This can be prevented by the administration of tubocurarine 6 mg five minutes before giving Scoline. Care should be taken with patients currently receiving systemic antibiotics such as streptomycin, neomycin, kanamycin, tobramycin, framycetin, amikacin, gentamicin, colistin and the polymyxins, as they can potentiate the action of Scoline.

Side-effects: Muscle pain (particularly in the muscles of the chest, abdomen and shoulder girdle) can occur following the use of Scoline. It occurs most frequently in patients who are ambulant in the early postoperative period and can be avoided by the prior administration of any of the non-depolarising muscle relaxants.

Other side-effects which have been reported include hypertension, fever and hypersensitivity reactions.

Overdosage: Because Scoline is usually administered by an anaesthetist, overdosage is unlikely. However, the unsuspected presence of low pseudocholinesterase levels in the serum, or this being replaced by the atypical enzyme, or the occurrence of dual block, can lead to a similar situation: prolonged apnoea. Management first consists of maintaining light anaesthesia and continued mechanical respiration to ensure an adequate supply of oxygen whilst the cause is determined. Dual block can be recognised by the response to edrophonium, and treatment then consists of reversal with neostigmine. Subsequently the patient should remain under observation as the dual block may outlast the duration of action of neostigmine (at least 20 minutes) and if apnoea recurs a further dose of neostigmine is indicated. Apnoea due to atypical or low serum cholinesterase levels can be corrected by intravenous administration of a highly concentrated preparation of pseudocholinesterase or transfusion of plasma or whole blood.

Pharmaceutical precautions Scoline should be stored at as low a temperature as possible above its freezing point and not exceeding 4°C; under these conditions it may be expected to retain its potency for at least two years from the date of preparation.

Legal category POM.

Package quantities Scoline is available in boxes of five 2 ml ampoules and in 10 ml multidose vials.

Further information Nil.

Product licence number 0021/5024.

ADSORBED TETANUS VACCINE BP (PTAH) (Tet/Vac/Ads)

Presentation Adsorbed Tetanus Vaccine BP (PTAH) is the detoxified toxin of *Clostridium tetani* adsorbed on aluminium hydroxide: each 0.5 ml dose contains not less than 40 i.u. of tetanus toxoid.

Uses Active immunisation against tetanus. Reinforcement of immunity to tetanus.

Vaccine should be administered by intramuscular injection.

Primary immunisation: The course consists of 3 doses each of 0.5 ml; the second dose is administered after an interval of 6–8 weeks and the third dose after a further interval of four to six months.

Reinforcing doses: A reinforcing dose of 0.5 ml should be given 5 years after basic course; subsequently at 5–15 year intervals. At the time of an injury likely to carry risk of tetanus (although it is not usually necessary for any subject who is known to have received a booster dose in the preceding year).

A full course is unnecessary for such subjects who have completed the basic three dose course of toxoid. A booster or recall dose given at any time afterwards can be expected to provide reinforcement of immunity.

Contra-indications, warnings, etc

Contra-indications: Acute infection is a contra-indication to routine tetanus immunisation, except in the presence of a tetanus-prone wound.

Warnings: A sterile syringe and Adrenaline Injection BP

should be ready for use, in case the need arises for emergency treatment of an allergic reaction.

Not for intradermal use.

Side-effects: Transient pyrexia, headache, malaise, local swelling, redness and tenderness may occur especially in adults.

A small painless nodule may form at the injection site.

Acute allergic reactions, pallor, dyspnoea, urticaria, angioneurotic oedema and acute anaphylactic reactions, are sometimes seen.

Pharmaceutical precautions Protect from light. Store between 2°C and 8°C (36°F and 46°F). Do not freeze. Partly used multi-dose containers should be discarded within 3 hours of the withdrawal of the first dose.

Legal category POM.

Package quantities Single-dose ampoules containing 0.5 ml and multidose vials containing 5 ml.

Further information Adsorbed tetanus vaccine may be administered at the same time as, but at a different site from Human Tetanus Immunoglobulin or Tetanus Antitoxin.

Product licence number 0021/0060.

TIGLYSSIN* TABLETS

Presentation A white tablet engraved DF/T, each tablet containing tigloidine hydrobromide 250 mg.

Uses Tigloidine, the tiglic acid ester of pseudotropine, possesses certain properties of atropine but lacks anticholinergic activity. Tiglyssin can assist the relief of muscular spasticity and spasms due to organic upper motor neurone disease or damage occurring as a result of partial or complete rupture of the cord; multiple sclerosis; transverse myelitis; cerebrovascular accidents; subacute combined degeneration of the cord.

Dosage and administration **Adults:** The optimum therapeutic dose lies between 4 and 8 tablets per day. Tiglyssin is not recommended for children.

The appropriate level for each patient should be found by starting at 3–4 tablets and increasing the dose until either no further improvement is noted, or mild atropine-like side-effects appear. The dose should be divided and given three times daily with meals. Administration for up to four weeks is usually required for the full therapeutic effect to become apparent; the value of the drug may then be assessed.

Contra-indications, warnings, etc There are no contra-indications.

Precautions: Tiglyssin should be given with care to patients with glaucoma.

Notice should be taken of current views that any drug should be prescribed with caution during pregnancy.

Side-effects: Slight atropine-like effects are sometimes seen, particularly at the higher dosage levels.

Overdosage: Standard procedures, similar to those for atropine, should be employed: gastric aspiration and lavage with dilute tannic acid solution, followed by a saline purge.

Pharmaceutical precautions No special requirements or precautions.

Legal category POM.

Package quantities Tiglyssin Tablets are available in tainers of 100.

ther information The effect of Tiglyssin is purely ative. It can have no curative effect nor can it delay advance of progressive diseases such as multiple rosis. Nevertheless, apart from increasing comfort

and making nursing easier, relief of spasticity and spasms may, in some patients, help in rehabilitation and in others reveal a useful amount of normal function yet remaining.

Product licence number 0021/5076.

** Trade Mark*

Duphar Laboratories Limited
Gaters Hill
West End
Southampton SO3 3JD



COLOFAC®

Presentation White sugar-coated tablets each containing 135 mg mebeverine hydrochloride.

Uses Mebeverine is a musculotropic antispasmodic with a direct action on the smooth muscle of the gastro-intestinal tract, relieving spasm without affecting normal gut motility. Since this action is not mediated by the autonomic nervous system, the usual anticholinergic side-effects are absent. Mebeverine is suitable for patients with prostatic hypertrophy and glaucoma.

Indications:

1. Irritable bowel syndrome and other conditions usually included in this grouping such as: chronic irritable colon, spastic constipation, mucous colitis, spastic colitis. Colofac is effectively used to treat the symptoms of these conditions, such as: abdominal pain and cramps, persistent, non-specific diarrhoea (with or without alternating constipation) and flatulence.

2. Gastro-intestinal spasm secondary to organic diseases such as diverticular disease, gastritis, duodenitis, oesophagitis, cholecystitis, Crohn's disease, ulcerative colitis, peptic ulcer, gall bladder disease, hiatus hernia and specific and non-specific inflammatory disease of the gastro-intestinal tract.

Dosage and administration *Adults:* One tablet three times a day, preferably 20 minutes before meals.

After a period of several weeks when the desired effect has been obtained the dosage may be gradually reduced.

Children under 10: Not applicable.

Contra-indications, warnings, etc

Contra-indications: None known.

Warnings: Animal experiments have failed to show any teratogenic effects. However, the usual precautions concerning the administration of any drug during pregnancy should be observed.

Treatment of overdosage: On theoretical grounds it may be predicted that CNS excitability will occur in cases of overdosage. No specific antidote is known; gastric lavage and symptomatic treatment is recommended.

Pharmaceutical precautions Store in a dry place, at room temperature, protected from light.

Legal category POM.

Package quantities Available in packs of 100 (5 strips of 20 blister-packed tablets).

Further information Results from a preliminary study show that mebeverine does not produce false positive reactions in standard diagnostic urine tests.

Product licence number 0512/0044.

DUPHALAC®

Presentation A colourless to pale yellow syrup containing lactulose 3.35 g/5 ml. Also contains lactose 0.3 g/5 ml, galactose 0.55 g/5 ml.

Uses The action of Duphalac in treating constipation depends on the inability of the enzymes in the small intestine to hydrolyse the synthetic disaccharide, lactulose, into its component molecules of fructose and galactose. Therefore, as lactulose is virtually unabsorbed, it passes into the large bowel chemically unchanged and forms a substrate for commensal saccharolytic bacteria.

The resulting breakdown products, simple organic compounds like lactic and acetic acid, give rise to increased intra-colonic osmotic pressure, with consequent increased faecal bulk, and stimulate peristalsis. The growth of saccharolytic bacteria is favoured and the normal colonic flora restored.

A soft stool is formed, and normal bowel action encouraged without irritation or direct interference with the gut mucosa.

In patients with hepatic encephalopathy larger doses of Duphalac are used; a significant reduction in the pH of the colonic contents results, which reduces markedly the formation and absorption of ammonium ions and other nitrogenous toxins into the portal circulation. Rapid decrements in blood ammonia concentration have been reported following Duphalac treatment.

Indications: 1. Constipation.

2. Hepatic encephalopathy (Portal systemic encephalopathy); hepatic coma.

Dosage and administration *Constipation:* Initially Duphalac may be given twice daily. In due course the dose should be adjusted to the needs of the individual but the following serves as a guide.

Starting dose

Adults	15 ml twice daily
Children 5 to 10 years	10 ml twice daily
Children under 5 years	5 ml twice daily
Babies	2.5 ml twice daily

Each dose of Duphalac may, if necessary, be taken with water or fruit juices, etc.

Hepatic encephalopathy: Initially 30–50 ml. (6–10 × 5 ml spoonfuls) three times a day. Subsequently adjust the dose to produce two or three soft stools each day.

Contra-indications, warnings, etc

Contra-indications: Galactosaemia. In common with other preparations used for the treatment of constipation Duphalac should not be used when there is evidence of gastro-intestinal obstruction.

Precaution: Lactose intolerance.

Pharmaceutical precautions Store below 20°C. Do not freeze. Dilution and subsequent storage not recommended.

Legal category P.

Package quantities Available in bottles of 300 ml and 1 litre.

Further information Because of Duphalac's physiological mode of action it may take up to 48 hours before effects are obtained. However, clinical experience has shown that this medicament does exhibit a 'carry-over' effect which may enable the patient to reduce the effective dose gradually over a period of time.

A maintenance dose of 15 ml per day provides only 58 kJ (14 kcals), and is therefore, unlikely to adversely affect diabetics.

Product licence number 0512/5001.

DUPHASTON®

Presentation White, flat, round tablet imprinted DUPHA- on one side, scored on reverse, each containing 10 mg Dydrogesterone BP.

Uses Dydrogesterone is an orally active progestogen which produces a complete secretory endometrium in an oestrogen-primed uterus. It is indicated in all cases of endogenous progesterone deficiency.

Indications: Dysmenorrhoea, endometriosis, threatened and habitual abortion (associated with proven progesterone deficiency), infertility, irregular cycles, functional bleeding (with added oestrogen), secondary amenorrhoea (with added oestrogen), premenstrual syndrome, conditions of progesterone deficiency and to counteract the effects of unopposed oestrogen in Hormone Replacement Therapy.

Dosage and administration *Dysmenorrhoea:* 10 mg twice daily from day 5 to 25 of the cycle.

Endometriosis: 10 mg two to three times daily from day 5 to 25 of the cycle, or continuously.

Threatened abortion: 40 mg at once then 10 mg every eight hours until symptoms remit. If symptoms persist or return during treatment the dose can be increased by one tablet every eight hours. The effective dose must be maintained for a week after symptoms have ceased and then be gradually decreased unless symptoms return.

Habitual abortion: Treatment should be started as early as possible, preferably before conception. 10 mg should be given twice daily from day 11 to day 25 of the cycle until conception and then continuously (10 mg twice daily) until the twentieth week of pregnancy, then dosage may be gradually reduced.

Infertility or irregular cycles: 10 mg twice daily from day 1 to day 25 of the cycle. Treatment should be maintained for at least six consecutive cycles. If the patient conceives, it is advisable to continue treatment or the first few months of pregnancy as described under 'habitual abortion'.

Unfractional bleeding – to arrest bleeding: 10 mg twice daily together with an oestrogen once daily for five to seven days.

Unfractional bleeding – to prevent bleeding: 10 mg twice daily together with an oestrogen once daily from day 11 to 25 of the cycle.

Amenorrhoea: An oestrogen once daily from day 1 to 25 of the cycle, together with 10 mg dydrogesterone twice daily from day 11 to 25 of the cycle.

Pre-menstrual syndrome: 10 mg twice daily from day 12 to 26 of the cycle. The dosage may be increased if necessary.

Contra-indications, warnings, etc

Contra-indications: None known.

Warning: Breakthrough bleeding may occur in a few patients. It can, however, be prevented by increasing the dosage.

Treatment of overdosage: No reports of ill effects from overdosage have been recorded and remedial action is generally unnecessary. If a large overdosage is discovered within 2–3 hours and treatment seems desirable, gastric lavage is recommended. There are no special antidotes and treatment should be symptomatic.

Pharmaceutical precautions Store in a dry place, at room temperature, protected from light.

Legal category POM.

Package quantities Available in packs of 40 (4 strips of 10 blister-packed tablets).

Further information Duphaston is non-androgenic, non-oestrogenic, non-thermogenic, non-corticoid, non-anabolic and is not excreted as pregnanediol.

Results from a preliminary study show that dydrogesterone does not produce false positive reactions in standard diagnostic urine tests.

Product licence number 0512/5004.

DUVADILAN®

Presentation 1. Round, pink tablets imprinted with the name 'Duvadilan' on one face, scored on the reverse, each tablet containing 20 mg isoxsuprine hydrochloride.

2. Ampoules containing a clear, colourless solution of isoxsuprine hydrochloride 5 mg/ml.

Uses Duvadilan (isoxsuprine hydrochloride) is a vaso-relaxant which acts through stimulation of the beta-receptors situated in the walls of blood vessels, especially cerebral vessels and the deeper vessels of the limbs. In high doses it also relaxes skin vessel walls, where alpha-sympathetic receptors predominate. Isoxsuprine also lowers blood viscosity. In addition, isoxsuprine has a stimulating action on the beta-adreno-receptors of the myometrium with a resulting inhibition of uterine contractions. In high doses, it also has a direct papaverine-like action on the smooth muscle of the uterus.

Indications: Peripheral vascular disorders: arteriosclerosis, Buerger's disease, Raynaud's syndrome, ischaemic and vasospastic symptoms (e.g. intermittent claudication, night cramps, pain in limbs, paraesthesia, cold extremities, ulcers).

Cerebral vascular disorders: cerebral insufficiency, occlusive and thromboembolic disorders, transient ischaemic episodes (e.g. dizziness, headache, insomnia, confusion, forgetfulness).

Premature labour.

Dosage and administration *Cerebral and peripheral vascular disease:* 1. Intravenous infusion: 100 mg isoxsuprine hydrochloride in 500 ml normal saline or 20 mg isoxsuprine hydrochloride in 100 ml normal saline in a burette apparatus.

Recommended infusion rates: For maximum infusion time of one hour twice daily, start at:

0.5 ml/min (0.1 mg/min) for 10 minutes.

1.0 ml/min (0.2 mg/min) for next 10 minutes.

1.5 ml/min (0.3 mg/min) for next 10 minutes.

2.0 ml/min (0.4 mg/min) for the remaining 30 minutes.

Note: If after 10 minutes at 2.0 ml/min there are no side-effects observed an infusion rate of 2.5 ml/min (0.5 mg/min) may be adopted for the remaining 20 minutes.

2. Intramuscular/intra-arterial injection: Duvadilan Injection (10 mg in 2 ml) may be given by intramuscular or intra-arterial routes up to four times daily.

3. Oral: Tablets, 20 mg isoxsuprine hydrochloride, four times daily. Capsules, equivalent of 40 mg isoxsuprine hydrochloride in a sustained release formulation, morning and evening (see Duvadilan Retard).

Premature labour:

1. Intravenous infusion: To be administered at the onset of premature labour and continued until control is obtained.

Infusion solution: Duvadilan 100 mg in 500 ml normal saline.

Infusion rate: 1.0–1.5 ml/min (0.2–0.3 mg/min) increasing up to 2.5 ml/min (0.5 mg/min) until control is obtained.

Blood pressure and heart rate should be checked regularly during intravenous infusion. Adjustment of the drip rate should be made according to the result and possible side-effects such as a serious drop in blood pressure.

2. Intra-muscular injection: When labour is arrested: Duvadilan 10 mg (1 × 2 ml ampoule) three hourly for 24 hours, then four to six-hourly for a further 48 hours.

3. Oral: When contractions have ceased for 48 hours Duvadilan 1 × 20 mg tablet four times a day.

Contra-indications, warnings, etc

Contra-indications: Recent arterial haemorrhage, par- enteral use in patients with known heart disease, premature detachment of placenta, and severe anaemia.

Precaution: Patients in premature labour should be maintained in the lateral position during infusion. Blood pressure and heart rate should be recorded regularly during infusion. If a prolonged fall in blood pressure occurs the rate of infusion should be reduced or the infusion discontinued.

Side-effects: Hypotension (see Precautions); transient tachycardia, mild flushing, nausea and vomiting have been noted. If it is necessary to reverse the cardiovascular effects, treatment with a non-selective beta-blocker should be considered.

Treatment of overdosage: Gross overdosages have not been reported, treatment would be gastric lavage, and if necessary, a non-selective beta-blocker may be administered intramuscularly.

Pharmaceutical precautions Injections should be stored above 0°C but below 20°C, protected from light. The infusion may be prepared with dextrose or isotonic saline.

Legal category

Tablets P.

Injection POM.

Package quantities Ampoules containing isoxsuprine hydrochloride 5 mg/ml in packs of 6 × 2 ml and 2 × 10 ml.

Tablets containing 20 mg isoxsuprine hydrochloride in packs of 100 (5 strips of 20 blister packed tablets).

Further information Results from a preliminary study show that isoxsuprine does not produce false positive reactions in standard diagnostic urine tests.

Product licence numbers

Duvadilan Tablets 0512/5002

Duvadilan Injection 0512/5003

DUVADILAN* RETARD

Presentation Isoxsuprine in a graded release formulation. Red/opaque white, hard gelatine capsules, im printed 'DUV.RET. duphar'. Each capsule contain isoxsuprine (equivalent to 40 mg of the hydrochloride complexed with a sulphonated polystyrene resin).

Uses The active ingredient is isoxsuprine, which has direct vasorelaxant effect on the vascular wall and has also viscosity lowering properties. Its vasodilating action is more marked on the intracerebral vessels, arteries and arterioles where the beta-sympathetic receptors predominate.

Indications: Cerebral and peripheral arteriosclerosis; cerebral and peripheral vasospasm; acute vascular occlusion; Buerger's disease; acrocyanosis; thrombophlebitis; Raynaud's disease.

Dosage and administration *Adults:* 1 capsule morning and evening.

The product is not intended for administration to children.

Contra-indications, warnings, etc

Contra-indication: Recent arterial haemorrhage.

Side-effects: Side-effects in the form of flushing and palpitations are rare and transient.

Treatment of overdosage: Gross overdosages have not been reported; treatment would be gastric lavage, and necessary, a non-selective beta-blocker may be administered intramuscularly.

Pharmaceutical precautions Store in a dry place at a temperature below 20°C.

Legal category P.

Package quantities Compliance pack of 56 capsules (4 strips of 14 blister packed capsules).

Further information Duvadilan Retard can be given to patients with hypertension, diabetes, coronary insufficiency, peptic ulcer and glaucoma. Duvadilan Retard may also be given with the commonly used diuretics, corticosteroids and antihypertensive drugs.

Results from a preliminary study show that isoxsuprine does not produce false positive reactions in standard diagnostic urine tests.

Product licence number 0512/0030.

INFLUVAC*

Presentation Disposable syringes and ampoules containing 0.5 ml, vials containing 5 ml and 25 ml of colourless, opalescent suspension of inactivated influenza virus strains. The product contains appropriate quantities of the A and B strains currently recommended by WHO.

Uses Prophylaxis of influenza. Particularly recommended in:

1. Chronic pulmonary disease, e.g. chronic bronchitis and emphysema, asthma, bronchiectasis, pulmonary tuberculosis and fibrosis.
2. Chronic heart disease, e.g. valvular and hypertensive heart disease.
3. Chronic renal disease, e.g. chronic nephritis, including patients with renal disease on immunosuppressive drugs.
4. Diabetes and possibly other less common endocrine disorders.
5. Elderly people.
6. Key workers in essential services, such as personnel in hospitals, public services and in industry, where temporary absence may constitute a serious problem.

Dosage and administration

Adults and children (over 13 years): 0.5 ml.

Children (9–13 years): 0.5 ml, followed by a second injection of 0.5 ml not less than 4 weeks later, unless previously primed with H₁N₁ antigen, in which case one dose of 0.5 ml is sufficient.

Children (under 9 years): Not recommended.

to be given by intramuscular injection after allowing the vaccine to reach room temperature. It is recommended that the contents of multi-dose vials are used within 8 hours of opening. The vaccine may be expected to protect the recipient 10–21 days after injection for a period of approximately 12 months.

Contra-indications, warnings, etc

Contra-indications: Persons with hypersensitivity to eggs, chicken proteins or feathers should not be vaccinated.

Immunisation should be postponed in patients with febrile illness.

Warnings: Although the incidence of side-effects with influenza, purified by zonal centrifugation, is minimal, a transient erythema, painful arm or tenderness at the site of injection or mild fever may appear within the first forty-eight hours.

Neurological disorders such as encephalomyelitis and neuritis after influenza vaccination have rarely been reported. An association has not been demonstrated except in the case of the Guillain Barré Syndrome (USA mass vaccination programme 1976).

The vaccine contains a maximum per dose of 0.00625 Units polymyxin and 0.00625 mcg neomycin. Use with caution in patients hypersensitive to these antibiotics.

Pharmaceutical precautions Store at 2–10°C, protected from light. Do not freeze.

Legal category POM.

Package quantities Single-dose (0.5 ml) disposable syringes and ampoules, 10 dose (5 ml) and 50 dose (25 ml) vials.

Further information Nil.

Product licence number 0512/0053.

MONOTRIM®

Presentation Tablets – white, flat, round, with bevelled edges, imprinted with the manufacturer's symbol  on one face, with a single break bar on the other and coded $\frac{AE}{2}$. Each tablet contains 200 mg trimethoprim BP.

Tablets – white, flat, round, with bevelled edges, imprinted with the manufacturer's symbol  on one face, with a single break bar on the other and coded $\frac{AE}{2}$.

Each tablet contains 100 mg trimethoprim BP.

Suspension – white, sugar free, aniseed flavoured suspension containing 50 mg trimethoprim per 5 ml.

Uses Trimethoprim is active *in-vitro* against most Gram-positive and Gram-negative aerobic organisms. The antimicrobial activity is due to selective inhibition of bacterial dihydrofolate reductase.

Indications: Treatment of susceptible infections caused by trimethoprim-sensitive organisms including urinary and respiratory tract infections.

Dosage and administration Acute infections:

Tablets:

Adults and children over 12 years: 200 mg twice daily

Children 6 years to 12 years: 100 mg twice daily

Children 6 months to 5 years: 50 mg twice daily

Suspension:

Adults and children over 12 years: 200 mg (20 ml) twice daily

Children 6 years to 12 years: 100 mg (10 ml) twice daily

Children 6 months to 5 years: 50 mg (5 ml) twice daily

Children 6 weeks to 5 months: 25 mg (2.5 ml) twice daily

Treatment should continue for at least one week. The first dose can be doubled. The approximate dosage in children is 8 mg trimethoprim per kg body weight per day.

Long-term treatment and prophylactic therapy:

Tablets:

Adults and children over 12 years: 100 mg at night

Children 6 years to 12 years: 50 mg at night

Suspension:

Adults and children over 12 years: 100 mg (10 ml) at night

Children 6 years to 12 years: 50 mg (5 ml) at night

Children 6 months to 5 years: 25 mg (2.5 ml) at night

The approximate dosage in children is 2 mg trimethoprim per kg body weight per day.

Dosage advised where there is reduced kidney function:

Creatinine clearance (ml/sec)	Plasma creatinine (micromol/l)	Dosage advised
Over 0.45	men < 250 women < 175	normal
0.25–0.45	men 250–600 women 175–400	normal for 3 days then half dose
Under 0.25	men > 600 women > 400	half the normal dose

Contra-indications, warnings, etc

Contra-indications: Pregnancy, trimethoprim hypersensitivity, blood dyscrasias, severe renal insufficiency where blood levels cannot be monitored.

Precautions: Caution should be exercised in the administration of trimethoprim to patients with actual or potential folate deficiency and administration of folate supplement should be considered. Although an effect on folic acid metabolism is possible, interference with haematopoiesis rarely occurs at the recommended dose.

If any such change is seen, folic acid should reverse the effect. Elderly people may be more susceptible and a lower dose may be advisable. In neonates, trimethoprim should be used under careful medical supervision.

In patients with impairment of renal function, care should be taken to avoid accumulation.

Although trimethoprim is excreted in breast milk it is not a contra-indication for short-term therapy in lactating mothers.

Side-effects: Skin rashes, nausea and vomiting have been reported in rare instances.

Treatment of overdosage: Symptomatic treatment, gastric lavage and forced diuresis can be used. Depression of haematopoiesis by trimethoprim can be counteracted by intramuscular administration of calcium folinate.

Pharmaceutical precautions Monotrim Suspension may be diluted with water or sorbitol. The diluted suspension is stable for 14 days.

Legal category POM.

Package quantities

Tablets: 200 mg containers of 100 and 500 tablets
100 mg containers of 100 and 500 tablets

Suspension: Bottle of 100 ml.

Further information Trimethoprim is effective *in-vitro* against most Gram-positive and Gram-negative aerobic organisms, including *enterobacteria* – *E. coli*, *Proteus*, *Klebsiella pneumoniae*; *Streptococcus faecalis*; *Streptococcus pneumoniae*; *Haemophilus influenzae*; and *Staphylococcus aureus*.

It is not active against *Mycobacterium tuberculosis*, *Neisseria gonorrhoeae*, *Pseudomonas aeruginosa*, *Treponema pallidum*, or anaerobic bacteria.

Product licence numbers

Tablets: 200 mg 4012/0003

Tablets: 100 mg 4012/0001

Suspension: 100 ml 4012/0002

Product licence holder: GEA Limited, DK-2000, Copenhagen F, Denmark.

MONOTRIM® INJECTION

Presentation Ampoules containing a sterile, clear, colourless, aqueous solution (pH = 4.0), containing trimethoprim lactate equivalent to 20 mg trimethoprim base per ml. Each ampoule contains 5 ml corresponding to 100 mg of trimethoprim base.

Uses Trimethoprim is active *in-vitro* against most Gram-positive and Gram-negative aerobic organisms. The antimicrobial activity is due to selective inhibition of bacterial dihydrofolate reductase.

Indications: Treatment of susceptible infections caused by trimethoprim-sensitive organisms, particularly Gram-negative infections.

Dosage and administration **Dosage:** Adults and children over 12 years: 200 mg every 12 hours.

Children under 12 years: The approximate dosage in children is 8 mg trimethoprim per kg body weight per day, divided into two or three equal doses.

In severely ill patients, the initial doses may be higher or given more frequently.

Dosage advised where there is reduced kidney function:

Creatinine clearance (ml/sec)	Plasma creatinine (micromol/l)	Dosage advised
Over 0.45	men < 250 women < 175	normal
0.25–0.45	men 250–600 women 175–400	normal for 3 days then half dose
Under 0.25	men > 600 women > 400	half the normal dose

Administration: Monotrim Injection may be administered:

1. By direct intravenous injection, or intramuscular injection, or
2. Via the tubing of an established intravenous infusion.

It is compatible with the following commonly used infusion fluids:

Dextran 40 Injection BP 10% w/v in normal saline

Dextran 70 Injection BP 6% w/v in normal saline

Dextrose Injection BP 5% w/v

Laevulose Injection BP 5% w/v

Ringer's Injection USP

Sodium Chloride Injection BP 0.9% w/v

Sodium Chloride 0.45% w/v and Dextrose 2.5% w/v Injection BP

Sodium Lactate Injection BP

Compound Sodium Lactate Injection BP

Contra-indications, warnings, etc

Contra-indications: Pregnancy, trimethoprim hypersensitivity, blood dyscrasias, severe renal insufficiency where blood levels cannot be monitored.

Precautions: Caution should be exercised in the administration of trimethoprim to patients with actual or potential folate deficiency and administration of folate supplement should be considered. Although an effect on folic acid metabolism is possible, interference with haematopoiesis rarely occurs at the recommended dose. If any such change is seen, folic acid should reverse the effect. Elderly people may be more susceptible and a lower dose may be advisable.

In patients with impairment of renal function, care should be taken to avoid accumulation.

Although trimethoprim is excreted in breast milk, it is not a contra-indication for short-term therapy in lactating mothers.

Side effects: Skin rashes, nausea and vomiting have been reported in rare instances.

Treatment of overdosage: Symptomatic treatment, gastric lavage and forced diuresis can be used. Depressor of haematopoiesis by trimethoprim can be counteracted by intramuscular administration of calcium folinate.

Pharmaceutical precautions Store below 25°C protected from light.

Monotrim Injection is incompatible with solutions of sulphonamides and should not be mixed with such preparations.

Legal category POM.

Package quantities Boxes of 5 × 5 ml ampoules.

Further information Trimethoprim is effective *in-vitro* against most Gram-positive and Gram-negative

aerobic organisms, including *enterobacteria* – *E. coli*, *Proteus*, *Klebsiella pneumoniae*; *Streptococcus faecalis*; *Streptococcus pneumoniae*; *Haemophilus influenzae*; and *Staphylococcus aureus*.

It is not active against *Mycobacterium tuberculosis*, *Neisseria gonorrhoeae*, *Pseudomonas aeruginosa*, *Treponema pallidum*, or anaerobic bacteria.

Monotrim Injection may be given in conjunction with, but separately from, other parenterally administered antibacterials, for example, aminoglycosides, metronidazole or sulphonamides whenever such a combination seems suitable.

Product licence number 4012/0008.

Product licence holder: GEA Limited, DK-2000, Copenhagen F, Denmark.

SERC*

Presentation A white, flat, round tablet, imprinted 'Serc' on one face, scored on the reverse, each tablet containing 8 mg betahistine dihydrochloride.

Uses Betahistine is an orally effective treatment for Ménière's syndrome, which appears to exert its effect by reducing endolymphatic pressure. It is a histamine analogue which was developed following the successful parenteral use of histamine in patients with Ménière's syndrome. Animal studies have confirmed its specific effect. Clinical experience has demonstrated the efficacy of betahistine on all the principal symptoms of Ménière's syndrome, not only reducing vertiginous episodes and tinnitus but also arresting hearing loss.

Indications: Vertigo, tinnitus and hearing loss associated with Ménière's syndrome.

Dosage and administration **Adults:** One or two tablets three times a day, taken preferably with meals. The dosage may be adjusted according to response, up to a recommended maximum of 48 mg daily.

Children: No dosage recommendations are made for children.

Contra-indications, warnings, etc

Contra-indication: Phaeochromocytoma.

Precautions: Clinical intolerance to Serc in bronchial asthma patients has not been shown, but caution should be exercised when administering this histamine analogue to bronchial asthma patients.

High-dosage animal tests have shown no teratogenic properties, but the usual precautions should be observed when administering Serc to patients during pregnancy.

Though an antagonism between Serc and antihistamines could be expected on a theoretical basis, no such interactions have been reported.

Side-effects: There have been a small number of reports of gastric upset.

Pharmaceutical precautions As Serc Tablets are hygroscopic they should be stored and dispensed in the original unopened pack or an airtight container which should be kept in a cool dry place, away from light.

Legal category POM.

Package quantities Available in bottles of 100 tablets.

Further information Results from a preliminary study show that betahistine does not produce false positive reactions in standard diagnostic urine tests.

Product licence number 0512/5005.

TACHYROL*

Presentation A white, round, slightly biconvex tablet, imprinted 'DHT' on one face, and with a scoreline on the reverse. Each tablet contains 0.2 mg dihydrotachysterol₂ USP. XX.

Uses Dihydrotachysterol is a synthetic analogue of vitamin D. Like vitamin D and its active metabolites, dihydrotachysterol raises plasma calcium and promotes mineralisation of bone by its actions on intestinal transport of calcium and phosphate and possibly on other target tissues such as bone, kidney and the parathyroid glands. Dihydrotachysterol requires transformation by the liver (25-hydroxylation) to exert maximal biological effects but, unlike vitamin D, it does not require further metabolism by the kidney (1α -hydroxylation) for its activity.

Several disorders of mineral metabolism are known to be due in part to defective renal metabolism of vitamin D, including renal osteodystrophy, hypoparathyroidism and pseudohypoparathyroidism, and some forms of osteomalacia or rickets resistant to physiological doses of vitamin D. The use of dihydrotachysterol bypasses this metabolic block: moreover the onset and offset of action of dihydrotachysterol are more rapid than vitamin D, which facilitates titration of dose and reduces the risk of hypercalcaemia. Thus accidental hypercalcaemia can be rapidly reversed by stopping treatment.

Indications: Rickets or osteomalacia resistant to vitamin D. Post-operative hypoparathyroidism. Idiopathic hypoparathyroidism. Renal osteodystrophy.

Dosage and administration **Adults:** Initially 0.2 mg (1 tablet) daily. This dosage should be adjusted according to the requirements of individual patients as indicated by blood calcium levels (determined initially after two weeks, or earlier, then at least at monthly intervals), and appropriate clinical response.

Children: Dosage is adjusted to the requirements of individual patients as indicated by blood calcium levels.

Contra-indications, warnings, etc

Contra-indication: Hypercalcaemia.

Precautions: Overdosage is likely to cause hypercalcaemia which may be symptomless; symptoms which can occur include anorexia, nausea, vomiting, griping, polyuria and polydipsia. Chronic hypercalcaemia may lead to calcium deposition in soft tissues such as the kidney. In renal disease, hyperphosphataemia contributes to the tendency to extracellular calcium deposition, and should therefore be controlled if necessary by phosphate binding agents.

In patients with renal osteodystrophy, overdosage may increase the rate of deterioration of renal function.

Concurrent administration of barbiturates has been reported to influence vitamin D metabolism, and increased doses of dihydrotachysterol may therefore be required in patients taking barbiturates or anti-convulsant drugs.

Like all vitamin D analogues, dihydrotachysterol is excreted in breast milk. Animal experiments in rats show evidence of calcification in suckling neonatal rats, therefore it seems prudent, until human evidence is obtained to the contrary, to recommend that mothers receiving dihydrotachysterol do not nurse their infants.

Treatment of Overdosage: It is important to monitor plasma calcium, phosphate and creatinine levels, especially in patients with chronic renal failure.

There is no specific antidote to the effects of Tachyrol. As the drug is excreted rapidly from the patient, withdrawal should be sufficient in cases of overdosage.

Calcium supplements, if given, should also be stopped. Severe hypercalcaemia may be additionally treated using corticosteroids, 'loop diuretics' and i/v fluids. Hyperphosphataemia should be controlled if necessary by phosphate binding agents.

Pharmaceutical precautions Tachyrol tablets should be stored and dispensed in the original unopened pack or an airtight container. The product has a shelf-life of three years from the date of manufacture, if kept at temperatures below 20°C. Protect from light.

Legal category POM.

Package quantities Available in bottles of 75 tablets.

Further information Nil.

Product licence number 0512/0037.

YUTOPAR®

Presentation Tablets – Round, buff, with the inscription 'Yutopar' on one face; breakline on the reverse. Each tablet contains 10 mg ritodrine hydrochloride.

Injection – Clear, aqueous solution containing 10 mg/ml of ritodrine hydrochloride.

Uses Yutopar is a betamimetic drug developed for obstetric use. It mainly stimulates the beta₂-receptors, thereby decreasing uterine contractility. However, some chronotropic cardiac effect and peripheral vasodilation are also seen at therapeutic doses. Yutopar is active after oral, intramuscular and intravenous administration, and inhibits frequency and intensity of uterine contractions.

Indications:

The management of:

Uncomplicated Premature Labour.

Foetal Asphyxia in labour where it is desired to obtain uterine relaxation.

Dosage and administration *Premature labour: I/V:* To be administered as early as possible at the onset of premature labour. Initial dose 50 mcg (0.05 mg) per minute to be gradually increased according to the response by 50 mcg (0.05 mg)/minute every 10 minutes until the desired result is obtained, or the maternal heart rate reaches 140 beats per minute. The effective dosage usually lies between 150 mcg (0.15 mg) and 350 mcg (0.35 mg)/minute. The infusion should be continued for 12 to 48 hours after the uterine contractions have ceased.

I/M: If intravenous administration is considered to be inappropriate, intramuscular administration may be substituted, giving 10 mg intramuscularly every three to eight hours. The intramuscular regime should be continued for 12–48 hours following arrest of labour.

Oral: One tablet (10 mg) may be given approximately 30 minutes before the termination of intravenous therapy. The usual dosage schedule for the first 24 hours of oral maintenance is one tablet (10 mg) every two hours. Thereafter, the usual dose is one or two tablets (10–20 mg) every four to six hours depending on uterine activity and unwanted effects.

The total daily dose of oral ritodrine should not exceed 120 mg. The treatment may be continued as long as the physician considers it desirable to prolong pregnancy.

Foetal asphyxia: I/V: This treatment scheme is only recommended as a means of improving the condition of the foetus, so that intervention may be carried out under better conditions for the baby.

The recommended starting dose is 50 mcg (0.05 mg) per minute by intravenous infusion rapidly increasing the infusion rate until the uterine activity is suppressed, or the maternal heart rate reaches 140 beats per minute. The required dose is unlikely to exceed 350 mcg (0.35 mg) per minute. Whilst the infusion is given preparations should be made for the assisted delivery of the baby. Fifteen to 20 minutes after starting the infusion a foetal scalp blood sample should be taken. If the foetal scalp pH has not improved during the 15–20 minutes of infusion then the planned assisted delivery should be carried out. If the pH has significantly risen, the obstetrician may decide to continue the infusion for a further 15–30 minutes, with continued careful observation before proceeding with the delivery.

Contra-indications, warnings, etc

Contra-indications:

1. Antepartum haemorrhage which demands immediate delivery.
2. Eclampsia and severe pre-eclampsia.
3. Intra-uterine foetal death.
4. Chorioamnionitis.
5. Maternal cardiac disease.
6. Cord compression.

Precautions: Recent reports describe maternal pulmonary oedema in patients treated concomitantly with betamimetics and corticosteroids. Therefore, close monitoring under these conditions is advised.

Careful monitoring is required in patients with suspected heart disease, or those receiving other drugs, in particular those which could interact with ritodrine such as monoamine oxidase inhibitors, tricyclic antidepressants, corticosteroids, sympathomimetic amines, beta-adrenergic blocking drugs, anaesthetics used in surgery and potassium-depleting diuretics, as intravenous administration of Yutopar has been shown to decrease plasma potassium levels.

Experiments in animals have shown that even in high dosage Yutopar has no teratogenic properties. Nevertheless, in view of the limited available information from human studies, the administration of Yutopar is not recommended during the first trimester of pregnancy.

In diabetic patients, glucose levels should be closely monitored and insulin requirements adjusted accordingly during intravenous treatment. On oral treatment no alterations have been reported. It is also advisable to screen patients with potential cardiac risk before deciding on ritodrine treatment.

The drug should not be administered to patients with mild to moderate pre-eclampsia, hypertension or hyperthyroidism unless the attending physician considers that the benefits clearly outweigh the risks.

Side-effects: In appropriate dosage Yutopar is well tolerated. In particular no hypotension occurs if the recommended administration schedule is followed and the patient is maintained in the lateral position. It is only rarely that side-effects call for discontinuation of the treatment. The maternal pulse rate may progressively increase, usually to a moderate degree. This may lead to palpitations.

Any pronounced tachycardia that may arise during an intravenous infusion of Yutopar disappears shortly after decreasing the dosage or after the infusion is stopped.

Whether the maternal tachycardia is considered acceptable must be determined from case to case, but it is recommended that, in healthy patients, a heart rate of more than 140/min should be avoided.

Flushing, sweating, tremor, nausea and vomiting have been reported in a few cases. In cases of overdosage of 'utopar, a non-selective beta-sympatholytic agent may be given as an antidote.

Pharmaceutical precautions *Tablets:* Store in a cool dry place, protected from light.

Injection: Store in a cool place, protected from light. Do not use if solution is discoloured or contains a precipitate.

Compatible with commonly used infusion solutions, e.g. sterile isotonic saline or glucose/saline.

Legal category POM.

Package quantities *Tablets* – Packs of 40 tablets each containing 10 mg ritodrine hydrochloride.

Injection – Boxes of 6 × 1 ml ampoules, or 10 × 5 ml ampoules containing ritodrine hydrochloride 10 mg/ml.

Further information Less effect can be expected if the membranes are ruptured or the dilation of the cervix exceeds 4 cm.

Results from a preliminary study show that ritodrine does not produce false positive reactions in standard diagnostic urine tests.

Product licence numbers

Tablets	0512/0018
Injections (1 ml)	0512/0019
(5 ml)	0512/0020

***Trade Mark**

Du Pont (UK) Limited
Pharmaceuticals
Wedgwood Way
Stevenage
Herts SG1 4QN



NARCAN®
NARCAN® NEONATAL

Presentation A sterile, clear, colourless solution of naloxone hydrochloride in clear, colourless ampoules.

Narcan (1 ml ampoules): each 1 ml of solution contains 0.4 mg naloxone hydrochloride.

Narcan Neonatal (2 ml ampoules): each 1 ml of solution contains 0.02 mg naloxone hydrochloride.

Uses Narcan may be used for the complete or partial reversal of narcotic depression, including mild to severe respiratory depression induced by natural and synthetic narcotics, pentazocine, or dextropropoxyphene. It may also be used for the diagnosis of suspected acute narcotic overdosage. Narcan Neonatal may be used to counteract respiratory and other CNS depression in the new-born resulting from the administration of analgesics to the mother during childbirth.

Dosage and administration Narcan is for intravenous, intramuscular or subcutaneous injection.

1. *Narcotic Overdosage* (known or suspected). *Adults:* The usual initial adult dose of Narcan is 0.4 mg (1 ml) by i.v., i.m. or s.c. injection. If the desired degree of improvement in the respiratory function is not obtained immediately, this dose may be repeated at two to three minute intervals. Failure to obtain significant improvement after two or three doses suggests that causes other than narcotic overdosage may be responsible for the patient's condition.

Children: The usual initial dose of Narcan for children is 5–10 mcg (0.005–0.01 mg) per kg body weight. This dose may be repeated at two to three minute intervals in accordance with the adult administration guide lines.

2. *Post-operative Use:* When Narcan is used post-operatively, the dose should be titrated for each patient in order to obtain optimum respiratory response while maintaining adequate analgesia. Intravenous doses of 0.1–0.2 mg (1.5–3 mcg/kg body weight) are usually sufficient, but a full two minutes should be allowed between each 0.25 ml increment of Narcan administered. Further intramuscular doses may be needed within one to two hours, depending on the interval since the last narcotic administration and the amount and type (i.e. long or short acting) of drug used.

3. *Neonatal Use:* An adequate airway should be established in the apnoeic infant before Narcan is administered. The usual dose for narcotic induced depression is 0.01 mg/kg body weight administered i.v., i.m. or s.c. This dose may be repeated in accordance with adult administration guide lines. Alternatively, a single dose of 200 mcg (60 mcg/kg body weight) may be given intramuscularly at birth. It should however, be noted that onset of action is slower following i.m. injection.

Contra-indications, warnings, etc Narcan should not be given to patients who are known to be hypersensitive to it. It should be administered cautiously to patients who have received large doses of narcotics or to those physically dependent on narcotics since too rapid reversal of narcotic effects by Narcan may precipitate an acute withdrawal syndrome in such patients. The same caution is needed when giving Narcan to neonates delivered of such patients.

Although animal reproduction studies have not demonstrated any teratogenic or embryotoxic effects, Narcan should, like all drugs, be used with caution during pregnancy. However, Narcan may be administered to the mother during the second stage of labour to correct respiratory depression in the new-born caused by narcotics used to provide obstetrics analgesia.

Patients who have responded satisfactorily to Narcan should be kept under observation. Repeated doses of Narcan may be necessary since the duration of action of some narcotics may exceed that of Narcan.

Narcan is not effective against respiratory depression caused by non-opioid drugs.

Two patients with ventricular irritability have developed tachycardia or fibrillation following the administration of naloxone. Although a direct relationship has not been established, it is suggested that Narcan be used with caution in patients with cardiac irritability.

Overdosage: There have been no reports of acute overdosage with Narcan. Single doses of 10 mg intravenously and subcutaneous doses of 15 mg every four hours for two weeks (usual parenteral dose 0.4 mg) have been administered without producing either respiratory depression or psychotomimetic effects.

Adverse effects: Occasionally, nausea and vomiting have been reported in post-operative patients who have received Narcan in doses higher than those recommended; however, a cause and effect relationship has not been established.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Narcan ampoules each containing 1 ml are supplied in boxes of 10 ampoules.

Narcan Neonatal ampoules each containing 2 ml are supplied in boxes of 10 ampoules.

Further information Nil.

Product licence numbers

Narcan 4524/0001
Narcan Neonatal 4524/0002

**Trade Mark*

Ethicon Limited

Po Box 408
Bankhead Avenue
Edinburgh EH11 4HE

ABSELE* STERILE ABSORBABLE BONE SEALANT

Presentation A paste of putty-like consistency, sterilised by gamma irradiation and composed of:

Stabilised bovine fibrin	17.5% w/w
Solubilised bovine collagen	17.5% w/w
Dextran 70	8.0% w/w
Glycerol BP	30.0% w/w
Water	to 100

Physically it is a yellowish brown to brown, slightly sticky paste having a distinct honey-like odour. It is malleable and adheres to wet cut bone surfaces. Complete absorption of the paste has been shown experimentally in rats in two to three weeks.

Uses The paste is used to control bleeding from the divided, drilled or chipped edges of bone by physically plugging the osseous canals which contain the bleeding capillaries. It is suitable for use in neurosurgery, cardio-thoracic surgery and orthopaedic surgery.

Dosage and administration Implantation by application to bone as required to control haemorrhage.

Contra-indications, warnings, etc To date there have been no contra-indications to the use of this product.

Pharmaceutical precautions The product remains in optimum condition when stored at low temperatures. The shelf-life is two years when stored at 15°C, but storage under refrigeration will extend the expected shelf-life. Exposure to temperatures in excess of 30°C may cause irreversible adverse changes to the product.

Legal category P.

Package quantities Flat discs of approximately 2 grams in weight are packaged in a sealed inner aluminium foil pack. This pack is contained in a peel-apart secondary pack. The unit of sale is 12 packs contained in a film wrapped drawer-style carton.

Further information Absorbable bone sealant will harden if left exposed to the atmosphere for long periods, particularly under the heat of operating lights. The package should, therefore, only be opened immediately before use. The package will be damaged by caustics, chlorides and mercurials.

Product licence number 0508/0006.

BIETHIUM* STERILE ABSORBABLE OX FIBRIN PROSTHESIS

Presentation Moulded pliable implants in various shapes and sizes, sterilised by gamma irradiation and contained in a sealed foil sachet, which is in turn contained in a sterilised overwrap. The implant is composed of 65% heat treated bovine fibrin and 35%

Glycerol BP. Physically, it is a yellowish brown translucent product with a distinctive honey-like odour. It is pliable and resilient and has a specific gravity of 1.2. Absorption of the implant as observed experimentally in rats is approximately six weeks. However, if the implant is treated with a buffered formaldehyde solution prior to gamma irradiation, the absorption period can be extended for up to five months.

Uses

1. A bean-shaped prosthesis is used for the surgical correction of female stress incontinence. The bean is placed surgically at the urethro-vesical junction to reconstruct the normal angle of exit of the urethra from the bladder.

2. The buttress, buffer and button-shaped prostheses have the same basic function, namely to broaden the surface area of the suture which transfixes them in use. The buttress is rectangular and used in the repair of inguinal and incisional herniae, as well as in the resuture of the burst abdomen. The buffer is also rectangular and, used in pairs, effectively compresses the liver substance, following biopsy or liver resection, again by broadening the surface area of pressure of the ligating suture. The oval buttons are used in diaphragmatic hernia and in areas where a smaller implant is required to broaden the surface area of a suture.

Dosage and administration One bean only is required in stress incontinence, while in other procedures, several prostheses may be used, as required, according to the size of defect or damage. Administration is by implant at a surgical procedure.

Contra-indications, warnings, etc Biethium is supplied sterile and should not be resterilised.

Pharmaceutical precautions Store under normal shelf conditions. Observe expiry date.

Legal category P.

Package quantities One bean per foil pack, with five foil packs per box. Two buffers per foil pack, with five foil packs per box. Two buttons per foil pack, with five foil packs per box. Two buttresses per foil pack, with five foil packs per box. Each foil pack is overwrapped in a peel-open container. The boxes containing the foil packs are film overwrapped.

Further information *Storage:* Two years' shelf life. Avoid storing beside caustics, chlorides and mercurials which could damage the aluminium foil pack.

Product licence number 0508/0003.

POLYTEF* PASTE FOR INJECTION

Presentation A sterile, white, injectable paste in tin tubes within a see-through, peel-apart overwrap. Polytef Paste contains 50% of polytetrafluoroethylene powder

(which has been pyrolysed to purify it) in Glycerin USP containing polyoxyethylene sorbitan monolaurate (Tween 20).

Uses Polytef Paste for Injection is used for intravocal cord injection of the paralysed vocal cord. It is administered by injection directly into the cord.

Dosage and administration By injection. Dose varies according to size of cord, but should not exceed 0.6 cc per site of injection.

Contra-indications, warnings, etc Contra-indicated until at least six months have elapsed following the onset of paralysis, and/or until an intensive trial of rehabilitation by voice therapy has been given since many patients are capable of overcoming their vocal disability.

In bilateral laryngeal paralysis. In vocal disorders of psychogenic origin. In the presence of foreign bodies in the larynx (e.g. fragments of shells or bullets).

In the presence of an acute inflammation, infection or inadequately controlled malignancy, or a rapidly advancing disease, especially when these are in the laryngeal or upper respiratory tract area.

Warnings: Intra-cordal injection is a delicate procedure and should be conducted with precision and great caution. This product should be used only by trained ENT surgeons.

General anaesthesia is not advisable. Over-sedation may lead to an unco-operative patient and difficult airway problems. Intravascular injections must be avoided. Likewise, over-injection should be avoided.

It is safer to under-inject the involved cord than to over-inject because treatment may be repeated at a later time. If the procedure is followed by upper respiratory tract inflammatory changes in excess of the reaction expected at the site of injection, diagnostic and therapeutic procedures should be implemented. In acute fulminating reactions, steroid and antibiotic therapy may be indicated. This therapy should be at the discretion of the surgeon.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities Polytef Paste for Injection is packaged in tin tubes containing 7 cc and contained in a peel-apart overwrap.

Further information Nil.

Product licence number 0508/0002.

STERILISED FASCIA LATA

Presentation Straw-coloured strip 20 cm x 6 mm consisting of bovine connective tissue from below the hide. Fascia Lata is packaged in a tubing fluid containing isopropanol and water.

Uses In surgical operations upon the human body as a substitute for human fascia.

Dosage and administration By implantation.

Contra-indications, warnings, etc There are no contra-indications or warnings.

It is recommended that Fascia Lata is rinsed in sterile water or sterile saline solution to remove tubing fluid before use.

Pharmaceutical precautions Do not subject to heat. Store in a cool place.

Legal category P.

Package quantities Three heat-sealed foil packs overwrapped and placed in a film-wrapped plastic suture box.

Further information Individual unopened packs which have been removed from the overwrap may be re-sterilised by immersion in a solution of 1% w/v formaldehyde in 93% isopropanol q.s. water. Avoid contact with caustics, chlorides and mercurials which could cause damage to the aluminium foil pack.

Product licence number 0508/5004.

STERILISED SURGICAL BONEWAX

Presentation Solid wax. A white solid, somewhat translucent when in thin layers. Comprises:

Refined white beeswax	90%
Isopropyl palmitate	10%

Uses For controlling haemorrhaging in osseous surgery and the control of the escape of fluids from osseous tissues.

Dosage and administration By implantation and application to bone as required to control haemorrhage.

Contra-indications, warnings, etc There are no contra-indications or warnings.

Pharmaceutical precautions Store under normal warehouse conditions.

Legal category P.

Package quantities Slabs (5 x 2 x 0.13 cm) of approximately 2.5 g in weight packed in a paper slide and sleeve which is overwrapped packed. The overwraps are presented in a film-wrapped plastic box containing one dozen.

Further information Avoid contact with caustics, chlorides and mercurials which could cause damage to the aluminium foil pack.

Product licence number 0508/5001.

STERILISED SURGICAL CATGUT BP – ETHICON® BRAND

Presentation An absorbable strand, with or without a needle attached, consisting of collagen derived from the intestinal tract or gut of healthy mammals uniformly twisted to produce virtually a monofilament strand with a diameter conforming to the requirements set out in the British Pharmacopoeia.

It is capable of being absorbed by living mammalian tissue but may be treated to modify its resistance to absorption.

Plain catgut is Sterilised Surgical Catgut which has not been treated to prolong its resistance to digestion. It is straw coloured.

Chromic catgut is material which has been hardened by treatment with chromium salts in trivalent form and with oxidised pyrogallol (oxidised pyrogallous acid) to prolong its resistance to absorption. It is brown coloured.

Extra chromic catgut is chromic catgut which has been treated to prolong its resistance slightly further.

Plain and chromic catgut may be dyed with a blue (indigo) dye.

Sterilised Surgical Catgut is packed in tubing fluid containing isopropanol and water.

Uses Sterilised Surgical Catgut is used in surgical operations upon the human body.

Dosage and administration By implantation.

Contra-indications, warnings, etc Should not be used in situations where a non-absorbable suture would normally be used.

Pharmaceutical precautions Do not subject absorbable surgical suture to heat. Do not rinse or soak in fluids other than the tubing fluid. Store in a cool place.

Legal category P.

Package quantities Various lengths (40 cm to 1.5 m) in heat-sealed foil packs. The foil packs are contained in a peel-open overwrap and packed into film-wrapped boxes containing one dozen sutures.

Further information Individual unopened packs which have been removed from the overwrap may be re-sterilised by immersion in a solution of 1% w/v formaldehyde in 93% isopropanol q.s. water. Avoid contact with caustics, chlorides and mercurials which could cause damage to the aluminium foil pack.

Product licence number 0508/5002.

STERILISED SURGICAL COLLAGEN

Presentation An absorbable strand of re-constituted collagen with or without a needle attached, or an absorbable tape with or without a needle attached. Available plain or chromicised. Sterilised Surgical Collagen is packed in tubing fluid containing isopropanol and water.

Uses Used in surgical operations upon the human body.

Dosage and administration By implantation.

Contra-indications, warnings, etc Should not be used in situations where a non-absorbable suture would normally be used.

Pharmaceutical precautions Do not subject absorbable surgical suture to heat. Do not rinse or soak in fluids other than the tubing fluid. Store in a cool place.

Legal category P.

Package quantities Various lengths in heat-sealed foil packs. The foil pack is contained in a peel-open overwrap and packed into film-wrapped boxes which hold one dozen sutures, or Collagen Tape (chromic) 60 cm × 3 mm, 3 packs per box.

Further information Individual unopened packs which have been removed from the overwrap may be re-sterilised by immersion in a solution of 1% w/v formaldehyde in 93% isopropanol q.s. water. Avoid contact with caustics, chlorides and mercurials which could cause damage to the aluminium foil pack.

Product licence number 0508/5008.

ZENODERM* CORIUM IMPLANT

Presentation A white biscuit-like matrix of enzyme treated, glutaraldehyde cross-linked, lyophilised or air dried porcine dermis. All non-collagenous elements are removed by immersion in a proteolytic enzyme whilst glutaraldehyde treatment crosslinks the collagen for strength. Individual sheets are cut to various sizes and thicknesses depending upon their ultimate clinical application.

Uses As a biological implant for tissue replacement in areas where tissue is weak, deficient or absent, e.g. in: Dural Replacement, Fascia Lata Substitute, Bladder Sling, Oro Antral Fistulae, Senile Entropion, Repair of Herniae, Perforations of the Tympanic Membrane and Retropubic Sling.

Dosage and administration By implantation.

Contra-indications, warnings, etc No situation has presented, to date, in the areas listed above, where the use of the material is contra-indicated. Supplied sterile, Zenoderm Corium Implant should not be re-sterilised. Open unused Zenoderm implant should be discarded.

Pharmaceutical precautions Under normal storage conditions, a shelf life of 5 years is recommended for Zenoderm Corium Implant. It should be stored in a cool place and not subjected to heat.

Legal category P.

Package quantities Supplied sterile in double peel apart overwrap envelopes (foil backing transparent fronts), Zenoderm Corium Implant is available in the following sizes, packaged 5 sheets per box.

25 cm × 12 cm × 0.6 mm	(ZD 6251)
10 cm × 10 cm × 0.3 mm	(ZD 3101)
30 cm × 2 cm × 0.6 mm	(ZD 6301)
20 cm × 1.5 cm × 0.6 mm	(ZD 6201)
30 cm × 1.5 cm × 0.6 mm	(ZD 6311)
10 cm × 5 cm × 0.6 mm	(ZD 6101)

Further information Zenoderm Corium Implant is crosslinked in a buffered solution of glutaraldehyde then freeze or air dried before sterilisation by gamma irradiation. After implantation into the human body Zenoderm is gradually replaced by host tissue.

Product licence number 0508/0007.

***Trade Mark**

BCG VACCINE (INTRADERMAL)

Presentation Multidose ampoules containing a white freeze-dried pellet which easily disperses to form an opalescent liquid on reconstitution. This vaccine is a suspension containing living *Bacillus Calmette-Guérin*, a bovine strain of tubercle bacillus which has been attenuated by growth on a special medium.

Development of the culture medium by Glaxo research has resulted in a vaccine which, in the dry state, resists the effects of heat.

This vaccine complies with the specifications for *Bacillus Calmette-Guérin* Vaccine BP, and *Vaccinum Tuberculosis* (BCG) *Cryodesiccatum* (Ph Eur), and is of standardised potency.

Uses BCG Vaccine induces active immunity to tuberculosis. Patients normally become Mantoux-positive after a period of eight weeks has elapsed but sometimes about 14 weeks are needed.

Dosage and administration *Adults and children over three months of age:* 0.1 ml by **intradermal** injection (subcutaneous injection should be avoided).

Neonates: 0.05 ml by **intradermal** injection.

No special precautions are necessary when opening the ampoules, as the dextran content produces a solid plug of dried vaccine which is not dispersed, despite the ampoule being sealed under reduced pressure. The vaccine must not be contaminated with any antiseptic or detergent. If alcohol is used to swab the skin, it must be allowed to evaporate before the vaccine is injected.

The solution is prepared by adding 1 ml Water for Injections or Sodium Chloride Injection BP (sterile isotonic saline) to the 1 ml multidose ampoule. When using the 5 ml multidose ampoule, 5 ml of Sodium Chloride Injection BP (not Water for Injections) should be added. Do not shake as this causes frothing. Allow to stand for one minute, then draw it into the syringe once or twice to ensure homogeneity. Once the liquid vaccine has been prepared, it should be used on the same day.

The injection site is best left uncovered to facilitate healing.

Contra-indications, warnings, etc

Contra-indications: Unless specifically indicated, BCG Vaccine should not be given to patients suffering from generalised eczema, infective dermatoses, hypogammaglobulinaemia, or to those with a history of deficient immunity, particularly to bacterial infections. The same applies to patients being treated with antimetabolites, irradiation, systemic corticosteroids, or any substance that depresses the immune response. The effect of BCG vaccine may be exaggerated in these patients, and a more generalised infection is possible.

Tuberculin-positive patients, i.e. those in Heaf grades 2 to 4, or with induration greater than 5 mm in diameter in the Mantoux test, should not receive BCG Vaccine.

Pregnancy: When, however, there is a risk of tuberculous

infection, the importance of vaccination may outweigh the possible risk of BCG to the fetus.

Warnings: BCG Vaccine may be given at the same time as oral poliomyelitis vaccine. With other live vaccines it is preferable to allow an interval of three weeks between administration of BCG and the other vaccine, but the interval can be reduced to 10 days if a longer period is not available. In neonates concomitant administration of BCG and smallpox vaccines is effective, but could result in ulceration of both arms for up to three weeks, as different arms must be used.

In general, vaccines containing toxoids or killed organisms should be given at least seven days before BCG Vaccine, or 10 days after. However, diphtheria/tetanus vaccine has been given at the same time as BCG Vaccine (but in different arms) with satisfactory results.

Any prepared vaccine remaining at the end of the day should be discarded, and preferably incinerated or treated with a disinfectant such as strong hypochlorite solution.

Side-effects: Occasionally an excessive response to BCG Vaccine results in a discharging ulcer. Frequently this is attributable to inadvertent subcutaneous injection, or to excessive dosage. The ulcer should be encouraged to dry by avoiding abrasion, e.g. by tight clothes. Waterproof dressings should not be used. If the ulcer persists, it can be treated by application of a cream containing neomycin and a corticosteroid, or by local application of isoniazid powder.

In the rare cases of severe local reactions with abscess formation, aspiration should be carried out, perhaps with streptomycin replacement. Enlargement of axillary lymph glands is unlikely, except occasionally in young infants.

Overdosage: If gross overdosage occurs, and there is reason to suspect the development of a more generalised infection with BCG, systemic treatment with isoniazid should be given.

Pharmaceutical precautions Protect from light and keep in a refrigerator at a temperature below 10°C, but avoid freezing ampoules of diluent. Refrigeration during actual delivery is not essential but the vaccine should be kept as cool as possible.

Legal category POM.

Package quantities 1 ml multidose ampoules in boxes of 10.

Composite pack of five 1 ml multidose ampoules with five 1 ml ampoules of Water for Injections.

5 ml multidose ampoules with 5 ml ampoules of Sodium Chloride Injection BP are available to United Kingdom Health Authorities and hospitals through Department of Health and Social Security contract.

Further information No batch of vaccine is released until it has been shown to resist a temperature of 37°C for 28 days.

Measles or rubella infection can cause tuberculin positive patients to revert temporarily to tuberculin negative.

BCG Vaccine (Intradermal) has also been given by jet injector.

Product licence number 0004/0245.

BCG VACCINE (PERCUTANEOUS)

Presentation Multidose ampoules containing a freeze-dried white pellet which is easily dispersed to form an opalescent suspension on reconstitution. This vaccine contains dextran and living *Bacillus Calmette-Guérin* (BCG) with a higher viable bacterial count than BCG Vaccine (Intradermal). The BCG is an attenuated form of a bovine strain of tubercle bacillus. This vaccine complies with the specification for Percutaneous BCG Vaccine BP, and is of standardised potency.

Uses Percutaneous BCG Vaccine induces active immunity to tuberculosis. Patients normally become Mantoux-positive after a period of eight weeks has elapsed, but sometimes up to 14 weeks are needed.

Dosage and administration Percutaneous BCG Vaccine is used with a multiple puncture apparatus equipped with not less than 20 needles giving reliable penetration of the skin to a depth of 2 mm. Ethyl or isopropyl alcohol may be used to prepare the skin, which must be dry before the vaccine is used.

With a dry syringe add 0.3 ml of Water for Injections or Sodium Chloride Injection to the ampoule of BCG, and allow to stand for about one minute to allow a suspension to form. Do NOT shake, as this causes rothing. A small amount of the suspension is spread on the skin by means of a glass rod, platinum loop or spatula. The treated area of skin is then immediately punctured with the multiple puncture apparatus.

Once the vaccine has been prepared for use, it should be used forthwith; any remaining at the end of the day should be discarded after boiling or treatment with a disinfectant, e.g. strong hypochlorite solution.

The injection site is best left uncovered; waterproof dressings are particularly undesirable. The multiple puncture apparatus should be sterilised according to the maker's instructions. Any alcohol or ether used should be burnt off before the apparatus is used, and IT MUST BE ALLOWED TO COOL before use. Detergents or antiseptics should not be used.

Contra-indications, warnings, etc

Contra-indications: Unless specifically indicated, percutaneous BCG Vaccine should not be given to patients suffering from generalised eczema, infective dermatoses, hypogammaglobulinaemia or a history of deficient immunity, especially to bacterial infections. This vaccine is also contra-indicated in patients treated with antimetabolites, irradiation, systemic corticosteroid, or any substance which depresses the immune response.

Tuberculin-positive patients, i.e., those in Heat grades 1 to 4 or with induration greater than 5 mm in diameter with the Mantoux test, should not receive percutaneous BCG vaccine.

Pregnancy: When, however, there is a risk of tuberculous infection, the importance of vaccination may outweigh the possible risks of BCG to the fetus.

Warnings: Percutaneous BCG Vaccine must NOT be given by intradermal injection or by Dermojet.

BCG Vaccine may be given at the same time as oral poliomyelitis vaccine. With other live vaccines it is preferable to allow an interval of three weeks between administration of BCG and the other vaccine, but the interval can be reduced to 10 days if a longer period is not available. In general, vaccines containing toxoids or killed organisms should be given at least seven days before BCG vaccine, or 10 days after.

Any prepared vaccine remaining at the end of the day should be discarded, and incinerated or treated with a disinfectant such as strong hypochlorite solution.

Side-effects: Occasionally an excessive response to percutaneous BCG vaccine results in a discharging ulcer. This should be encouraged to dry by avoiding abrasion, e.g. by tight clothes. Waterproof dressings should not be used. If the ulcer persists, it can be treated by application of a cream containing a corticosteroid, with neomycin to prevent secondary infection, or by local application of isoniazid powder.

In the rare cases of severe local reactions with abscess formation, aspiration should be carried out, perhaps with streptomycin replacement. Enlargement of axillary lymph glands is unlikely, except occasionally in young infants.

Overdosage: If gross overdosage occurs, and there is reason to suspect the development of a generalised infection with BCG, systemic treatment with isoniazid should be given.

Pharmaceutical precautions Protect from light and keep in a refrigerator at a temperature below 10°C. Refrigeration during actual delivery is not essential, but the vaccine should be kept as cool as possible.

Legal category POM.

Package quantities Multidose ampoules in boxes of 10.

Further information Infections such as measles or rubella may cause tuberculin-positive patients to revert temporarily to tuberculin-negative.

Product licence number 0004/0247.

NEPENTHE* INJECTION

Presentation A clear, colourless, sterile solution containing the equivalent of 0.84% w/v (4.2 mg/0.5 ml) anhydrous morphine of which 0.05% w/v is derived from Papaveretum BPC and 0.79% w/v from Morphine Hydrochloride BP.

Uses To relieve severe pain, especially when it causes anxiety and/or sleeplessness.

Dosage and administration

Not to be used for Children under 6 year of age.

6-12 years: Maximum single dose 0.5-1.0 ml.

Adults: Usual single dose 1-2 ml but not to be repeated more than four hourly.

Nepenthe Injection should be administered by the subcutaneous or intramuscular routes using a syringe graduated in 1/100ths of a ml. It must not be given intravenously.

When doses of fractional of a ml are prescribed special care should be taken in view of the small volumes involved.

Contra-indications, warnings, etc Nepenthe Injection should not be given concurrently with other opiates,

with monoamine oxidase inhibitors, nor within two weeks of discontinuation of treatment with them.

Nepenthe Injection is contra-indicated in respiratory depression and obstructive airways disease. Use with care in the elderly. Safety in pregnancy has not been established. Use with caution in myxoedema and chronic hepatic disease. Administration in labour may cause respiratory depression in the new born infant.

Tolerance and dependence may occur and nausea and vomiting may be troublesome.

Effects of overdosage and their treatment: Signs of morphine overdosage include pin-point pupils, depressed respiration and coma. In severe poisoning there may be dilatation of the pupils, shock, severe respiratory depression and pulmonary oedema.

Naloxone, nalorphine or levallorphan tartrate may be given as an antidote.

Pharmaceutical precautions Protect from light.

Legal category POM: MDA.

Package quantities Ampoules of 0.5 ml in boxes of 5.

Further information Any requests for further information should be made to Evans Medical Limited, Beaconsfield, Buckinghamshire HP9 2JH. Telephone Beaconsfield 6111.

Product licence number 0039/0063R.

NEPENTHE* ORAL SOLUTION

Presentation A brown, bright solution with characteristic odour containing 0.84% w/v anhydrous morphine of which 0.79% w/v is derived from Morphine alkaloid and 0.05% w/v is derived from Tincture of Opium BP. 1 ml contains 8.4 mg anhydrous morphine.

Uses To relieve severe pain, especially when it causes anxiety and/or sleeplessness.

Dosage and administration Nepenthe Oral Solution is for use as an ingredient in the preparation of narcotic analgesic mixtures. The recommended diluent is Syrup BP.

This product must always be diluted when being dispensed by the pharmacist and the dosage expressed in units of 5 ml.

Children under 1 year: not recommended.

1–5 years: 0.25–0.5 ml maximum single dose.

6–12 years: 0.5–1.0 ml maximum single dose.

Adults: Usual single dose 1–2 ml, not to be repeated more often than four hourly.

Contra-indications, warnings, etc

Nepenthe Oral Solution should not be given concurrently with other opiates, with monoamine oxidase inhibitors nor within two weeks of discontinuation of treatment with them.

Nepenthe Oral Solution is contra-indicated in respiratory depression and obstructive airways disease. Use with care in the elderly. Safety in pregnancy has not been established. Use with caution in myxoedema and chronic hepatic disease. Administration in labour may cause respiratory depression in the new born infant.

Tolerance and dependence may occur and nausea and vomiting may be troublesome.

Effects of overdosage and their treatment: Signs of morphine overdosage include pin-point pupils, de-

pressed respiration and coma. In severe poisoning there may be dilatation of the pupils, shock, severe respiratory depression and pulmonary oedema.

Gastric lavage should be performed as soon as possible after ingestion and intensive supportive therapy carried out.

Naloxone, nalorphine or levallorphan tartrate may be given as an antidote.

Pharmaceutical precautions Nepenthe Oral Solution should be diluted with Syrup BP. Any diluted portion not used within four weeks should be discarded. Protect from light. Nepenthe Oral Solution is compatible with Ethanol BP, Chloroform Spirit BP and Glycerol BP. It is incompatible with alkalis.

Because of the volatile nature of the solvent, Nepenthe Oral Solution should be stored in a cool place and the bottle should be tightly closed. If evaporation is thought to have occurred during storage, the solution must not be used.

Legal category POM: MDA.

Package quantities Bottle of 100 ml.

Further information Any requests for further information should be made to Evans Medical Limited, Beaconsfield, Buckinghamshire HP9 2JH. Telephone Beaconsfield 6111.

Product licence number 0039/0062R.

STREPTOMYCIN SULPHATE BP

Presentation Streptomycin sulphate is supplied in vials as a white sterile powder for preparation of Streptomycin Sulphate Injection BP.

Uses Streptomycin has antibacterial activity particularly against *Mycobacterium tuberculosis*, *Klebsiella pneumoniae* and *Escherichia coli*.

Streptomycin may be used in the treatment of: tuberculosis; non-tuberculous infections, including chronic respiratory infections, septicaemia and bacterial endocarditis (usually in conjunction with penicillin); pneumonia due to *Klebsiella pneumoniae*; infections with *Escherichia coli*, particularly of the urinary tract; tularaemia and plague; brucellosis (normally in conjunction with a tetracycline).

Dosage and administration *Tuberculosis: Adults.* Commonly 1 g daily, but in patients over 40 years of age 0.75 g daily by intramuscular injection may be appropriate. Streptomycin is given in conjunction with other antituberculous drugs. The injection should be given deeply into muscle, and the site changed for each injection. A 1 g dose is usually dissolved in 2 or 3 ml of Water for Injections.

Children: Usually 30 mg/kg (13.6 mg/lb) body weight daily up to 1 g a day by intramuscular injection.

Tuberculous meningitis: Intramuscular dosage 30–40 mg/kg (13.6–18 mg/lb) body weight up to 1 g a day. In addition to this streptomycin may be given intrathecally: adults, 50 mg a day; infants and children, 1 mg per kilogram body weight daily. The antibiotic is dissolved in Sodium Chloride Injection, using 5 ml for infants and 10 ml or more for children and adults. The concentration of streptomycin in the injection must not exceed 5 mg/ml. After withdrawal of an equal volume of cerebrospinal fluid, the solution is injected slowly, taking at least 1 l

minutes. An injection may be given once a day for 10 days, perhaps followed by a dose on three alternate days.

Use of a sterile disposable membrane filter of 0.45 micron pore size is convenient to ensure clarity of the solution.

Non-tuberculous infections. Adults: Usually 1 g a day by intramuscular injection for three to seven days.

Children: 22–40 mg/kg (10–18 mg/lb) body weight daily. Divided doses are often used.

N.B. In urinary-tract infections the urine should be kept alkaline.

Contra-indications, warnings, etc

Contra-indications: Allergy to streptomycin.

Diseases of the ear, particularly suppurative otitis media and labyrinthine disturbances.

Precautions: In the presence of actual or suspected renal insufficiency, treatment of non-tuberculous infections may start with a dose of 250–500 mg streptomycin. No further dose should be given until the blood level has fallen to 20 mcg/ml or less (*Brit. Med. J.* 1963, 1, 1393).

In tuberculous patients over 60 years of age, the serum level of streptomycin 24 hours after injection should not exceed 1 mcg/ml. It is important to repeat this estimation several times in the early weeks of treatment (*Brit. Med. J.* 1963, 1, 1527).

Skin sensitisation may occur in persons handling the antibiotic and care should be taken to avoid contact with the substance. Use of rubber gloves is recommended.

Side-effects: Ototoxicity: Some impairment of vestibular function (less often of auditory function) can occur, particularly with prolonged or intensive therapy, in the presence of renal dysfunction, and in the elderly patient. Prolonged streptomycin therapy given during pregnancy can cause deafness and vestibular dysfunction in the child.

Sensitivity: Occasional allergic-type reaction, rarely severe, often responding to antihistamine treatment. Anaphylactic reaction is rarely reported.

Overdosage: Streptomycin can be removed from the body by haemodialysis.

Pharmaceutical precautions Sterile solutions of streptomycin should be used as soon as possible but they can be kept for up to 28 days in a refrigerator (below 4°C). Limited storage (up to seven days) is permissible in a cool place (below 20°C) if protected from light.

Although solutions may discolour slightly on keeping, potency is not decreased.

Legal category POM.

Package quantities Vials each containing 1 g streptomycin base as sulphate, box of 10.

Further information To obtain fractional doses:

Volume of water to be added to 1 g vial	Streptomycin per ml of solution
4.2 ml	200 mg
3.2 ml	250 mg
1.2 ml	500 mg
1 g streptomycin in solution displaces 0.82 ml.	

Product licence number 0039/6002.

TUBERCULIN PURIFIED PROTEIN DERIVATIVE (PPD) BP

Presentation Sterile aqueous solutions for intradermal

injection containing Tuberculin PPD BP are prepared from human strains of *Mycobacterium tuberculosis*.

Use As a diagnostic test for hypersensitivity to tubercle bacilli.

Dosage and administration

1. **Mantoux Test:** The Mantoux test enables an estimate to be obtained of the degree of hypersensitivity of a particular patient. It consists of injecting intradermally ready diluted Tuberculin PPD.

First, clean the skin of the volar surface of the left forearm with acetone or ether. Then using a disposable syringe inject 0.1 ml so that a weal 7 mm in diameter is raised.

The following doses are given, the second and subsequent injections being given only if a negative reaction is obtained from the previous injection.

- 0.1 ml of 10 units per ml Tuberculin dilution (1 unit).
- 0.1 ml of 100 units per ml Tuberculin dilution (10 units).
- 0.1 ml of 1,000 units per ml Tuberculin dilution (100 units).

An interval of two days is allowed between the injections. A further injection of 0.1 ml containing 1,000 units may be given if no reaction has been obtained to the third injection. Children are given one half of the above dose but the 1,000 units in 0.1 ml is not usually given. A positive reaction is characterised by an area of 6 mm or greater of palpable induration, which may sometimes be surrounded by erythema and the results should be read at 48 to 96 hours, preferably after 72 hours.

This test may be carried out and at the same time the control solution may be used to assess individual patients response to the vehicle used.

2. **Heaf test:** This test is performed using undiluted Tuberculin PPD at a strength of 100,000 units per ml. 1 ml is sufficient for 50–100 tests and in addition to the tuberculin the solution contains in each ml 0.2 g glycerol and phenol 2.5 mg, together with phosphate buffers.

Cleanse the skin as for the Mantoux test and allow to dry, then transfer undiluted tuberculin using a syringe needle or loop and smooth over a circular area of about 1 cm in diameter. Using the Heaf multiple puncture apparatus set the apparatus to give a puncture of 1 mm for children under the age of two years or 2 mm for older children and adults. Holding the apparatus at right angles to the skin, place the end plate firmly and evenly in the centre of the film of tuberculin and press the handle to release the needles. No dressing need be applied and the gun should be sterilised after each application or a disposable end plate should be used.

The test should be read at 3 to 10 days. A positive result should be recorded only when there is palpable induration around at least four puncture points. The induration is best felt by passing the finger lightly over the punctures, and if no resistance is felt, a negative result should be recorded.

Four grades of positive response are recognised.

- at least 4 small indurated papules
- an indurated ring formed by confluent papules
- a solid induration 5 to 10 mm wide
- induration over 10 mm wide.

For further information on methods of use see DHSS leaflet No. 322/BCG (1972).

Contra-indications, warnings, etc Temporary diminution of skin sensitivity to tuberculin may occur after

ultra-violet light treatment, during treatment with corticosteroids or immunosuppressive agents, and for 4 weeks or longer following measles or measles vaccination.

Tuberculin can cause a severe acute local reaction in some individuals if the solution is allowed to come into contact with open cuts, the eyes and the mouth.

The affected area should be washed with copious quantities of water followed, if necessary, by local corticosteroids.

The potency of tuberculins may be affected if they are diluted with diluents which differ in composition from the vehicle used in their preparation.

Pharmaceutical precautions Dilutions of tuberculins do not retain their potency for long periods and should therefore be ordered only as required and used before the expiry date shown on the package. Use contents of ampoule at once or within one hour provided adequate aseptic precautions are taken. Any unused solution should be disposed of by flushing away to waste with copious water. Care should be taken to avoid contamination of the ampoule contents.

Legal category POM.

Package quantities *Undiluted*: – ampoules of 1 ml in packs of 5.

Dilutions: – ampoules of 1 ml in packs of 5.

Control solution: – ampoules of 1 ml in packs of 5 for Mantoux Test.

Tuberculin undiluted and Tuberculin 100 units per ml (dilution 1 in 1,000), 5 × 1 ml ampoule packs are available to United Kingdom Health Authorities and hospitals through Department of Health & Social Security Contract.

Further information Nil.

Product licence numbers

Tuberculin PPD BP undiluted 100,000 units per ml
0039/5975R for Heaf Multiple Puncture Test

Tuberculin PPD BP dilutions for Mantoux Test

10 units per ml	1/10,000 dilution	0039/5976R
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100 units per ml	1/1,000 dilution	0039/5977R
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1,000 units per ml	1/100 dilution	0039/5978R
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Control Solution for Mantoux Test		0039/5984R
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*Trade Mark

FAIR Laboratories Limited
Squibb House
141–149 Staines Road
Hounslow
Middlesex TW3 3JA



ECOSTATIN* CREAM, LOTION, POWDER, SPRAY POWDER, AND SPRAY SOLUTION

Presentation Cream: White cream containing 1% w/w econazole nitrate.

Lotion: Milky white homogeneous lotion containing 1% w/w econazole nitrate.

Powder and spray powder: White powder containing 1% w/w econazole nitrate in a talc base.

Spray solution: Alcoholic solution containing 1% w/w econazole nitrate.

Uses Actions: Econazole nitrate is a broad spectrum antifungal agent, active against dermatophytes (*Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum* and *Malassezia furfur*); pathogenic yeasts; *Candida albicans* and other *Candida* species. Also active against some Gram-positive bacteria, e.g. staphylococci and streptococci.

Indications All fungal skin infections due to dermatophytes (e.g. *Trichophyton* species), yeasts (e.g. *Candida* species), moulds and other fungi. These include ringworm (tinea) infections, athlete's foot, paronychia, pityriasis versicolor, erythrasma, intertrigo, fungal nappy rash, candidal vulvitis and candidal balanitis.

Dosage and administration Cream: To be massaged gently into the affected and surrounding skin area morning and evening. The cream is particularly suitable for moist or weeping lesions.

Lotion: To be applied twice daily to the affected and surrounding skin area. In the treatment of fungal infections of the nail, apply once daily with an occlusive dressing.

Powder and spray powder: To be applied to the affected area twice daily. The powder is particularly suitable for use in skin folds, e.g. inguinal and interdigital.

Spray solution: To be applied twice daily. See precautions.

All preparations are suitable for topical application to both adults and children.

Clinical improvement usually occurs promptly; however, complete disappearance of the symptoms of the disease may require prolonged treatment. Therapy should continue for several days following both clinical and mycological cure in order to prevent relapse.

Contra-indications, warnings, etc

Contra-indications: None known.

Precautions: Ecostatín cream, lotion, powder, spray powder or spray solution should not be used in or near the eyes. Ecostatín spray solution should not be used on mucous membranes. Care should be taken in the presence of eczematous dermatitis.

Side-effects: Ecostatín is well tolerated. Side-effects are

limited to occasional local irritation manifested by erythema, burning or stinging sensation, and pruritus.

Pharmaceutical precautions *Storage:* Cream, lotion, powder: Store at room temperature.

Spray powder, spray solution: Store in a cool place.

Legal category P.

Package quantities *Ecostatín cream:* Tubes of 30 g and 15 g.

Ecostatín lotion: 30 ml.

Ecostatín powder: 30 g.

Ecostatín spray powder: 200 g.

Ecostatín spray solution: 150 g.

Further information Nil.

Product licence numbers

Ecostatín Cream 0085/0014

Ecostatín Lotion 0085/0021

Ecostatín Powder 0085/0023

Ecostatín Spray Powder 0085/0020

Ecostatín Spray Solution 0085/0022

ECOSTATIN* PESSARIES AND TWIN PACK

Presentation Pessaries: White, opaque, oval pessaries each containing 150 mg econazole nitrate in an hydro-genated vegetable oil base.

Twin pack: Three Ecostatín pessaries with applicator plus 15 g Ecostatín cream (containing 1% w/w econazole nitrate).

Uses Actions: Econazole nitrate has a broad spectrum of antifungal activity. It is highly active against *Candida albicans* and other *Candida* species and is effective in controlling infections of the vagina and vulva caused by such organisms (thrush).

Indications: Vulvovaginal candidosis. In addition to vaginal treatment the Twin Pack contains cream for topical application to the anogenital area.

Dosage and administration Pessaries: One pessary to be inserted at bedtime for three consecutive nights. Administration should be continued even if menstruation occurs, and despite the disappearance of signs and symptoms of the infection.

The pessary should be inserted high into the vagina while the patient is supine.

Cream: The cream is applied twice daily, in the morning and evening, to the anogenital area.

Note: To prevent re-infection with *Candida*, the male consort should be treated concurrently with Ecostatín cream, applied twice daily to the external genital area during the treatment period.

Although a three day course of therapy usually suffices, it may be necessary to institute a second course of therapy.

Contra-indications, warnings, etc

Contra-indications: None known.

Precautions: Ecostatín pessaries are effective in the candidal vaginitis associated with pregnancy. However, as with other agents, Ecostatín should not be used during the first trimester of pregnancy unless the physician deems its use essential for the welfare of the patient. In pregnancy, extra care should be taken in using an applicator to prevent the possibility of mechanical trauma. Avoid contact between contraceptive diaphragms and this product, since the rubber may be damaged by the preparation.

Side-effects: Patients may rarely complain of discomfort; this is usually transitory and disappears with continued treatment. Seldom is it necessary to discontinue econazole pessary treatment.

Ecostatín cream is well tolerated. Side-effects are limited to occasional local irritation manifested by erythema, burning or stinging sensation, and pruritus.

Pharmaceutical precautions *Storage:* Store at room temperature.

Legal category Cream P.
Pessaries POM.

Package quantities *Pessaries:* Pack of three pessaries with applicator.

Twin pack: Three pessaries with applicator plus 15 g cream.

Further information Nil.

Product licence numbers

Ecostatín Pessaries 0085/0013

Ecostatín Cream 0085/0014

HALCICOMB* CREAM

Presentation Pale yellow in a vanishing cream base, containing in each gram the following:

Halcinonide	0.1%
Neomycin (as sulphate)	0.25%
Nystatin	100,000 units

Uses *Actions:* Halcinonide is a potent corticosteroid with rapid anti-inflammatory, anti-pruritic and anti-allergic actions.

Neomycin provides comprehensive antibacterial therapy against a wide range of Gram-negative and Gram-positive bacteria, including those responsible for most bacterial skin infections.

Nystatin is an anti-fungal antibiotic, active against a wide range of yeasts and yeast-like fungi, including *Candida albicans*.

Indications: The topical treatment of superficial bacterial infections, cutaneous candidosis and dermatological conditions known to respond to topical steroid therapy when threatened or complicated by bacterial or candidal superinfection. These include: atopic eczema, contact eczema, follicular eczema, infantile eczema, otitis externa, anogenital pruritus (pruritus ani et vulvae), nummular eczema, post-traumatic infective eczema, seborrhoeic or flexural eczema, neurodermatitis, psoriasis.

Dosage and administration *Adults and children:* Apply to the affected areas two to three times daily.

Contra-indications, warnings, etc *Contra-indications:* In tuberculous and most viral lesions of the skin, particularly herpes simplex, vaccinia and varicella. Also in fungal lesions not susceptible to nystatin. It is not intended for ophthalmic use, nor should it be applied to the external auditory canal of patients with perforated eardrums.

Precautions: Since the use of occlusive dressings may increase the risk of sensitivity, such dressings should be avoided. In infants long-term continuous topical steroid therapy should be avoided. Adrenal suppression may occur, even without occlusion.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to humans has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

Side-effects: Halcinonide and nystatin are well tolerated and local irritation is not common. Sensitivity reactions to neomycin may occur.

Pharmaceutical precautions *Storage:* Store at room temperature; avoid freezing.

Dilution: Not recommended, as this would reduce the concentration of the antibiotics to below therapeutic levels.

Consult manufacturers for advice if dilution required.

Legal category POM.

Package quantities Tubes of 25 g.

Further information Nil.

Product licence number 0085/0009.

MULTILIND* OINTMENT

Presentation Pale yellow ointment containing 100,000 iu nystatin per gram in an emollient base thickened with 5% w/w zinc oxide.

Uses *Actions:* Nystatin is an antifungal antibiotic active against a wide range of yeasts and yeast-like fungi, including *Candida albicans*.

Indications: For the treatment of cutaneous and mucocutaneous mycoses, especially those caused by *C. albicans*. Multilind ointment is particularly indicated for the treatment of napkin rash where super-infection with *C. albicans* has occurred.

Dosage and administration To be applied liberally to the affected area two to four times daily.

Contra-indications, warnings, etc

Contra-indications: There are no known contra-indications or special precautions for topical application of nystatin.

Side-effects: There have been no substantiated reports of sensitivity associated with the topical use of nystatin.

Pharmaceutical precautions *Storage:* At room temperature. Avoid freezing.

Dilution: Nystatin products should not be diluted as this may reduce therapeutic efficacy.

Legal category POM.

Package quantities Tubes of 30 g and 100 g.

Further information Nil.

Product licence number 0085/0015.

*Trade Mark

Farmitalia Carlo Erba Limited

Kingmaker House,
Station Road, New Barnet,
Hertfordshire EN5 1NU



ADRIAMYCIN®

Presentation Sterile, pyrogen-free, orange-red, freeze-dried powder in vials of 10 mg and 50 mg each containing doxorubicin hydrochloride and lactose.

Uses Antimitotic and cytotoxic. Adriamycin has been used successfully to produce regression in a wide range of neoplastic conditions including acute leukaemias, lymphomas, soft-tissue and osteogenic sarcomas, paediatric malignancies and adult solid tumours, in particular breast and lung carcinomas.

Adriamycin is frequently used in combination chemotherapy regimens involving other cytotoxic drugs.

Dosage and administration For reconstitution the contents of the 10 mg vial may be dissolved in 5 ml Water for Injections or Sodium Chloride Injection and those of the 50 mg vial in 25 ml of the same solvents.

Intravenous administration: This is the most frequently used route of administration. The reconstituted solution is given via the tubing of a freely-running intravenous infusion, taking two to three minutes over the injection. This technique minimises the risk of thrombosis or perivenous extravasation which can lead to severe cellulitis and vesication. Commonly used acceptable solutions are Sodium Chloride Injection, Dextrose Injection 5% or Sodium Chloride and Dextrose Injection.

Dosage is usually calculated on the basis of body surface area. On this basis, 60–75 mg/m² may be given every three weeks when Adriamycin is used alone. If it is used in combination with other antitumour agents having overlapping toxicity, the dosage of Adriamycin may need to be reduced to 30–40 mg/m² every three weeks. If dosage is to be calculated on the basis of body weight, 1.2–2.4 mg/kg should be given as a single dose every three weeks.

It has been shown that giving Adriamycin as a single dose every three weeks greatly reduces the distressing toxic effect, mucositis; however, there are still some who believe that dividing the dose over three successive days (0.4–0.8 mg/kg or 20–25 mg/m² on each day) gives greater effectiveness even though at the cost of higher toxicity.

Dosage may need to be reduced for patients who have had prior treatment with other cytotoxics and for the elderly.

Intra-arterial administration: More recently, intra-arterial injection has been used in attempts to produce intense local activity while keeping the total dose low and therefore reducing general toxicity. It should be emphasised that this technique is potentially extremely hazardous and can lead to widespread necrosis of the perfused tissues unless due precautions are taken. Intra-arterial injection should only be attempted by those fully conversant with the published literature on the method.

Intravesicular administration: Adriamycin is being increasingly used by intravesicular administration for the

treatment of transitional cell carcinoma, papillary bladder tumours and carcinoma in situ. It should not be employed in this way for the treatment of invasive tumours which have penetrated the bladder wall. It has also been found useful to instil Adriamycin into the bladder at intervals after transurethral resection of a tumour in order to reduce the probability of recurrence. While at present many regimens are in use, making interpretation difficult, the following may be helpful guides:

The concentration of Adriamycin in the bladder should be 50 mg per 50 ml.

To avoid undue dilution with urine, the patient should be instructed not to drink any fluid in the 12 hours prior to instillation. This should limit urine production to approximately 50 ml per hour.

Exposure to the drug solution for one hour is generally adequate and the patient should be instructed to void at the end of this time.

Contra-indications, warnings, etc Adriamycin is intended for use under the direction of those experienced in cytotoxic therapy.

Dosage should not be repeated in the presence of bone-marrow depression or buccal ulceration. The latter may be preceded by premonitory buccal burning sensations and repetition in the presence of this symptom is not advised. Cardiotoxicity may be manifested in tachycardia and ECG changes, routine ECG monitoring is recommended and caution should be exercised in patients with impaired cardiac function.

A cumulative dose of 550 mg/m² should be exceeded only with extreme caution; above this level the risk of irreversible congestive cardiac failure appears to increase greatly.

Haematological monitoring should be undertaken regularly in both haematological and non-haematological conditions in view of the possibility of bone-marrow depression which may occur around ten days from the time of administration. Alopecia is usual and nausea, vomiting and diarrhoea may occur. The risk of thrombophlebitis at the injection site may be minimised by following the procedure for administration recommended above.

Adriamycin imparts a red colour to the urine, particularly to the first specimen passed after the injection, and patients should be advised that this is no cause for alarm.

In the presence of liver impairment, the dosage of Adriamycin should be reduced, moderate dysfunction (bilirubin 1.2–3 mg/100 ml or BSP retention 9–15%) requires a 50% reduction of the dose while severe impairment (bilirubin > 3 mg/100 ml or BSP retention > 15%) necessitates a dose reduction of 75%.

There is no conclusive information as to whether Adriamycin may adversely affect human fertility, or cause teratogenesis. Experimental data, however, suggest that Adriamycin may harm the foetus. This product should not normally be administered to patients who are pregnant or to mothers who are breast-feeding.

Accidental contact with the skin or eyes should be treated immediately by copious lavage with water or soap and water, or, if available, sodium bicarbonate solution.

Overdosage: Single doses of 250 mg and 500 mg of Adriamycin have proved fatal. Such doses may cause acute myocardial degeneration within 24 hours and severe myelosuppression, the effects of which are greatest between 10 and 15 days after administration. Treatment should aim to support the patient during this period and should utilise such measures as blood transfusions and reverse barrier nursing. Delayed cardiac failure may occur up to six months after the overdose. Patients should be observed carefully and should signs of cardiac failure arise, be treated along conventional lines.

Pharmaceutical precautions Reconstitution occasionally results in the formation of a gelatinous mass which will completely dissolve on further shaking. The resulting solution may be stored for up to 24 hours at room temperature or 48 hours at 4°C without significant deterioration. Prolonged contact with any solution of an alkaline pH should be avoided as it will result in hydrolysis of the drug. Adriamycin should not be mixed with heparin as a precipitate may form and it is not recommended that Adriamycin be mixed with other drugs. Exposure to sunlight can result in degradation.

It is recommended that personnel handling Adriamycin should wear protective gloves.

Legal category POM.

Package quantities 10 mg and 50 mg vials for injection.

Further information Nil.

Product licence number 3433/0025.

CYCLOPHOSPHAMIDE

Presentation White, biconvex, sugar-coated tablets containing cyclophosphamide monohydrate 50 mg.

Cyclophosphamide for injection is a sterile white powder in clear glass vials, with rubber caps and aluminium seals, containing 100 mg, 200 mg, 500 mg or 1,000 mg of cyclophosphamide monohydrate with sodium chloride.

Uses Alkylating, antineoplastic agent. Cyclophosphamide has been used successfully to induce and maintain regressions in a wide range of neoplastic conditions, including leukaemias, lymphomas, soft tissue and osteogenic sarcomas, paediatric malignancies and adult solid tumours; in particular, breast and lung carcinomas.

Cyclophosphamide is frequently used in combination chemotherapy regimens involving other cytotoxic drugs.

Dosage and administration The dosage regimen should be tailored to the individual requirements of the patient, depending on his general condition, concurrent therapy, the type and state of tumour, and the patient's response. Three sample regimens may serve as guides:

<i>Low dose</i>	80 to 240 mg/m ² (2 to 6 mg/kg) as a single dose weekly i.v., or in divided doses orally.
<i>Medium dose</i>	400 to 600 mg/m ² (10 to 15 mg/kg) as a single dose weekly i.v.
<i>High dose</i>	800 to 1,600 mg/m ² (20 to 40 mg/kg) as a single dose i.v. at 10–20 day intervals.

Higher doses should be used only at the discretion of a physician experienced in cytotoxic chemotherapy.

It is recommended that the calculated dose of cyclophosphamide be reduced when it is given in combination with other anti-neoplastic agents or radiotherapy, and in patients with bone marrow depression.

Cyclophosphamide tablets should be swallowed whole, preferably on an empty stomach, but if gastric irritation is severe, they may be taken with meals.

Cyclophosphamide injection should be reconstituted with Water for Injections, 5 ml for each 100 mg of cyclophosphamide. After reconstitution the solution will remain stable at room temperature for 2–3 hours. It should be given by slow intravenous injection over a period of 2–3 minutes or into the tubing of a freely running intravenous infusion over a period of 2–3 minutes.

Contra-indications, warnings, etc Cyclophosphamide should be used only under the direction of physicians experienced in cytotoxic or immunosuppressant therapy.

Contra-indications: Hypersensitivity and haemorrhagic cystitis.

Warnings: Cyclophosphamide should be withheld in the presence of severe bone marrow depression and reduced doses should be used in the presence of lesser degrees of bone marrow depression. Single doses will produce a leucopenia which may be severe but usually returns to normal within 21 days. Regular blood counts should be performed in patients receiving cyclophosphamide. This product should not normally be administered to patients who are pregnant or to mothers who are breast-feeding. It should not normally be given to patients with severe infections and should be withdrawn if such infections become life-threatening.

Cyclophosphamide should be used with caution in debilitated patients and those with renal and/or hepatic failure. In all such cases, dosage should be reduced. Oral hypoglycaemic agents may be potentiated by cyclophosphamide.

Amenorrhoea and azoospermia often occur during treatment with cyclophosphamide but in most cases are reversible. Alkylating agents, including cyclophosphamide, have been shown to possess mutagenic, teratogenic and carcinogenic potential. Pregnancy should therefore be avoided during cyclophosphamide therapy and for three months thereafter.

Cyclophosphamide is excreted mainly in the urine largely in the form of active metabolites which may give rise to a chemical cystitis which may be haemorrhagic. Because of this, a high fluid intake should be maintained with frequent emptying of the bladder. However, cyclophosphamide may give rise to fluid retention with subsequent water intoxication. Should this arise, a diuretic may be given. Cyclophosphamide may cause myocardial toxicity, especially at high dosage.

Cyclophosphamide may induce permanent sterility in children.

Side-effects: In addition to those noted above, the following may accompany cyclophosphamide therapy: hair loss, which may be total, although generally reversible; mucosal ulceration, anorexia, nausea and vomiting, pigmentation typically affecting the palms and nails of the hands and the soles of the feet, and interstitial pulmonary fibrosis.

Overdosage: If the drug has been taken in the form of tablets, early gastric lavage may reduce the amount of

drug absorbed. In all cases, forced alkaline diuresis with copious fluid intake, using diuretics if necessary, should be employed. Patients should be observed for signs of water overload and monitored for electrolyte disturbances. Profound myelo-suppression should be anticipated and may require such measures as blood transfusions, antibiotic therapy and reverse barrier nursing. Bleeding, possibly severe, may occur from the bladder and gastro-intestinal tract.

Pharmaceutical precautions *Tablets:* Store in a cool dry place and protect from light.

Injection: Store in a cool place and protect from light.

If heated above 32°C, cyclophosphamide may decompose to a damp-looking gel. It is, therefore, recommended that this product is never stored where heat build-up may occur such as near radiators, etc.

Legal category POM.

Package quantities

Tablets: Containers of 100 and 250 tablets of 50 mg.

Injection:

Vials of 100 mg in packs of 6 and 24.

Vials of 200 mg in packs of 6 and 24.

Vials of 500 mg in packs of 6.

Vials of 1,000 mg in packs of 6.

Each vial contains dry powder for reconstitution.

Further information Nil.

Product licence numbers

Cyclophosphamide Tablets 50 mg	3433/0036
Cyclophosphamide Injection 100 mg	3433/0037
Cyclophosphamide Injection 200 mg	3433/0038
Cyclophosphamide Injection 500 mg	3433/0039
Cyclophosphamide Injection 1,000 mg	3433/0040

EUHYPNOS®

Presentation Green soft gelatin capsules, marked '10' on white, containing temazepam 10 mg in solution.

Uses Euhypnos is indicated for the short-term treatment of sleep disturbances.

It is particularly suitable for patients with transient sleep disorders in whom the re-establishment of normal sleep patterns is anticipated following the resolution of precipitating factors.

Euhypnos is also indicated for pre-medication for minor surgical and investigatory procedures, especially in the case of out-patients.

Dosage and administration *Insomnia - Adults:* One or three capsules by mouth on retiring. A dose of two capsules will be found satisfactory for most patients. This may be increased to four or six capsules in patients who do not respond to the lower dose.

Elderly: Half the normal adult dose may be sufficient for a therapeutic response in the elderly (see Warnings and Adverse Effects).

Children: Not recommended.

Pre-medication: 2 to 4 capsules from half an hour to one hour prior to surgery or investigatory procedures.

Contra-indications, warnings, etc *Contra-indications:* Known sensitivity to benzodiazepines. Acute pulmonary insufficiency.

Warnings: Although hangover effect is uncommon, patients should be warned against driving or operating

dangerous machinery if so affected. Doses of 30 mg and above are more likely to cause hangover effects to persist into the following day than lower doses, particularly in patients unused to hypnotics and in the elderly. As with all compounds which have an effect on the CNS, patients should be advised not to consume alcohol whilst taking Euhypnos.

Use in pregnancy: There is no evidence as to drug safety in human pregnancy, nor is there evidence from animal work that the drug is free from hazard. Do not use during pregnancy, especially during the first and last trimesters unless there are compelling reasons.

Adverse effects: Common adverse effects of benzodiazepines include drowsiness, sedation, blurring of vision, unsteadiness and ataxia. These symptoms are liable to be potentiated by alcohol. The elderly are more liable to experience such effects. (See also under Dependence Potential and Withdrawal Symptoms).

Abnormal psychological reactions to benzodiazepines have been reported. Rare behavioural adverse effects include paradoxical aggressive outbursts, excitement, confusion and the uncovering of depression with suicidal tendencies.

Other rare adverse effects, including hypotension, gastro-intestinal and visual disturbances, skin rashes, urinary retention, headache, vertigo, changes in libido, blood dyscrasias and jaundice have been reported.

Precautions: Give with caution to patients with chronic pulmonary insufficiency, or renal or hepatic dysfunction. Avoid benzodiazepines if possible during lactation.

The concurrent use of other CNS depressant drugs should be avoided.

Dependence potential and withdrawal symptoms: In general, the dependence potential of benzodiazepines is low, but this increases when high dosage is used, especially when given over long periods. This is particularly so in patients with a history of alcoholism, drug abuse or in patients with marked personality disorders. Regular monitoring of treatment in such patients is essential and routine repeat prescriptions should be avoided.

Treatment in all patients should be withdrawn gradually as symptoms such as depression, nervousness, rebound insomnia, irritability, sweating and diarrhoea have been reported following abrupt cessation of treatment with benzodiazepines in patients receiving even normal therapeutic doses for short periods of time.

Abrupt withdrawal following excessive dosage may produce confusion, toxic psychosis, convulsions or a condition resembling delirium tremens.

Overdosage: Doses substantially in excess of those recommended, have been taken without ill effect. As with other benzodiazepines, treatment of overdosage should be symptomatic with general supportive measures as required. Although temazepam in this formulation is rapidly absorbed, gastric lavage may be useful if performed shortly after ingestion.

Pharmaceutical precautions Dispense in glass or plastic containers.

Legal category POM.

Package quantities Containers of 50, 100, 500 or 1,000 capsules.

Further information The formulation of temazepam as a solution in soft gelatin capsules ensures rapid and complete absorption which, with its short half-life and

lack of active metabolites, results in prompt induction of sleep and a low incidence of hangover effects.

Temazepam is a short-acting benzodiazepine. As accumulation tends not to occur, patients are less likely to experience excessive drowsiness or impairment in the performance of skilled tasks. The short half-life of this drug may offer advantages in the treatment of the elderly, in patients with impaired renal or liver function, and in situations where day-time alertness is desirable.

Product licence number 3433/0024.

EUHYPNOS[®] FORTE

Presentation Green soft gelatin capsules, marked '20' in white, containing temazepam 20 mg in solution.

Uses Euhypnos Forte is indicated for the short-term treatment of sleep disturbances, particularly where lower doses of temazepam are not sufficient.

Euhypnos Forte is also indicated for pre-medication in minor surgical or investigatory procedures, especially in the case of out-patients.

Dosage and administration *Insomnia – Adults:* For those patients resistant to a low hypnotic dosage, two or three capsules before retiring.

Elderly: Half the normal adult dose may be sufficient for a therapeutic response in the elderly (see Warnings and Adverse Effects).

Children: Not recommended.

Pre-medication: 1 to 2 capsules from half to one hour prior to surgical or investigatory procedures.

Contra-indications, warnings, etc *Contra-indications:* Known sensitivity to benzodiazepines. Acute pulmonary insufficiency.

Warnings: Although hangover effect is uncommon, patients should be warned against driving or operating dangerous machinery if so affected.

Doses of 30 mg and above of temazepam are more likely to cause hangover effects to persist into the following day than lower doses, particularly in patients unused to hypnotics and in the elderly.

As with all compounds which have an effect on the CNS, patients should be advised not to consume alcohol whilst taking Euhypnos Forte.

Use in pregnancy: There is no evidence as to drug safety in human pregnancy nor is there evidence from animal work that the drug is free from hazard. Do not use during pregnancy especially during the first and last trimesters unless there are compelling reasons.

Adverse effects: Common adverse effects of benzodiazepines include drowsiness, sedation, blurring of vision, unsteadiness and ataxia. These symptoms are liable to be potentiated by alcohol. The elderly are more liable to experience such effects. (See also under Dependence Potential and Withdrawal Symptoms).

Abnormal psychological reactions to benzodiazepines have been reported. Rare behavioural adverse effects include paradoxical aggressive outbursts, excitement, confusion and the uncovering of depression with suicidal tendencies.

Other rare adverse effects, including hypotension, gastro-intestinal and visual disturbances, skin rashes, urinary retention, headache, vertigo, changes in libido, blood dyscrasias and jaundice have been reported.

Precautions: Give with caution to patients with chronic pulmonary insufficiency, or renal or hepatic dysfunction.

Avoid benzodiazepines if possible during lactation. The concurrent use of other CNS depressant drugs should be avoided.

Dependence potential and withdrawal symptoms: In general the dependence potential of benzodiazepines is low, but this increases when high dosage is used, especially when given over long periods. This is particularly so in patients with a history of alcoholism, drug abuse or in patients with marked personality disorders. Regular monitoring of treatment in such patients is essential and routine repeat prescriptions should be avoided.

Treatment in all patients should be withdrawn gradually as symptoms such as depression, nervousness, rebound insomnia, irritability, sweating and diarrhoea have been reported following abrupt cessation of treatment with benzodiazepines in patients receiving even normal therapeutic doses for short periods of time.

Abrupt withdrawal following excessive dosage may produce confusion, toxic psychosis, convulsions or a condition resembling delirium tremens.

Overdosage: Doses substantially in excess of those recommended, have been taken without ill effect. As with other benzodiazepines, treatment of overdosage should be symptomatic with general supportive measures as required. Although temazepam in this formulation is rapidly absorbed, gastric lavage may be useful if performed shortly after ingestion.

Pharmaceutical precautions Dispense in glass or plastic containers.

Legal category POM.

Package quantities Containers of 50, 250 or 500 capsules.

Further information The formulation of temazepam as a solution in soft gelatin capsules ensures rapid and complete absorption which, with its short half-life and lack of active metabolites, results in prompt induction of sleep and a low incidence of hangover effects.

Temazepam is a short-acting benzodiazepine. As accumulation tends not to occur, patients are less likely to experience excessive drowsiness or impairment in the performance of skilled tasks. The short half-life of this drug may offer advantages in the treatment of the elderly, in patients with impaired renal or liver function and in situations where day-time alertness is desirable.

Product licence number 3433/0041.

EUHYPNOS[®] ELIXIR

Presentation A clear, green, lemon-mint flavoured elixir containing 10 mg temazepam per 5 ml.

Uses Euhypnos Elixir is indicated for the short-term treatment of sleep disturbances particularly where a liquid formulation is preferable.

Euhypnos Elixir is particularly suitable for patients with transient sleep disorders in whom the re-establishment of normal sleep patterns is expected following the resolution of precipitating factors.

Euhypnos Elixir is also indicated for pre-medication for minor surgery and investigatory procedures, especially in out-patients.

Dosage and administration

Insomnia: Adults: Each 5 ml spoonful of Euhypnos Elixir is equivalent to 10 mg temazepam.

The usual dose is 5 to 15 ml orally on retiring; a dose of 10 ml will be found satisfactory for most patients and is equivalent to 20 mg temazepam in capsule form.

This may be increased to 20 or 30 ml (40–60 mg emazepam) in patients who do not respond to the lower dose.

Elderly: Half the normal dose may be sufficient for a herapeutic response in the elderly (see Warnings and dverse Effects).

Children: Not recommended.

Pre-medication: 10 to 20 ml from half an hour to one our prior to surgery or investigatory procedures.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to benzodiazepines. Acute pulmonary insufficiency.

Warnings: Although hangover effect is uncommon, atients should be warned against driving or operating langerous machinery if so affected.

Doses of 15 ml and above are more likely to cause angover effects to persist into the following day than ver doses, particularly in patients unused to hypnotics nd in the elderly. As with all compounds which have an ffect on the CNS, patients should be advised not to onsume alcohol whilst taking Euhypnos Elixir.

Use in pregnancy: There is no evidence as to drug safety n human pregnancy, nor is there evidence from animal ork that the drug is free from hazard. Do not use during regnancy, especially during the first and last trimesters, nless there are compelling reasons.

Adverse effects: Common adverse effects of benzodiazepines include drowsiness, sedation, blurring of vision, nsteadiness and ataxia. These symptoms are liable to e potentiated by alcohol. The elderly are more liable to xperience such effects. (See also under Dependence 'ontential and Withdrawal Symptoms). Abnormal psy- chological reactions to benzodiazepines have been ported. Rare behavioural adverse effects include aradoxical aggressive outbursts, excitement, confusion nd the uncovering of depression with suicidal endencies.

Other rare adverse effects, including hypotension, astro-intestinal and visual disturbances, skin rashes, rinary retention, headache, vertigo, changes in libido, lood dyscrasias and jaundice have been reported.

Precautions: Give with caution to patients with chronic ulmonary insufficiency, or renal or hepatic dysfunction. void benzodiazepines if possible during lactation. The oncurrent use of other CNS depressant drugs should be voided.

Dependence potential and withdrawal symptoms: In eneral, the dependence potential of benzodiazepines is w, but this increases at high dosage, especially over ng periods. This is particularly so in patients with a istory of alcoholism or drug abuse or in patients with arked personality disorders. Regular monitoring of eatment in such patients is essential and routine repeat rescriptions should be avoided.

Treatment in all patients should be withdrawn gradu- ally as symptoms such as depression, nervousness, ound insomnia, irritability, sweating and diarrhoea ave been reported following abrupt cessation of eatment with benzodiazepines in patients receiving ven normal therapeutic doses for short periods of time.

Abrupt withdrawal following excessive dosage may roduce confusion, toxic psychosis, convulsions or a ondition resembling delirium tremens.

Overdosage: Doses of temazepam substantially in excess of those recommended have been taken without ill effect. As with other benzodiazepines, treatment of overdosage should be symptomatic with general sup- portive measures as required. Although temazepam in this formulation is rapidly absorbed, gastric lavage may be useful if performed shortly after ingestion.

Pharmaceutical precautions Store below 25°C and protect from direct light.

Legal category POM.

Package quantities Bottles of 300 ml and 2 litres.

Further information The formulation of temazepam as an elixir ensures rapid and complete absorption which, with its short half-life and lack of active metabolites, results in prompt induction of sleep and a low incidence of hangover effects.

Temazepam is a short-acting benzodiazepine. As accumulation tends not to occur, patients are less likely to experience excessive drowsiness or impairment in the performance of skilled tasks. The short half-life of this drug may offer advantages in the treatment of the elderly, in patients with impaired renal or liver function, and in situations where daytime alertness is desirable.

Product licence number 3433/0054.

FARLUTAL®

Presentation White, sterile suspension for i.m. injection, which settles on standing and readily disperses on shaking, containing 500 mg of medroxyprogesterone acetate in 2.5 ml or 1,000 mg in 5.0 ml.

Uses Palliative treatment of hormone-dependent malignancies. Farlital has been successfully used to produce regressions in breast, endometrial, prostatic and renal cell carcinoma. High dose Farlital therapy has proved especially useful for breast carcinoma and in achieving subjective improvements in terminally ill patients, notably pain relief and improved performance status.

Farlital may be used in combination with cytotoxic drugs.

Dosage and administration Suggested dosage schemes are as follows:

Breast carcinoma:

Initial dose 500–1,000 mg/day i.m. for 4 weeks.
Maintenance 500 mg i.m. twice a week.

Endometrial carcinoma:

Initial dose 500 mg i.m. twice weekly for 3 months.
Maintenance 500 mg i.m. weekly.

Renal adenocarcinoma:

Initial dose 500 mg i.m. on alternate days for 30 days.
Maintenance 500 mg i.m. twice weekly until 60th day then 250 mg i.m. weekly.

Prostatic carcinoma:

Initial dose 500 mg i.m. twice weekly.
Maintenance 500 mg i.m. weekly.

Administration should be by deep injection into alternate gluteal muscles using a long wide-bore needle such as 21 G × 1½ (8/10 40 mm). Narrow-bore or short needles must not be used.

Contra-indications, warnings, etc

Contra-indications: Thrombophlebitis, thrombo-embolic disorders, severe hepatic insufficiency and hypercalcaemia as may occur in patients with osseous metastases; also, suspected or early breast carcinoma, missed abortion, metrorrhagia, pregnancy and known hypersensitivity to hydroxybenzoates (excipients) and/or medroxyprogesterone acetate.

Warnings: Farlutal should be used under the direction of those experienced in cancer chemotherapy.

Since medroxyprogesterone acetate appears to enhance blood clotting potential, treatment should be discontinued upon the appearance of thrombo-embolic episodes, migraine or associated ocular problems such as sudden partial or total loss of vision, diplopia or vascular lesions of the retina.

In the event of vaginal bleeding occurring, an accurate diagnosis should be made. If a histological examination is indicated, the laboratory should be informed that the patient has been receiving a progestogen.

Precautions: Animal studies have shown that medroxyprogesterone acetate possesses adrenocorticoid activity and this effect has also been observed in humans. Patients treated with high doses continuously over long periods should be carefully observed for signs normally associated with adrenocorticoid therapy, such as hypertension, sodium retention, oedema, etc, and care is needed in treating patients with diabetes and/or arterial hypertension.

Farlutal may raise plasma calcium levels; some cases of hypercalcaemia have been reported in the treatment of breast carcinoma.

Administration of progesterone during the first months of pregnancy may possibly be associated with the occurrence of congenital cardiac malformations in the neonate. In addition, instances of masculinisation of female foetuses have been reported following high dose therapy during pregnancy. For these reasons, Farlutal is contra-indicated during pregnancy.

It should be noted that long term administration of medroxyprogesterone acetate to beagle dogs has resulted in the development of mammary nodules which were occasionally found to be malignant. The relevance of these findings to humans has, however, not been established.

Side effects: As is generally found after intramuscular administration of large volumes of suspension, this preparation may cause local lesions at the injection site, such as sterile abscesses or inflammatory infiltrates. The suspension should, therefore, be well shaken before use and injected deeply into healthy gluteal muscle.

In common with other progestogens, Farlutal may cause mastodynia, galactorrhoea, vaginal bleeding, changes in menstrual flow, amenorrhoea, cervical erosions and modifications of cervical secretions. Farlutal also exerts a corticoid-like effect which may lead to facies lunaris, Cushingoid syndrome and weight changes; and an adrenergic-like action which may result in fine hand tremors, sweating and cramps in the calves at night. Cholestatic jaundice has occasionally been reported.

Pharmaceutical precautions Farlutal should be well shaken before use and should not be mixed with other agents. The vials are for single dose administration only. Farlutal should be stored between 15°–30°C and should not be frozen.

Package quantities 500 mg and 1,000 mg vials supplied in individual cartons.

Legal category POM.

Further information Analysis of the various dosage schedules so far employed indicates that higher response rates may be obtained by rapid attainment and maintenance of high plasma levels. The intramuscular injection of Farlutal as a 20% suspension of medroxyprogesterone acetate, enables these levels to be achieved while minimising the local side effects associated with high dose therapy using formulations of lower concentrations.

Product licence number 3433/0045.

FLOSINT* ▼

Presentation White, uncoated, biconvex, scored tablets containing 200 mg indoprofen.

Uses Flosint is an analgesic anti-inflammatory indicated for the treatment of the arthritides: rheumatoid arthritis, osteo-arthritis, ankylosing spondylitis and others. Its analgesic activity may be utilised in a variety of disorders characterised by mild to moderate pain such as lower limb ischaemia, episiotomy and other surgical and dental procedures, and malignancy.

Dosage and administration *Adults:* The recommended initial dosage of indoprofen is 200–600 mg daily in two to three divided doses. In some severe conditions it can be advantageous to increase the daily dosage to 800 mg. Maintenance therapy can be accomplished by reducing the dosage to the level which gives satisfactory relief of symptoms for prolonged periods. The tablets should be taken after food to increase tolerability.

Children: Paediatric usage has not been established.

Contra-indications, warnings, etc

Contra-indications: Indoprofen is a propionic acid derivative and a prostaglandin synthetase inhibitor. It should not be given to patients with known sensitivity to this class of compounds or to patients with active peptic ulceration.

Warnings: Bronchospasm may be precipitated in patients suffering from or with a previous history of bronchial asthma or allergic disease. Indoprofen is extensively protein-bound, and may displace oral anti-coagulants, sulphonylureas, etc. from binding sites. Dosage alterations may be needed in patients requiring concomitant treatment with these agents.

Dosage reduction may be required in renal or hepatic impairment.

Pregnancy: Animal experiments show no evidence of teratogenicity. However, this class of compounds has been shown to delay parturition in animals. The use of indoprofen during pregnancy should be avoided if possible.

Adverse effects: The most common adverse reaction caused by indoprofen are gastro-intestinal, including dyspepsia and nausea. Haemorrhage can occur rarely as well as exacerbation of latent peptic ulceration. Other effects include mild central nervous system symptoms such as dizziness and headache, and also skin rashes of various types. Decrease in platelet count has been observed rarely and blood dyscrasias may uncommonly occur. Limited data available suggests that abnormal liver function may be further impaired by treatment with indoprofen.

Overdosage: Gastric lavage and general supportive treatment should be carried out. There is no specific antidote.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Containers of 100 tablets.

Further information Nil.

Product licence number 3433/0034.

KELFIZINE* W

Presentation White, uncoated tablets each containing sulfametopyrazine 2 g stamped 'Kelfizine W' on one face, and 'Weekly Dose' on obverse.

Ivory-coloured suspension in syrup base, containing sulfametopyrazine 500 mg in each 5 ml.

Uses The treatment of infections due to sulphonamide sensitive organisms. It has been used in the management of: chronic bronchitis (including prophylaxis); urinary tract infections; ear, nose and throat infections; bacillary dysentery; meningitis.

Dosage and administration

Adults: 2 g once weekly by mouth.

Children: 30 mg/kg once weekly by mouth.

The tablet should be stirred into half-a-tumblerful of water or orange squash.

Contra-indications, warnings, etc

Contra-indications: Not to be taken by persons sensitive to sulphonamides. The use of Kelfizine W is not recommended for infants under one year of age; it is, therefore, also not recommended for use in breast-feeding mothers. Sulfametopyrazine should be used with caution in patients with renal or hepatic dysfunction, dehydration, or blood dyscrasias. Sulphonamides should not be used during the last few weeks of pregnancy unless considered essential by the physician.

Overdosage: Doses up to 8 g have been taken over 36 hours without evidence of ill effects. A high fluid intake should be maintained for seven days and the urine rendered alkaline with Potassium Citrate mixture or Sodium Bicarbonate.

Pharmaceutical precautions The suspension may be diluted with Syrup BP if required.

Legal category POM.

Package quantities

Tablets: Pack of 5, individually foil wrapped.

Suspension: Paediatric single dose 10 ml bottle.

Adult single dose 20 ml bottle.

Further information The long half-life of sulfametopyrazine is due not to a high degree of serum protein binding (which is only 60%) but to a high degree of renal tubular re-absorption coupled with a low rate of hepatic metabolism of the drug. Accordingly, if it is required to accelerate elimination of the drug, this may be accomplished by rendering the urine alkaline (approximately pH 8) by means of Potassium Citrate Mixture BPC or other suitable agent. The sulphonamide will then be retained in the urine in higher concentrations in the form of the alkali metal salt.

Product licence numbers

Tablets 3433/5916

Suspension 3433/0027

KEMICETINE* SUCCINATE KEMICETINE* STERILE SURGICAL POWDER

Presentation

Kemicetine Succinate: Individual glass vials of chloramphenicol sodium succinate for injection containing the equivalent of 1 g of chloramphenicol.

Kemicetine Sterile Surgical Powder: Single glass vials with rubber caps in individual blister packs containing 1 g of sterile, pyrogen-free chloramphenicol.

Uses Kemicetine (chloramphenicol) is a broad-spectrum antibiotic and is active against many gram-positive and gram-negative organisms, spirillae and rickettsia. Kemicetine should not be used for trivial infections due to the possibility of severe blood dyscrasias, which may prove fatal.

Kemicetine succinate is indicated for typhoid, paratyphoid, meningitis caused by *H. influenzae* infections and other serious infections. It is also indicated wherever chloramphenicol is deemed the antibiotic of choice and oral administration is not possible, or higher than usual blood concentrations are required.

Kemicetine sterile surgical powder is applied locally before wound closure in general and especially after orthopaedic surgery, to assist in the prevention of infection.

Dosage and administration

Kemicetine Succinate: In order to ensure rapid attainment of high blood levels, Kemicetine Succinate is best administered by i.v. injection. Where this is not possible, however, intramuscular administration may be used, although it should be borne in mind that absorption may be slow and unpredictable.

The injection should be reconstituted with Water for Injections, Sodium Chloride Injection, or Dextrose Injection 5%. The following dilution table may be useful for the administration of a proportion of the contents of a vial:

Concentration	Solution strength	Volume of diluent to be added	Total volume after dilution
40%	400 mg/ml	1.7 ml	2.5 ml
25%	250 mg/ml	3.2 ml	4.0 ml
20%	200 mg/ml	4.2 ml	5.0 ml
10%	100 mg/ml	9.2 ml	10.0 ml

The dose administered and the concentration used is dependent on the severity of the infection. The recommended standard dosage is as follows:

Adults: The equivalent of 1 g chloramphenicol every 6–8 hours.

Children: The equivalent of 50 mg/kg chloramphenicol, according to body weight, daily in divided doses every 6 hours (this dose should not be exceeded). The patient should be carefully observed for signs of toxicity.

Neonates and premature infants: 25 mg/kg in divided doses.

Certain infections, such as meningitis or septicaemia, may require substantially higher doses.

The 10% solution should be given by intravenous injection over a period of about a minute, or in a larger volume of fluid, by slow intravenous infusion.

Kemicetine succinate has been applied locally in cases of acute peritonitis, perforated appendix and similar

states where doses of 10–20 ml of 10% solution were introduced into the peritoneal cavity during the operation, or during the following days, through drainage tubes. The concurrent administration of i.v. Kemicetine with topical treatment, has been found to be very effective in the treatment of osteomyelitic foci, abscesses, empyema and skin and urinary infections.

Kemicetine Sterile Surgical Powder: At the conclusion of surgery, particularly orthopaedic procedures, 1 g may be sprinkled into the wound before closure.

Contra-indications, warnings, etc Kemicetine is to be administered only under the direction of a medical practitioner. Chloramphenicol may cause severe bone marrow depression which may lead to agranulocytosis, thrombocytopenic purpura or aplastic anaemia. These effects on the haemopoietic system are usually associated with a high dose, prolonged administration, or repeated courses, but they may occur at relatively low doses. Chloramphenicol should not, therefore, be used in the treatment of any infection for which a less toxic antibiotic is available. It is also advisable to perform blood tests in the case of prolonged or repeated administration. Evidence of any detrimental effect on blood elements is an indication to discontinue therapy immediately.

Other adverse reactions which may become apparent after chloramphenicol treatment are: dryness of the mouth, nausea and vomiting, diarrhoea, urticaria, optic neuritis and blurring, or temporary loss of vision. Superinfection by fungi, e.g. *C. albicans* in the gastrointestinal tract, or vagina, may also occur due to the disturbance of normal bacterial flora.

Chloramphenicol has been shown to interact with, and enhance the effects of, coumarin anticoagulants, some hypoglycaemic agents (e.g. tolbutamide) and phenytoin. When given concurrently, a dose reduction of these agents may, therefore, be necessary. Chloramphenicol may also impede the development of immunity and should therefore not be given during active immunisation.

The drug should be used with great caution in patients with impairment of hepatic or renal function. 'The Grey Syndrome' may occur after administration, in patients with immature hepatic metabolic capacity, i.e. infants and neonates, usually in those treated with doses substantially in excess of those recommended.

Pharmaceutical precautions Any Kemicetine succinate solution remaining in the vial after use should be discarded, as chloramphenicol sodium succinate is not bactericidal or bacteriostatic.

Legal category

Kemicetine Succinate	POM.
Kemicetine Sterile Surgical Powder	POM.

Package quantities

Kemicetine Succinate:
Cartons containing 20 individual vials.

Kemicetine Sterile Surgical Powder: Cartons containing 20 vials each individually enclosed in a sterile blister.

Further information Nil.

Product licence numbers

Kemicetine Sterile Surgical Powder	3433/5902
Kemicetine Succinate	3433/5903

LEVIUS*

Presentation Uncoated, controlled-release tablets

each containing aspirin 500 mg microencapsulated with ethylcellulose.

Uses Analgesic, anti-inflammatory and antipyretic. For use as an alternative to Aspirin Tablets BP, particularly in chronic painful conditions such as rheumatoid arthritis, osteoarthritis, and chronic rheumatic conditions where prolonged treatment may be needed. This, however, does not diminish its suitability for the short-term treatment of, for example, feverish colds, influenza, sprains, lumbago and the relief of mild to moderate pain including headache, toothache and dysmenorrhoea.

Dosage and administration *Standard Dose:* One or two tablets every four hours or as prescribed by the physician. Maximum daily dose should generally not exceed 4 g except in the treatment of acute rheumatism for which 4–8 g in divided doses is recommended.

Children (up to the age of 12): One tablet every four hours or as prescribed by the physician. The daily dose should generally not exceed 80 mg/kg.

Contra-indications, warnings, etc

Contra-indications: Active peptic ulceration, haemophilia and hypersensitivity to aspirin or salicylates.

Precautions: Aspirin may prolong labour and contribute to maternal and neonatal bleeding, and is best avoided at term. There is clinical evidence of safety in human pregnancy. Aspirin may enhance the effect of anticoagulants and inhibit the action of uricosurics. It may precipitate bronchospasm or induce attacks of asthma in susceptible subjects.

Warnings and adverse effects: Levius may induce 'aspirin-type' hypersensitivity, asthma or gastrointestinal haemorrhage which may occasionally be severe.

Overdosage: The fatal dose varies, 10–30 g have caused death but much larger doses have been ingested without fatal outcome. The symptoms of overdosage include headache, epigastric pain, dizziness, tinnitus, sweating, nausea, vomiting, confusion and hyperventilation. More serious signs of toxicity include fever, ketosis, respiratory alkalosis and metabolic acidosis. Depression of the CNS may lead to coma, cardiovascular collapse and respiratory failure. Treatment is largely symptomatic and the patient should be hospitalised. Absorption from the G.I. tract may be reduced by emesis, gastric lavage and/or administration of activated charcoal. In severe poisoning, extra-renal measures such as exchange transfusion, peritoneal dialysis, haemodialysis and haemoperfusion are the most effective measures available for the removal of salicylate, while electrolyte imbalance may need constant monitoring and i.v. infusion correction.

Pharmaceutical precautions Store in a cool dry place.

Legal category P.

Package quantities Amber, child-resistant containers of 30 tablets and Securitainers of 500 tablets.

Further information Aspirin is released from the microcapsules by a process of dialysis over a period of about one hour. As this process is steady and progressive, no part of the alimentary tract receives the full irritant effect of all the aspirin contained in the tablet. Moreover, the analgesia resulting from the aspirin is more prolonged than from a conventional tablet.

Product licence number 3433/0018.

MINODIAB*

Presentation Minodiab is available as white, biconvex, scored 8 mm tablets containing 5 mg of glipizide.

Uses Minodiab is an orally active hypoglycaemic sulphonylurea and has been shown to be effective in the treatment of maturity-onset diabetes. In certain patients receiving insulin, the concurrent use of Minodiab allows a reduction in the daily dose of insulin.

Dosage and administration The usual dose range of Minodiab is 2.5–20 mg daily; this may be increased to a daily total of 30 mg at the clinician's discretion although the additional proportion of patients responding to this higher dosage may not be large. The initial dose, in patients previously untreated with oral hypoglycaemic agents is 2.5–5 mg daily. The dose, thereafter, can be adjusted to obtain the optimum effect.

Doses of up to 5 mg may be taken as a single dose with the main meal or in two divided doses with morning and evening meals. Doses of 7.5 mg or more may be taken in three divided doses with meals. The use of multiple divided doses is intended to produce more even control of post-prandial blood glucose peaks throughout the day. The dose must be adjusted according to the patient's response; the daily dose to be increased, or decreased by 2.5 or 5 mg every three to five days until the desired control is achieved.

When Minodiab replaces other oral antidiabetic agents, the recommended starting dose is 5 mg daily in a divided dose. If the dose given is considered adequate but the control is not, a biguanide may be added.

Contra-indications, warnings, etc

Contra-indications: Minodiab is contra-indicated in pregnancy, juvenile diabetes, diabetic ketoacidosis, diabetic coma, severe renal or hepatic insufficiency, infections and febrile conditions, gangrene and in severe trauma and major surgical procedures.

Warnings: Concurrent use of MAOIs, phenylbutazone, β -blockers, sulphonamides, coumarin derivatives or salicylates may enhance the hypoglycaemic effect. Conversely the effect may be diminished in the presence of adrenaline, corticosteroids, oral contraceptives and thiazide diuretics.

Patients should be instructed to take their meals regularly and not to exercise excessively without additional calorie intake. Failure to do so may result in a hypoglycaemic episode. The hypoglycaemia is controlled by giving carbohydrates.

Adverse reactions: Side-effects are not common with Minodiab. Those that do occur are associated with the gastro-intestinal tract, and include nausea, vomiting, anorexia, gastric pain, etc. Skin reactions have been reported, e.g. rash, urticaria, pruritus, etc. Other reactions include headache, dizziness and vertigo.

Overdosage: Gastric lavage should be performed as soon as possible. Hypoglycaemia should be treated as it occurs with appropriate measures including oral or i.v. glucose.

Pharmaceutical precautions None.

Legal category POM.

Package quantities *Minodiab 5 mg Tablets:* Bottles of 100 tablets and tins of 1,000 tablets.

Further information Glipizide can be considered to have a physiological action as its peak effect coincides with post-prandial peak blood-sugar levels. It is rapidly

absorbed from the gastro-intestinal tract; the absorption being practically complete. Peak concentrations are achieved in the blood within 60 minutes and the half-life is approximately three and a half hours. The excretion of glipizide and its metabolites, which are inactive, occurs mainly in the urine. During the first 24 hours, about 80–85% of the ingested drug is excreted in the urine and about 10% in the faeces. These properties make Minodiab particularly suitable for the treatment of maturity-onset diabetes. Taken with a meal, therapeutic effects are seen within 30 minutes and reach a peak at about 60 minutes. The rapid metabolism and excretion makes it unlikely that delayed hypoglycaemic episodes will occur.

Product licence number 3433/0023.

NAXOGIN* 500

Presentation Naxogin 500 is available as white or slightly yellow bi-convex tablets scored on one side and plain on the other. Each tablet contains 500 mg nimorazole.

Uses Naxogin is a trichomonocidal agent. It is indicated for the systemic treatment of trichomonal vaginitis. Sexual partners should also be treated even if they are free of symptoms.

Naxogin is also effective against other protozoa and thus may be used for the treatment of giardiasis, amoebiasis, and acute ulcerative gingivitis.

Dosage and administration *For the treatment of trichomoniasis:* 2 g (4 tablets) to be taken together as a single dose with a main meal. This may be repeated if there is no clinical improvement.

For acute ulcerative gingivitis: 500 mg twice daily for two days.

For giardiasis or amoebiasis: Adults: 500 mg twice daily for five days.

Children (over 10 kg body weight): 500 mg daily for five days.

Children (under 10 kg body weight): 250 mg daily for five days.

Contra-indications, warnings, etc Like all nitroimidazoles, Naxogin 500 is contra-indicated for nursing mothers as it is excreted in breast milk and the effect on the neonate is unknown. Also this group of drugs should not be given in the presence of active CNS disease. Treatment should be discontinued if ataxia or other CNS symptoms appear.

Naxogin 500 should be given with caution during pregnancy although there is no known teratogenicity. Clinical studies have been carried out during pregnancy and no untoward effects of any kind have been associated with this drug. As Naxogin 500 is excreted principally via the kidneys, overt renal insufficiency is also a contra-indication.

Unwanted effects are rare and may comprise transient gastro-intestinal effects such as nausea and vomiting. No blood dyscrasias have been reported. Intolerance to alcohol, similar to that induced by disulfiram, has been observed with the nitroimidazoles but is rarely troublesome with nimorazole.

Overdosage: There is no specific treatment but gastric lavage should be performed as soon as possible. Supportive measures should be instituted as required and a high fluid intake maintained.

Pharmaceutical precautions None.

Legal category P.

Package quantities *Tablets 500 mg:* Bottles of 8 and 100 tablets.

Further information Naxogin 500 is well absorbed after oral administration, achieving blood levels of 32 mcg/ml within two hours and 1.9 mcg/ml at 24 hours. The metabolites of the drug are trichomonacidal and are excreted mainly by the kidney so that there are high urinary concentrations. Concentrations are high in vaginal and salivary secretions.

Naxogin 500 is also recommended for the treatment of acute ulcerative gingivitis in patients hypersensitive to penicillin.

Product licence number 3433/5914.

PHARMIDONE*

Presentation Yellow, scored, tablets each containing:

Codeine Phosphate Ph Eur	10 mg
Diphenhydramine Hydrochloride BP	5 mg
Paracetamol Ph Eur	400 mg
Caffeine Ph Eur	50 mg

Uses Analgesic, in the treatment of headache, migraine, muscular pain and nerve pain.

Dosage and administration *For adults and children over 12 years of age:* One or two tablets orally every four hours, up to a maximum of ten tablets in 24 hours.

Contra-indications, warnings, etc Pharmidone may cause drowsiness, and if affected, the patient should not drive or operate machinery. The effect of alcohol and other sedatives may be potentiated.

Pharmidone should not be given to patients with known liver or renal impairment.

Pharmidone should not be administered to children.

Safety in pregnancy has not been established.

Overdosage: The effects of overdosage are predominantly those of paracetamol; vomiting, gastrointestinal haemorrhage, liver damage, cerebral oedema, and renal tubular necrosis may occur. Gastric lavage should be carried out and haemodialysis may be necessary if renal failure occurs.

Pharmaceutical precautions None.

Legal category P.

Package quantities Boxes of 12 and containers of 100 tablets.

Further information Nil.

Product licence number 3433/0042.

SINTISONE*

Presentation White, scored tablets each containing 6.65 mg of prednisolone teaglate, therapeutically equivalent to prednisolone 5 mg.

Uses Sintisone is a synthetic glucocorticoid and is indicated in all conditions that respond to corticosteroid treatment, such as: rheumatoid arthritis, rheumatic fever, asthma, ulcerative colitis, pemphigus, sarcoidosis, systemic lupus erythematosus, nephrotic syndrome, scleritis, skin conditions and polyarteritis nodosa.

Sintisone may also be used in cancer chemotherapy when a corticosteroid is indicated.

Dosage and administration *Adults:* The average initial dose for adults is 2–4 tablets, orally, twice daily, gradually reducing this to a maintenance dose of 1–3 tablets daily.

Children: Initial dose: 0.6–2 mg/kg body weight, orally in divided doses. Maintenance dose: 1 mg/kg body weight, orally in divided doses.

Treatment may be given in short (6–10 day) courses for the alleviation of the symptoms of acute inflammatory episodes.

Alternate-day corticosteroid therapy is known to reduce the incidence of unwanted effects. Sintisone may be used with advantage in this manner by giving twice the normal daily dose every other day.

Treatment with corticosteroids should not terminate abruptly but should be withdrawn gradually.

Contra-indications, warnings, etc The contra-indications are those common to other corticosteroids: active tuberculosis, peptic ulcer, acute psychosis, Cushing's disease, osteoporosis, hypertension, diabetes mellitus and a tendency to thromboembolic episodes. Corticosteroids are usually also contra-indicated in the presence of acute bacterial or viral infections.

Patients receiving corticosteroids or who have been prescribed them during the preceding two years should be given supplementary corticosteroids for one to two days before surgery, and continued until stress has ceased before tapering off the dose.

Corticosteroids should be used with caution in pregnancy, especially during the first trimester.

Overdosage: There is no specific treatment but gastric lavage should be performed as soon as possible. Supportive measures should be instituted as required.

Pharmaceutical precautions Store in airtight containers and protect from light.

Legal category POM.

Package quantities Bottles of 100 tablets.

Further information Sintisone is a lipid soluble ester of prednisolone which is absorbed intact from the gut more completely than prednisolone. It circulates in the blood as the ester and is slowly metabolised to prednisolone. These properties confer on Sintisone a reduced tendency to the side-effects associated with corticosteroid therapy such as suppression of the pituitary/adrenal axis (Metrapone test), salt and water retention, calcium loss and raised intraocular pressure.

Product licence number 3433/5906.

TETRALYSAL* 300

Presentation Tetralysal 300 is available as white, hard gelatin capsules, size 'O', containing 408 mg of lymecycline BP, equivalent to 300 mg tetracycline base.

Uses Tetralysal 300 is recommended in the treatment of all infections caused by tetracycline-sensitive organisms and may be utilised in all conditions where tetracycline therapy is indicated. In common with other tetracyclines they are also indicated in penicillin-sensitive patients for the treatment of staphylococcal and streptococcal infections. As a prophylactic agent, they may be used in chronic bronchitis.

Dosage and administration Tetralysal 300 – The usual recommended dose is 1 capsule b.d. If higher

A small fraction of the active ingredients in oral contraceptives has been identified in the milk of mothers receiving these drugs. The effects, if any, on the breast-fed child have not been determined. If possible the use of oral contraceptives should be deferred until the infant is weaned.

Reduced efficacy and increased incidence of breakthrough bleeding have been associated with concomitant use of oral contraceptives and rifampicin. A similar association has been suggested with oral contraceptives and barbiturates, phenylbutazone, phenytoin sodium and ampicillin.

Reasons for stopping oral contraceptives immediately: Early manifestations of thrombotic or thromboembolic disorders, thrombophlebitis, cerebrovascular disorders (including haemorrhage), myocardial infarction, pulmonary embolism. Gradual or sudden, partial or complete loss of vision. Proptosis or diplopia. Onset or aggravation of migraine or development of headaches of a new pattern which are recurrent, persistent or severe. Papilloedema or any evidence of retinal vascular lesions. During periods of immobility (e.g. after accidents). Pregnancy. Manifestations of liver tumours.

Precautions: Examination of the pelvic organs, breasts and blood pressure should precede the prescribing of any oral contraceptive, and should be repeated regularly. The following are some of the medical conditions reported to be influenced by the combined pill, and may be affected by Micronor. The physician will have to exercise medical judgement to commence, continue or discontinue therapy as appropriate.

- a) Pre-existing uterine fibromyomata may increase in size.
- b) A decrease in glucose tolerance in a significant number of women.
- c) An increase in blood pressure in a small but significant number of women.
- d) Cholestatic jaundice. Patients with a history of cholestatic jaundice of pregnancy are more likely to develop cholestatic jaundice during oral contraceptive therapy.
- e) Amenorrhoea during and after oral contraceptive therapy. Women with a past history of oligomenorrhoea or secondary amenorrhoea or women with irregular cycles may be more likely to remain anovulatory or to become amenorrhoeic post oral contraceptive therapy.
- f) Depression.
- g) Fluid retention. Conditions which might be influenced by this factor include epilepsy, migraine, asthma, cardiac or renal dysfunction.
- h) Varicose veins.
- i) Multiple sclerosis.
- j) Porphyria.
- k) Tetany.
- l) Wearing of contact lenses.

or any condition that is prone to worsen during pregnancy.

The following laboratory determinations may be altered in patients using oral contraceptives.

Hepatic: Increased BSP retention and other tests.

Coagulation: Increased prothrombin, Factors VII, VIII, IX and X, decreased antithrombin III, increased platelet aggregability.

Endocrine: Increased PBI and butanol extractable protein bound iodine and decreased T³ uptake, increased glucose blood levels.

Other: Increased phospholipids and tri-glycerides, de-

creased serum folate values and disturbance in tryptophan metabolism, decreased pregnanediol excretion, reduced response to metyrapone test.

These tests usually return to pre-therapy values after discontinuing oral contraceptive use. However, the physician should be aware that these altered determinations may mask an underlying disease.

Side-effects: Micronor has been found to be a well tolerated drug. Side-effects are usually self-limiting and of relatively short duration. Amongst the symptoms reported are headaches, nausea, vomiting, breast changes, change in weight, chloasma, break-through bleeding and spotting. Particularly in the early cycles of therapy the menstrual pattern becomes irregular, some cycles being short and others long. It is important that patients should be advised that whilst on Micronor therapy they will experience that variation in cycle length.

Overdosage: Serious ill effects have not been reported following acute ingestion of large doses of oral contraceptives by young children. Overdosage may cause nausea, and withdrawal bleeding may occur in females. An appropriate method of gastric emptying may be used if considered desirable.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Carton containing 3 pushpaks each of 28 tablets – sufficient for 3 cycles.

Further information Nil.

Product licence number 0076/0017.

MONISTAT* CREAM MONISTAT* PESSARIES

Presentation Cream: A white, water-miscible cream containing miconazole nitrate 2% w/w.

Pessaries: White egg-shaped pessaries each containing 100 mg miconazole nitrate and melting at 37°C.

Uses A potent antimycotic agent for the local treatment and rapid symptomatic relief of vulvovaginal moniliasis and balanitis.

Dosage and administration Cream: One applicatorful (approx. 5 g) intravaginally, with additional cream smeared onto other affected areas, once daily, preferably at night, for 14 days.

Pessaries: One pessary should be inserted high into the vagina at night for the same period.

Patients should be instructed not to discontinue treatment upon relief of symptoms, but to complete the prescribed course. The simultaneous treatment of the partner with Monistat Cream is advisable.

Contra-indications, warnings, etc Hypersensitivity to the product.

Side-effects: Isolated cases of vulvo-vaginal burning, itching and irritation have been reported after using the product. If this occurs administration of the product should be discontinued.

Overdosage: Monistat Cream and Pessaries are intended for intravaginal use. If accidental ingestion of large quantities of the product occurs, an appropriate method of gastric emptying may be used if considered desirable.

Pharmaceutical precautions Cream – none known.
Pessaries – store in a cool place.

Legal category POM.

Package quantities Cream: 78 g tube with ORTHO* Plastic Vaginal applicator.

Pessaries: Each pessary is completely sealed in PVC strips with seven pessaries to a strip. Each carton contains two strips of seven pessaries.

Both packs contain full patient instructions.

Further information Monistat Cream or Pessaries are particularly useful in the treatment of those patients with predisposing conditions for monilial vulvovaginitis – pregnancy, diabetes and those taking oral contraceptives or broad-spectrum antibiotics.

Product licence numbers

Cream 0076/0040

Pessaries 0076/0048

ORTHO-CREME* CONTRACEPTIVE CREAM

Presentation Ortho-Creme Contraceptive Cream is a white spermicidal cream which contains nonoxynol-9 2.0%.

Uses Ortho-Creme Contraceptive Cream is a spermicidal cream for the control of conception. A higher degree of protection against pregnancy will be afforded by using another method of contraception in addition to a spermicidal contraceptive.

Dosage and administration The cream should be spread over the surface of the diaphragm which will be in contact with the cervix, and on the rim. The diaphragm must be allowed to remain *in situ* for at least six to eight hours after coitus. A fresh application of cream or other spermicides, e.g. Orthoforms Contraceptive Pessaries, must be made prior to any subsequent act of coitus within this period of time, without removing the diaphragm. (A vaginal applicator should be used for inserting more cream or jelly.)

Contra-indications, warnings, etc Hypersensitivity to the product.

Warning: Where avoidance of pregnancy is essential, the choice of contraceptive should be made in consultation with a doctor or a family planning clinic.

Overdosage: Ortho-Creme Contraceptive Cream is intended for intravaginal use only, and if taken orally by mistake is likely to taste unpleasant. If excess quantities are swallowed, this may give rise to gastric irritation as the product contains a surfactant, and general supportive therapy should be carried out if necessary.

Pharmaceutical precautions None known.

Legal category GSL.

Package quantities Tubes containing 70 g.
ORTHO* Plastic Vaginal Applicator available separately.

Further information Nil.

Product licence number 0076/5008.

ORTHO* DIENOESTROL CREAM

Presentation A white non-staining cream containing 0.01% w/w dienioestrol.

Uses For intravaginal use only. Indicated in the treatment of atrophic vaginitis and kraurosis vulvae in postmenopausal women, and for the treatment of pruritis vulvae and dyspareunia when associated with the atrophic vaginal epithelium.

Dosage and administration Given for short term use only. The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible.

Attempts to discontinue or taper medication should be made at three to six month intervals, following physical examination. The usual dosage range is one or two applicatorfuls per day for one or two weeks, then gradually reduced to one half initial dosage for a similar period. A maintenance dose of one applicatorful, one to three times a week, may be used after restoration of the vaginal mucosa has been achieved. Treated patients with an intact uterus should be monitored closely for signs of endometrial cancer and appropriate diagnostic measures should be taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding. As a general rule it is advisable that patients receiving any form of oestrogen replacement therapy should have a complete physical examination at least once a year.

Contra-indications, warnings, etc Prolonged exposure to unopposed oestrogen may increase the risk of development of endometrial carcinoma, induction of other malignant neoplasms, and the risk of cancer of the breast: long term continuous administration of natural and synthetic oestrogens in certain animal species increases the frequency of carcinomas of the breast, cervix, vagina and liver. There is now evidence that oestrogens increase the risk of carcinoma of the endometrium in humans.

At the present time there is no satisfactory evidence that oestrogens given to post-menopausal women increase the risk of cancer of the breast, although a recent long-term follow up of a single physician has raised this possibility. However, because of animal data there is a need for caution in prescribing oestrogens for women with a strong family history of breast cancer or who have breast nodules, fibrocystic disease, or abnormal mammograms.

Pregnancy is an absolute contra-indication to the use of Dienioestrol cream since it may be harmful to the developing foetus.

Oestrogens should not be used in women with any of the other following conditions: known or suspected cancer of the breast, known or suspected oestrogen-dependent neoplasia, undiagnosed abnormal genital bleeding, active thrombophlebitis or thromboembolic disorders, a past history of thrombophlebitis, thrombosis, or thromboembolic disorders.

Thromboembolic disorders: While an increased rate of thromboembolic and thrombotic disease in postmenopausal users of oestrogens has not been found, this does not rule out the possibility that such an increase may be present or that subgroups of women who have underlying risk factors or who are receiving relatively large doses of oestrogens may have increased risk. Therefore oestrogens should not be used in persons with active thrombophlebitis or thromboembolic disorders, and they should not be used (except in treatment of malignancy) in persons with a history of such disorders. They should be used with caution in patients with cerebral vascular or coronary artery disease and only for those in whom oestrogens are clearly needed.

Gall bladder disease: A recent study has reported a two to three-fold increase in the risk of surgically confirmed gall bladder disease in women receiving post-menopausal oestrogens, similar to the two-fold increase previously noted in users of oral contraceptives.

Hepatic adenoma: Benign hepatic adenomas appear to be associated with the use of oral contraceptives. Although benign, and rare, these may rupture and may cause death through intra-abdominal haemorrhage. Such lesions have not yet been reported in association with other oestrogen or progestogen preparations but should be considered in oestrogen users having abdominal pain and tenderness, abdominal mass, or hypovolemic shock.

Elevated blood pressure: It has been reported that this may occur with the use of oestrogens in the menopause and blood pressure should be monitored with oestrogen use, especially if high doses are used.

Precautions: A complete medical and family history should be taken prior to the initiation of any oestrogen therapy. The pretreatment and periodic physical examinations should include special reference to blood pressure, breasts, abdomen, and pelvic organs, and should include a Papanicolaou smear.

A pathologist should be advised of oestrogen therapy when relevant specimens are submitted.

Certain patients may develop undesirable manifestations of excessive oestrogenic stimulations, such as abnormal or excessive uterine bleeding, mastodynia, etc. Pre-existing uterine fibroids may increase in size during oestrogen use.

Patients with a past history of jaundice during pregnancy have an increased risk of recurrence of jaundice while receiving oestrogen therapy. If jaundice develops in any patient receiving oestrogen, the medication should be discontinued while the cause is investigated.

Oestrogens may aggravate cases of porphyria.

Overdosage: Ortho Dienoestrol Cream is intended for intravaginal use. If accidental ingestion of large quantities of the product occurs, an appropriate method of gastric emptying may be used if considered desirable.

Pharmaceutical precautions Store at room temperature.

Legal category POM.

Package quantities Tubes of 78 g with or without the ORTHO* Plastic Vaginal Applicator.

Further information Nil.

Product licence number 0076/5010.

ORTHOFORMS* CONTRACEPTIVE PESSARIES

Presentation White, opaque pessaries. Each pessary contains nonoxonyl-9 5% w/w.

Uses Whenever the control of conception is desired. Placed in the vagina, the pessary melts and rapidly forms a smooth emollient cream which spreads, mixing intimately with secretions and seminal fluid. Orthoforms Contraceptive Pessaries melt rapidly between 34°C and 37°C – the normal vaginal temperature range.

Orthoforms Contraceptive Pessaries are intended to add reliability to the use of other methods, such as the diaphragm, the sheath, the cervical cap, the IUCD, or

when intercourse is repeated without removing the appliance.

A higher degree of protection against pregnancy will be afforded by using another method of contraception in addition to a spermicidal contraceptive.

Dosage and administration The Orthoforms Contraceptive Pessary should be inserted as high as possible into the vagina approximately 5 minutes before intercourse to permit the pessary to melt. It retains its spermicidal activity for approximately 1 hour. Any subsequent acts of intercourse should not be undertaken before the insertion of an additional pessary.

Contra-indications, warnings, etc Hypersensitivity to the product.

Side-effects: Irritation of the vagina or penis has been reported. In such cases the medication should be discontinued.

Warnings: Where avoidance of pregnancy is essential the choice of contraceptive should be made in consultation with a doctor or a family planning clinic.

Overdosage: Orthoforms Contraceptive Pessaries are intended for intravaginal use only, and if taken orally by mistake are likely to taste unpleasant. If excess quantities are swallowed this may give rise to gastric irritation as the product contains a surfactant, and general supportive therapy should be carried out if necessary.

Pharmaceutical precautions Orthoforms Contraceptive Pessaries should be stored in a cool place.

Legal category GSL.

Package quantities Pack of 15 pessaries.

Further information Nil.

Product licence number 0076/5006.

ORTHO* GYNE-T* INTRAUTERINE COPPER CONTRACEPTIVE DEVICE

Presentation Each device consists of a polyethylene 'T' shaped support with 120 mg pure copper wire (providing a surface area of 200 sq. mm) wound around the vertical section of the 'T'.

The support is impregnated with a radiopaque substance and has a polyethylene suture attached to the base of the 'T'.

Uses Contraception.

Dosage and administration Ortho Gyne-T Intra-uterine Copper Contraceptive Device may be used in any woman of child-bearing age including nulligravidae patients.

One device is inserted by its introducer into the uterus. The device should be removed after three years of use. If continued contraception is required a new device should be inserted. The device should be placed as high as possible within the uterine cavity and the patient should check periodically, particularly after menstruation, to ensure that the threads still protrude from the cervix. She should return to her doctor if she becomes aware that the device has been expelled. When the threads cannot be felt by the patient and cannot be seen by her doctor further investigation is necessary.

Contra-indications, warnings, etc

Contra-indications: The use of the device is contraindicated in the following conditions:

1. Pregnancy or suspicion of pregnancy.
2. Abnormalities of the uterus resulting in distortion of the uterine cavity.
3. Pelvic inflammatory disease or a history of repeated pelvic inflammatory disease.
4. Post-partum endometritis or infected abortion in the past three months.
5. Known or suspected uterine or cervical malignancy including unresolved abnormal cervical smear.
6. Uterine bleeding of unknown aetiology.
7. Cervicitis until infection is controlled.
8. Known allergy to copper.

Warnings: The expulsion, perforation and removal rates may be increased when insertions are made before normal uterine involution occurs post partum.

The device should be removed for the following reasons:

1. Excessive and persistent bleeding or cramping.
2. Perforation of the uterus and location of the device outside the uterine cavity. In this case hospital investigation and surgical removal will be required.
3. Partial downward displacement of the device within the cervical canal.

Pregnancy: If a patient is found to be pregnant with an Ortho Gyne-T *in situ* and the thread is visible it is recommended that in the absence of reasons to the contrary the device be removed as soon as possible. As with other intrauterine devices the possibility exists that should a second trimester abortion occur sepsis may supervene, and hence the desirability of removing the device as early as possible. If the thread is not visible then it is recommended that the device is left *in situ* until the pregnancy goes to term or a decision is made to terminate the pregnancy.

Ectopic pregnancy: A pregnancy that occurs with an IUCD in place is more likely to be ectopic than a pregnancy that occurs without an IUCD in place. Accordingly patients who become pregnant while using an IUCD should be carefully evaluated for the possibility of ectopic pregnancy.

Pelvic infection: An increased risk of pelvic infection has been reported in women with IUCD's *in situ*.

Precautions: Prior to insertion of an IUCD a thorough history and physical examination, including a pelvic examination and Papanicolaou smear, should be performed. Insertion of an IUCD into a uterine cavity measuring less than 6.5 cm by sounding may increase the incidence of expulsion, bleeding, pain and perforation. The patient should be re-examined within three months after insertion and thereafter at yearly intervals to ensure the device is still in place. The patient should be advised to contact her doctor immediately if she misses a menstrual period or has any other reason to think she may be pregnant.

IUCDs should be used with caution in patients with anaemia, menorrhagia or hypermenorrhoea or in patients receiving anticoagulants or having any disorder of coagulation.

Syncope, bradycardia or other neuro-vascular episodes may occur during insertion or removal of IUCDs especially in patients susceptible to these conditions. Patients with known or suspected cardiac abnormalities should receive appropriate antibiotic cover during insertion of the device. No method of contraception is 100% effective. In some cases it may be appropriate to recommend the use of an additional reliable method of contraception at mid-cycle.

Overdosage: Not applicable.

Pharmaceutical precautions If the seal of the sterile pack is broken the device inside should not be used.

Legal category POM. Also available through family planning clinics.

Package quantities Each sterile Ortho Gyne-T Intra-uterine Copper Contraceptive Device unit is supplied in a sealed transparent envelope together with a sterile disposable GYNEPROBE* intrauterine sound for measuring the depth of the uterus. Full fitting instructions and advice for the patient are supplied with each device.

Further information Nil.

Product licence number 0076/0046.

ORTHO-GYNOL* CONTRACEPTIVE JELLY

Presentation Ortho-Gynol Contraceptive Jelly is a water-dispersible spermicidal jelly having a pH of 4.5, which contains *p*-diisobutylphenoxyethoxyethanol 1.0% w/w.

Uses Ortho-Gynol Contraceptive Jelly is a spermicidal jelly for use in conjunction with an occlusive vaginal diaphragm, whenever the control of conception is desirable.

A higher degree of protection against pregnancy will be afforded by using another method of contraception in addition to a spermicidal contraceptive.

Dosage and administration The jelly should be spread over the surface of the diaphragm which will be in contact with the cervix and on the rim. The diaphragm must be allowed to remain *in situ* for at least six to eight hours after coitus. A fresh application of jelly or other spermicides, e.g. Orthoforms Contraceptive Pessaries, must be made prior to any subsequent act of coitus within this period of time, without removing the diaphragm. (A vaginal applicator should be used for inserting more cream or jelly.)

Contra-indications, warnings, etc Hypersensitivity to the product.

Warning: Where avoidance of pregnancy is essential, the choice of contraceptive should be made in consultation with a doctor or family planning clinic.

Overdosage: Ortho-Gynol Contraceptive Jelly is intended for intravaginal use only, and if taken orally by mistake is likely to taste unpleasant. If excess quantities are swallowed this may give rise to gastric irritation as the product contains a surfactant, and general supportive therapy should be carried out if necessary.

Pharmaceutical precautions None known.

Legal category GSL.

Package quantities Tube containing 81 g.

ORTHO* Plastic Vaginal Applicator available separately.

Further information Nil.

Product licence number 0076/5007

ORTHO-NOVIN* 1/50 ORAL CONTRACEPTIVE TABLETS

Presentation White $\frac{1}{4}$ inch diameter, circular tablets with flat faces and bevelled edges, bearing on each face

the engraving 'ORTHO'. Each tablet contains 1 mg Norethisterone BP and 50 mcg Mestranol BP.

Uses Contraception and the recognised indications for such oestrogen/progestogen combinations.

Action: Through the mechanism of gonadotrophin suppression by the oestrogenic and progestational actions of the ingredients. Although the primary mechanism of action is inhibition of ovulation, alterations to the cervical mucus and to the endometrium may also contribute to the efficacy of the product.

Dosage and administration The basic dosage regimen is a 28-day cycle of 1 tablet daily for 21 days followed by seven tablet-free days. For initial therapy the first tablet is taken on the fifth day of the menstrual cycle, counting the first day of bleeding as Day 1. Each subsequent course is started after seven tablet-free days have followed the preceding course. Contraception can be initiated immediately post partum in the non-nursing patient. The possibility of ovulation and conception prior to the initiation of medication should be considered. The patient should be advised that during the first 14 days of the first course an additional reliable non-hormonal form of contraception should be used. If the patient misses more than one tablet she should begin taking tablets again as soon as remembered and an additional reliable method of contraception used until the next withdrawal bleed.

If the patient has vomiting or diarrhoea, absorption of the hormones will be impaired, making it advisable to use an additional reliable method of contraception until her next menstrual period. Should a bleeding fail to occur at the usual time, the possibility of pregnancy should be excluded before starting the next pack.

Contra-indications, warnings, etc

Contra-indications: Existing thrombophlebitis, thromboembolic disorders, cerebral vascular disease, myocardial infarction, or a past history of these conditions. Sickly-cell anaemia. Markedly impaired liver function. Congenital or existing disorders of lipid metabolism. Known or suspected carcinoma of the breast. Known or suspected oestrogen-dependent neoplasia. History during pregnancy of idiopathic jaundice, severe pruritis, shingles or deterioration of otosclerosis. Dubin-Johnson syndrome. Rotor syndrome. Undiagnosed abnormal genital tract bleeding. Known or suspected pregnancy.

Warnings: An increased risk of thrombophlebitis, cerebrovascular disorders, myocardial infarction and pulmonary embolism associated with the use of oral contraceptives has been reported in several retrospective case control studies. The increased risk has been estimated in these studies to be approximately 4 to 11 times higher (for cerebral haemorrhage two times higher) for users when compared to non users. This reported risk according to two of the studies is not related to duration of use nor does it persist after discontinuance according to one of the studies. An interim report of a large scale continuing prospective study has tended to confirm these retrospective studies for thrombophlebitis and possible cerebrovascular disorders. This study also reported that the risk of superficial and deep vein thrombosis was lower in women using preparations containing 50 mcg of oestrogen or less. There may not be full recovery from such disorders and it should be realised that in a few cases they are fatal.

Because of a possible increased risk of post surgery thromboembolic complications in oral contraceptive

users, therapy should be discontinued at least six weeks prior to elective surgery. Caution should be exercised in administering oestrogen/progestogen combinations to women with a history of hypertension. An increased risk of surgically confirmed gall bladder disease associated with the use of oral contraceptives has been reported in a retrospective case control study.

Liver tumours, occasionally fatal, have been reported in women using oral contraceptives. These tumours may present as an abdominal mass, intra-abdominal bleeding and/or with signs and symptoms of acute abdomen. These have been reported in short term as well as long term users of oral contraceptives.

A small fraction of the active ingredients in oral contraceptives has been identified in the milk of mothers receiving these drugs. The effects, if any, on the breast-fed child have not been determined. If possible the use of oral contraceptives should be deferred until the infant is weaned.

When women have taken hormones during pregnancy there have been some reports of the possibility of adverse effects on the developing child. A direct relationship between such effects and oral contraceptives has not been confirmed, but as with any other drug, avoidance of continuing oral contraception in early pregnancy is desirable. Therefore pregnancy should be ruled out before initiating or continuing the administration of oral contraceptives to patients who have missed one menstrual period.

Certain factors may entail some risk of thrombosis, e.g. smoking, obesity, varicose veins, cardiovascular diseases, diabetes, and migraine. The suitability of a combined oral contraceptive should be judged according to the severity of such conditions in the individual case, and should be discussed with the patient before she decides to take it. The risk of arterial thrombosis associated with combined oral contraceptives increases with age and this risk is aggravated by cigarette smoking. The use of combined oral contraceptives in women in the older age group, especially those who are cigarette smokers, should therefore be discouraged and alternative methods advised.

Reduced efficacy and increased incidence of breakthrough bleeding have been associated with concomitant use of oral contraceptives and rifampicin. A similar association has been suggested with oral contraceptives and barbiturates, phenylbutazone, phenytoin sodium and ampicillin.

Reasons for stopping oral contraceptives immediately: Early manifestations of thrombotic or thromboembolic disorders, thrombophlebitis, cerebrovascular disorders (including haemorrhage), myocardial infarction, pulmonary embolism or retinal thrombosis. Hypertension. Gradual or sudden, partial or complete loss of vision. Proptosis or diplopia. Onset or aggravation of migraine or development of headaches of a new pattern which are recurrent, persistent or severe. Papilloedema or any evidence of retinal vascular lesions. During periods of immobility (e.g. after accidents). Pregnancy. Manifestations of liver tumours.

Precautions: Examination of the pelvic organs, breasts and blood pressure should precede the prescribing of any oral contraceptive, and should be repeated regularly. The following are some of the medical conditions reported to be influenced by oral contraceptive therapy, and where the physician will have to exercise medical judgement to commence, continue or discontinue therapy as appropriate:

1. Pre-existing uterine fibromyomata may increase in size.
2. A decrease in glucose tolerance in a significant number of women.
3. An increase in blood pressure in a small but significant number of women.
4. Cholestatic jaundice. Patients with a history of cholestatic jaundice of pregnancy are more likely to develop cholestatic jaundice during oral contraceptive therapy.
5. Amenorrhoea during and after oral contraceptive therapy. Women with a past history of oligomenorrhoea or secondary amenorrhoea or women with irregular cycles may be more likely to remain anovulatory or to become amenorrhoeic post oral contraceptive therapy.
6. Depression.
7. Fluid retention. Conditions which might be influenced by this factor include epilepsy, migraine, asthma, cardiac or renal dysfunction.
8. Varicose veins.
9. Multiple sclerosis.
10. Porphyria.
11. Tetany.
12. Wearing of contact lenses

or any condition that is prone to worsen during pregnancy.

The following laboratory determinations may be altered in patients using oral contraceptives:

Hepatic: Increased BSP retention and other tests.

Coagulation: Increased prothrombin, Factors VII, VIII, IX and X; decreased antithrombin III; increased platelet aggregability.

Endocrine: Increased PBI and butanol extractable protein bound iodine and decreased T^3 uptake; increased glucose blood levels.

Other: Increased phospholipids and tri-glycerides, decreased serum folate values and disturbance in tryptophan metabolism. Decreased pregnanediol excretion, reduced response to metyrapone test.

These tests usually return to pre-therapy values after discontinuing oral contraceptive use. However, the physician should be aware that these altered determinations may mask an underlying disease.

Side-effects: Side-effects most commonly reported in early cycles of oral contraceptive therapy include breakthrough bleeding, spotting, nausea, vomiting and other gastro-intestinal disturbances. These frequently decrease with continued use. Other common side-effects include: change in menstrual flow, change in weight, oedema, chloasma (which may persist post therapy), amenorrhoea, breast changes (tenderness, enlargement and secretion).

In addition to the conditions and disorders discussed above, the following have been reported as adverse reactions in patients using combined oral contraceptives:

Neuro-ocular lesions
Rash
Cervical erosion and secretions
Suppression of lactation
Pre-menstrual-like syndrome
Changes in libido
Leg cramp
Relative pyridoxine deficiency
Haemorrhagic eruptions
Cystitis like syndrome
Headache
Nervousness

Fatigue
Hirsutism
Loss of scalp hair
Erythema multiforme
Erythema nodosum
Itching
Vaginal candidiasis
Porphyria

Overdosage: Serious ill effects have not been reported following acute ingestion of large doses of oral contraceptives by young children. Overdosage may cause nausea, and withdrawal bleeding may occur in females. An appropriate method of gastric emptying may be used if considered desirable.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Carton containing 3 pushpaks each of 21 tablets – sufficient for 3 cycles.

Further information Nil.

Product licence number 0076/5000.

OVYSMEN* 0.5/35 ORAL CONTRACEPTIVE TABLETS

Presentation White $\frac{1}{2}$ inch diameter, circular tablets with flat faces and bevelled edges, bearing the engraving **ORTHO** on each face. Each tablet contains 0.5 mg Norethisterone BP and 35 mcg Ethinyloestradiol BP.

Uses Contraception and the recognised indications for such oestrogen/progestogen combinations.

Action: Through the mechanism of gonadotrophin suppression by the oestrogenic and progestational actions of the ingredients. Although the primary mechanism of action is inhibition of ovulation, alterations to the cervical mucus and to the endometrium may also contribute to the efficacy of the product.

Dosage and administration The basic dosage regimen is a 28-day cycle of 1 tablet daily for 21 days followed by seven tablet-free days. For initial therapy the first tablet is taken on the fifth day of the menstrual cycle, counting the first day of bleeding as Day 1. Each subsequent course is started after seven tablet-free days have followed the preceding course. Contraception can be initiated immediately post partum in the non-nursing patient. The possibility of ovulation and conception prior to initiation of medication should be considered. The patient should be advised that during the first 14 days of the first course an additional reliable non-hormonal form of contraception should be used. If the patient misses more than 1 tablet, she should begin taking tablets again as soon as remembered and an additional reliable method of contraception used until the next withdrawal bleed.

If the patient has vomiting or diarrhoea, absorption of the hormones will be impaired, making it advisable to use an additional reliable method of contraception until her next menstrual period. Should a bleeding fail to occur at the usual time, the possibility of pregnancy should be excluded before starting the next pack.

Contra-indications, warnings, etc

Contra-indications: Existing thrombophlebitis, thromboembolic disorders, cerebral vascular disease, myocardial infarction, or a past history of these conditions. Sick-cell anaemia. Markedly impaired liver function.

Congenital or existing disorders of lipid metabolism. Known or suspected carcinoma of the breast. Known or suspected oestrogen-dependent neoplasia. History during pregnancy of idiopathic jaundice, severe pruritus, shingles or deterioration of otosclerosis. Dubin-Johnson syndrome. Rotor syndrome. Undiagnosed abnormal genital tract bleeding. Known or suspected pregnancy.

Warnings: An increased risk of thrombophlebitis, cerebrovascular disorders, myocardial infarction and pulmonary embolism associated with the use of oral contraceptives has been reported in several retrospective case control studies. The increased risk has been estimated in these studies to be approximately 4 to 11 times higher (for cerebral haemorrhage two times higher) for users when compared to non users. This reported risk according to two of the studies is not related to duration of use nor does it persist after discontinuance according to one of the studies. An interim report of a large scale continuing prospective study has tended to confirm these retrospective studies for thrombophlebitis and possible cerebrovascular disorders. This study also reported that the risk of superficial and deep vein thrombosis was lower in women using preparations containing 50 mcg of oestrogen or less. There may not be full recovery from such disorders and it should be realised that in a few cases they are fatal.

Because of a possible increased risk of post surgery thromboembolic complications in oral contraceptive users, therapy should be discontinued at least six weeks prior to elective surgery. Caution should be exercised in administering oestrogen/progestogen combinations to women with a history of hypertension. An increased risk of surgically confirmed gall bladder disease associated with the use of oral contraceptives has been reported in a retrospective case control study.

Liver tumours, occasionally fatal, have been reported in women using oral contraceptives. These tumours may present as an abdominal mass, intra-abdominal bleeding and/or with signs and symptoms of acute abdomen. These have been reported in short-term as well as long-term users of oral contraceptives.

A small fraction of the active ingredients in oral contraceptives has been identified in the milk of mothers receiving these drugs. The effects, if any, on the breast-fed child have not been determined. If possible the use of oral contraceptives should be deferred until the infant is weaned.

When women have taken hormones during pregnancy there have been some reports of the possibility of adverse effects on the developing child. A direct relationship between such effects and oral contraceptives has not been confirmed, but as with any other drug, avoidance of continuing oral contraception in early pregnancy is desirable. Therefore pregnancy should be ruled out before initiating or continuing the administration of oral contraceptives to patients who have missed one menstrual period.

Certain factors may entail some risk of thrombosis, e.g. smoking, obesity, varicose veins, cardiovascular diseases, diabetes, and migraine. The suitability of a combined oral contraceptive should be judged according to the severity of such conditions in the individual case, and should be discussed with the patient before she decides to take it. The risk of arterial thrombosis associated with combined oral contraceptives increases with age and this risk is aggravated by cigarette smoking. The use of combined oral contraceptives in women in the older age group, especially those who are cigarette

smokers, should therefore be discouraged and alternative methods advised.

Reduced efficacy and increased incidence of breakthrough bleeding have been associated with concomitant use of oral contraceptives and rifampicin. A similar association has been suggested with oral contraceptives and barbiturates, phenylbutazone, phenytoin sodium and ampicillin.

Reasons for stopping oral contraceptives immediately: Early manifestations of thrombotic or thromboembolic disorders, thrombophlebitis, cerebrovascular disorders (including haemorrhage), myocardial infarction, pulmonary embolism or retinal thrombosis. Hypertension. Gradual or sudden, partial or complete loss of vision. Proptosis or diplopia. Onset or aggravation of migraine or development of headaches of a new pattern which are recurrent, persistent or severe. Papilloedema or any evidence of retinal vascular lesions. During periods of immobility (e.g. after accidents). Pregnancy. Manifestations of liver tumours.

Precautions: Examination of the pelvic organs, breasts and blood pressure should precede the prescribing of any oral contraceptive, and should be repeated regularly. The following are some of the conditions reported to be influenced by oral contraceptive therapy, and where the physician will have to exercise medical judgement to commence, continue or discontinue therapy as appropriate.

- a) Pre-existing uterine fibromyomata may increase in size.
 - b) A decrease in glucose tolerance in a significant number of women.
 - c) An increase in blood pressure in a small but significant number of women.
 - d) Cholestatic jaundice. Patients with a history of cholestatic jaundice of pregnancy are more likely to develop cholestatic jaundice during oral contraceptive therapy.
 - e) Amenorrhoea during and after oral contraceptive therapy. Women with a past history of oligomenorrhoea or secondary amenorrhoea or women with irregular cycles may be more likely to remain anovulatory or to become amenorrhoeic post oral contraceptive therapy.
 - f) Depression.
 - g) Fluid retention. Conditions which might be influenced by this factor including epilepsy, migraine, asthma, cardiac or renal dysfunction.
 - h) Varicose veins.
 - i) Multiple sclerosis.
 - j) Porphyria.
 - k) Tetany.
 - l) Wearing of contact lenses.
- or any condition that is prone to worsen during pregnancy.

The following laboratory determinations may be altered in patients using oral contraceptives:

Hepatic: Increased BSP retention and other tests.

Coagulation: Increased prothrombin, Factors VII, VIII, IX and X; decreased antithrombin III; increased platelet aggregability.

Endocrine: Increased PBI and butanol extractable protein bound iodine and decreased T³ uptake, increased glucose blood levels.

Other: Increased phospholipids and tri-glycerides, decreased serum folate values and disturbance in tryptophan metabolism. Decreased pregnanediol excretion, reduced response to metyrapone test.

These tests usually return to pre-therapy values after discontinuing oral contraceptive use. However, the physician should be aware that these altered determinations may mask an underlying disease.

Side-effects: Side-effects most commonly reported in early cycles of oral contraceptive therapy include breakthrough bleeding, spotting, nausea, vomiting and other gastro-intestinal disturbances. These frequently decrease with continued use. Other common side-effects include: change in menstrual flow, change in weight, oedema, chloasma (which may persist post therapy), amenorrhoea, breast changes (tenderness, enlargement and secretion).

In addition to the conditions and disorders discussed above, the following have been reported as adverse reactions in patients using combined oral contraceptives:

- Neuro-ocular lesions
- Rash
- Cervical erosion and secretions
- Suppression of lactation
- Pre-menstrual like syndrome
- Changes in libido
- Leg cramp
- Relative pyridoxine deficiency
- Haemorrhagic eruptions
- Cystitis-like syndrome
- Headache
- Nervousness
- Fatigue
- Hirsutism
- Loss of scalp hair
- Erythema multiforme
- Erythema nodosum
- Itching
- Vaginal candidiasis
- Porphyria

Overdosage: Serious ill effects have not been reported following acute ingestion of large doses of oral contraceptives by young children. Overdosage may cause nausea, and withdrawal bleeding may occur in females. An appropriate method of gastric emptying may be used if considered desirable.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Carton containing 3 pushpaks each of 21 tablets – sufficient for 3 cycles

Further information Nil.

Product licence number 0076/0047.

PEVARYL* CREAM

PEVARYL* LOTION

PEVARYL* SPRAY POWDER

Presentation *Cream:* A white cream containing 1% econazole nitrate.

Lotion: A white water-miscible lotion containing 1% econazole nitrate.

Spray Powder: A white powder containing 1% econazole nitrate, emitted as a spray by means of an aerosol container.

Uses Econazole nitrate is a broad-spectrum antifungal agent.

Cream: All fungal skin infections due to dermatophytes (e.g., *Trichophyton* species), yeasts (e.g., *Candida* species), moulds and other fungi. These include ringworm (tinea) infections, athlete's foot, paronychia, pityriasis versicolor, erythrasma and vulvitis, balanitis and napkin rash due to *Candida*.

Lotion: As Pevaryl Cream, but particularly suitable for hairy and moist areas and for fungal otitis externa.

Spray Powder: As Pevaryl Cream, but particularly suitable in intertriginous areas. Also for the protection of areas at risk and as yet unaffected by such infections.

Dosage and administration *Cream:* Apply to the affected area 2-3 times daily and rub in gently.

In nail infections, apply once daily and cover with an occlusive dressing.

Lotion: As for Pevaryl* Cream.

Spray Powder: Apply to the affected area twice daily until the lesions have healed.

In order to prevent relapse, treatment should be continued for 2 weeks after clinical cure.

Contra-indications, warnings, etc *Contra-indications:* None known.

Side effects: Rarely, transient local mild irritation may occur immediately after application.

Precautions: *Cream and Lotion:* Hypersensitivity has rarely been recorded, if it should occur, administration of the product should be discontinued.

Spray Powder: As for Pevaryl Cream and Pevaryl Lotion. The spray should be kept away from the eyes and mucous membranes.

Overdosage: Pevaryl Cream, Lotion and Spray Powder are intended for topical use. If accidental ingestion of large quantities of the product occurs, an appropriate method of gastric emptying may be used if considered desirable.

Pharmaceutical precautions

Cream and Lotion: None.

Spray Powder: Shake well before use. Contents are under pressure. Store in a cool place away from heat and sunlight; do not burn or puncture, even when empty.

Legal category

Cream: P.

Lotion: P.

Spray Powder: P.

Package quantities *Cream:* Each tube contains 30 g.

Lotion: Each bottle contains 30 ml.

Spray Powder: 200 g aerosol can contains 20 g econazole nitrate powder 1%.

Further information The infected area should be kept clean and dry during treatment.

Pevaryl Spray Powder is suitable for use in conjunction with Pevaryl Cream or Pevaryl Lotion. It is also useful for the treatment of clothing such as shoes and socks in cases of tinea pedis.

Cream: 0076/0059

Lotion: 0076/0066

Spray powder 0076/0063

RETIN-A* ACNE TREATMENT

Presentation Retin-A* Acne Treatment is available as either a clear yellow solution of 0.025% w/w tretinoin

supplied in amber bottles or in tubes of tretinoin gel 0.025% w/w or tretinoin cream 0.05% w/w.

Uses For topical application in the treatment of acne vulgaris in which comedones, papules and pustules predominate.

Retin-A Lotion is best suited for large areas such as the back.

Retin-A Gel is best suited for severe acne, for initial therapy and for oily and dark skin.

Retin-A Cream is best suited for use on dry and fair skin.

Dosage and administration Retin-A Acne treatment should be applied once or twice daily to the area of skin where acne lesions occur. Only apply sufficient to cover the affected area lightly, using a gauze swab, cotton wool or the tips of clean fingers. Avoid over-saturation to the extent that excess medication could run into eyes, angles of the nose or other areas where treatment is not intended.

Initial application may cause transitory stinging and a feeling of warmth. The correct frequency of administration should produce no more than an erythema similar to that of mild sunburn. In patients with sensitive skin, application once daily may be sufficient. In patients with normal skin, increasing the frequency of application to twice daily is usually necessary.

If Retin-A is applied excessively, no more rapid or better results will be obtained and marked redness, peeling or discomfort may occur. Should this occur accidentally or through over-enthusiastic use, application should be discontinued for a few days.

Patience is needed in this treatment, since therapeutic effects will not usually be observed until after 6-8 weeks of treatment. During the early weeks of treatment, an apparent exacerbation of inflammatory lesions may occur. This is due to the action of the medication on deep, previously unseen comedones and papules. Once the acne lesions have responded satisfactorily, it should be possible to maintain the improvement with less frequent applications.

Cosmetics may be used, but the areas to be treated should be thoroughly washed beforehand. Astringent toiletries should be avoided.

Contra-indications, warnings, etc Use of the product should be discontinued if hypersensitivity to any of the ingredients should occur. Retin-A Acne Treatment should be kept away from the eye and eyelids, the mouth and other mucous membranes. Care should also be taken not to let the medication accumulate in folds of the skin and the angles of the nose. Retin-A should not be applied to eczematous skin, nor to cuts and abrasions.

Retin-A should not be used concomitantly with other skin medications, particularly those containing peeling agents such as sulphur, resorcinol, benzoylperoxide or salicylic acid.

Recent studies in mice treated with the active ingredient (tretinoin) of Retin-A and exposed to artificial sunlight suggest that tretinoin may speed up the appearance of sunlight induced skin tumours. Laboratory mice treated with tretinoin but not exposed to sunlight did not develop skin tumours. The significance of these studies as related to human beings is unknown. However it is important to avoid or minimise exposure of Retin-A treated areas to sunlight or sunlamps during the course of treatment.

Retin-A should not be used in patients with a personal or family history of cutaneous epithelioma.

Side effects: The application of excessive amounts of Retin-A to the skin may cause severe erythema, irritation and discomfort. Should this occur, the frequency of application should be reduced or the use of Retin-A discontinued temporarily. Temporary hypo or hyperpigmentation has been reported in a few individuals treated with Retin-A. All side effects so far reported have been reversible upon discontinuation of Retin-A therapy.

Overdosage: Retin-A is intended for topical use only. Excessive use is dealt with under side effects. Taken orally by mischance Retin-A is liable to taste unpleasant. Unless the amount is small an appropriate method of gastric emptying should be used as soon as possible.

Pharmaceutical precautions Store in a cool place. The 80 ml bottle of lotion should be protected from light and any remaining medicine discarded on completion of treatment.

Legal category POM.

Package quantities *Lotion:* Amber glass bottle containing 80 ml.

Gel and Cream: Tubes containing 60 g.

Further information Nil.

Product licence numbers

Lotion 0076/0037

Gel 0076/0050

Cream 0076/0056

SULTRIN* TRIPLE SULFA CREAM

Presentation A white, non-staining cream containing Sulphathiazole 3.42% w/w, Sulphacetamide 2.86% w/w and Sulphabenzamide 3.70% w/w.

Uses For the treatment of infections caused by *Haemophilus Vaginalis* and non-specific bacterial vaginitis and cervicitis. It may also be used in the prevention of bacterial complications following cervical and vaginal surgery and vulvectomy and as an anti-infective in the post-partum state.

Dosage and administration One applicatorful intra-vaginally twice daily for 10 days. The dosage may then be reduced to once a day if necessary.

Contra-indications, warnings, etc Sulphonamide sensitivity and kidney disease.

Overdosage: Sultrin Triple Sulfa Cream is intended for intravaginal use. If accidental ingestion of large quantities of the product occurs, an appropriate method of gastric emptying may be used if considered desirable. Elimination of sulphonamides in the urine may be assisted by giving alkalis such as sodium bicarbonate and increasing fluid intake.

Pharmaceutical precautions Store at room temperature, avoid excessive heat.

Legal category POM.

Package quantities Tube containing 78 g with or without the ORTHO* Plastic Vaginal Applicator.

Further information The three sulphonamides exert optimal bacteriostatic action at different specific pH levels. The point of optimal activity for each drug is:

Sulphathiazole pH 7.0

Sulphacetamide pH 5.2
Sulphabenzamide pH 4.6

Product licence number 0076/5012.

SULTRIN* VAGINAL TABLETS

Presentation Sultrin Vaginal Tablets are white, non-staining, water-dispersible, lozenge-shaped tablets engraved with the Ortho shield design. Each tablet contains:

Sulphathiazole 172.5 mg
Sulphacetamide 143.75 mg
Sulphabenzamide 184.0 mg

in a rapidly disintegrating base.

Uses For the treatment of infections caused by *Haemophilus vaginalis* and non-specific bacterial vaginitis and cervicitis. It may also be used in the prevention of bacterial complications following cervical and vaginal surgery and vulvectomy and as an anti-infective in the post-partum state.

Dosage and administration One tablet placed high in the vagina twice daily for 10 days. Repeat if necessary.

Contra-indications, warnings, etc Sulphonamide sensitivity; renal disease.

Overdosage: Sultrin Vaginal Tablets are intended for intravaginal use. If accidental ingestion of large quantities of the product occurs, an appropriate method of gastric emptying may be used if considered desirable. Elimination of sulphonamides in the urine may be assisted by giving alkalis such as sodium bicarbonate and increasing fluid intake.

Pharmaceutical precautions None known.

Legal category POM.

Package quantities Packages of 20 foil-wrapped tablets with vaginal applicator.

Further information The three sulphonamides exert optimal bacteriostatic action at different specific pH levels. The point of optimal activity for each drug is:

Sulphathiazole pH 7.0
Sulphacetamide pH 5.2
Sulphabenzamide pH 4.6

Product licence number 0076/5013.

TOLECTIN* TABLETS ▼ TOLECTIN* DS CAPSULES

Presentation *Tablets:* White, flat, circular tablet (12 mm diameter) with bevelled edges. The word TOLECTIN is engraved on one side with a score line on the reverse. For oral administration.

Tolectin (tolmetin sodium) 200 mg tablets each contain 246 mg of tolmetin sodium dihydrate, which is equivalent to 200 mg tolmetin. Each tablet contains 18 mg (0.784 m Eq) of sodium.

Capsules: A size 'O' hard gelatin capsule with an ivory opaque body and a light blue opaque cap containing a yellow powder. For oral administration.

Tolectin (tolmetin sodium) 400 mg capsules each contain 490 mg of tolmetin sodium dihydrate, which is equivalent to 400 mg of tolmetin. Each capsule contains 36 mg (1.568 m Eq) of sodium.

Uses Tolectin is a non-steroidal anti-inflammatory

agent with analgesic and antipyretic properties. It is indicated for:

rheumatoid arthritis
juvenile rheumatoid arthritis (Still's Disease)
osteoarthritis
ankylosing spondylitis
peri-articular disorders such as fibrositis and bursitis

Dosage and administration The initial adult dosage is 400 mg three times daily. This may be adjusted within the range 600–1800 mg daily in 2, 3 or 4 divided doses depending on patient response and the severity of the disease.

In juvenile rheumatoid arthritis the dosage is 20–25 mg/kg/day in 3–4 divided doses. The maximum dose is 30 mg/kg/day or 1800 mg/day whatever the body weight. Half a tablet (100 mg) is a suitable unit for most children's doses.

Contra-indications, warnings, etc *Contra-indications:* active peptic ulcer; previous sensitivity to Tolectin, aspirin, or other non-steroidal anti-inflammatory agents, which have induced symptoms of asthma, rhinitis or urticaria.

Warnings: Tolectin should be used with caution in patients with a history of upper gastrointestinal tract disease. Tolectin prolongs bleeding time and patients who may be adversely affected should be carefully monitored during Tolectin therapy.

No teratogenic effects have been found in animals, but, as in the case of all new drugs, caution should be exercised in the prescribing of Tolectin to pregnant women. Safety for use during pregnancy or lactation has not been established.

Renal papillary necrosis has occurred in animals after long term administration although there has been no evidence of renal toxicity in clinical trials. However, since Tolectin is eliminated primarily by the kidneys, caution should be observed and patients with impaired renal function should be closely monitored and may require lower doses.

In patients with rheumatoid arthritis who have received certain anti-rheumatic drugs, eye changes have been observed. During clinical studies of up to 2 years with Tolectin no such changes have occurred.

Side effects: epigastric discomfort, headache (rare), water and sodium retention, skin rash. Gastro-intestinal disturbance may occur but blood loss due to Tolectin is rare.

Small and transient decreases in haemoglobin and haematocrit not associated with gastrointestinal bleeding have occurred. A few cases of granulocytopenia have been observed.

Management of overdosage: In the event of overdosage, the stomach should be emptied by inducing vomiting or by gastric lavage followed by the administration of activated charcoal. Studies in rats indicate that the urinary excretion of the drug is enhanced when the urine is made alkaline with sodium bicarbonate.

Pharmaceutical precautions *Tablets and Capsules:* Extremes of temperature and humidity should be avoided.

Legal category POM.

Package quantities Containers of 100 and 250 tablets
Container of 100 capsules.

Further information In clinical trials Tolectin has

shown no interaction with concomitantly administered drugs, such as gold, corticosteroids and paracetamol.

Preliminary studies indicate that Tolectin does not interact with anti-coagulant drugs.

In adult diabetic patients under treatment with either sulphonylureas or insulin no changes have been observed in the clinical effects of either Tolectin or the hypoglycaemic agents.

The metabolites of tolmetin in urine have been found to give positive tests for proteinuria using tests which rely on acid precipitation as their endpoint. No interference is seen in the tests for proteinuria using dye-impregnated commercially available reagent strips.

Product licence numbers

Tablets: 0076/0021

Capsules: 0076/0075

ZOMAX* TABLETS ▼

Presentation Pale yellow flat faced irregular hexagon shaped tablets, scored, bevelled, imprinted ORTHO on one side and imprinted ZOMAX on the reverse.

Each Zomax 100 mg tablet contains 120 mg zomepirac sodium dihydrate equivalent to 100 mg zomepirac. Each 100 mg tablet contains 8 mg (0.34 mEq) of sodium.

Uses Zomax is indicated for the treatment of pain associated with the following conditions:

Post traumatic pain related to musculoskeletal injury.

Pain in osteoarthritis and rheumatoid arthritis.

Post operative pain following orthopaedic surgery.

Post operative pain following general surgery.

Pain secondary to oral surgery.

Post partum episiotomy pain.

Pain secondary to malignancy.

Dysmenorrhoea.

Dosage and administration The recommended oral dose of Zomax is 100 mg every 4-6 hours as required. Dosage may be adjusted to the patient's response. Dosages larger than 600 mg per day have not been studied and are not recommended. Single doses larger than 100 mg have not been adequately studied and are not recommended.

Contra-indications, warnings, etc Zomax should not be used in patients in whom salicylates or other non-steroidal anti-inflammatory drugs induce bronchospasm, rhinitis, urticaria, or other sensitivity reactions.

As with other non-steroidal anti-inflammatory drugs, anaphylactoid reactions have been reported. Because of the possibility of cross-sensitivity due to structural relationships which exist among non-steroidal anti-inflammatory drugs anaphylactoid reactions may be more likely to occur in patients who have exhibited allergic reactions to these compounds, particularly tolmetin sodium. Patients presenting with an allergic reaction to Zomax should be evaluated as to the severity of the reaction and treated appropriately with conventional therapy. This may include the use of epinephrine, antihistamines, pressors, fluids, and/or steroids.

Peptic ulceration and gastrointestinal bleeding have rarely been reported in patients receiving Zomax tablets. However, the drug should be given under close super-

vision to patients with a history of these disorders, and should be avoided in patients with active peptic ulcer.

Although zomepirac sodium has a more transient effect on bleeding time than aspirin, it is an inhibitor of platelet function; therefore, as with aspirin, patients who have coagulation disorders should be carefully observed when Zomax is administered.

As with other non-steroidal anti-inflammatory drugs, elevations of BUN and serum creatinine have been reported with Zomax administration. Therefore, periodic kidney function tests are recommended for those patients undergoing long-term treatment with Zomax. Rarely, acute renal failure has been reported in patients receiving Zomax.

Since Zomax is eliminated primarily by the kidneys, patients with impaired renal function should be closely monitored and lower doses of Zomax used.

Rarely, in long-term studies, reversible elevations of liver enzymes have occurred.

Zomax is not recommended during pregnancy or lactation since safety in pregnant women or nursing mothers has not been established.

The safety and effectiveness of Zomax has not been established in children under the age of 12 years, and the use of Zomax in children is not recommended.

Side effects: Zomax is a well tolerated drug and the side effect incidence is low.

Adverse reactions were usually mild and as with other products of this type incidence was nearly always lower during short term therapy. The most common side effects were related to the gastrointestinal tract and included nausea, GI distress, diarrhoea, abdominal pain and dyspepsia. Dizziness, oedema and allergic reactions have been reported, rarely.

Management of overdosage: The absence of experience with acute overdosage precludes characterization of sequelae and assessment of antidotal efficacy at this time. It is reasonable to assume, however, that the standard practices of gastric evacuation, activated charcoal administration, and general supportive therapy would apply.

Pharmaceutical precautions None known.

Legal category POM.

Package quantities Containers of 100 tablets.

Further information The binding of warfarin to human plasma proteins is unaffected by Zomax.

Zomax produces significant analgesia within a $\frac{1}{2}$ hour and maximum analgesia within 1-2 hours following oral administration. The duration of analgesia is generally 4 to 6 hours.

Zomax is a non-narcotic, non-addicting analgesic, and in adequate and well controlled clinical studies no patient tolerance to the drug has been observed.

Since antacids do not interfere with the bioavailability of zomepirac, Zomax may be administered with antacids (other than bicarbonate) if gastrointestinal symptoms occur.

Product licence number 0076/0073.

*Trade Mark

Paines & Byrne Limited
Pabyrn Laboratories
Greenford
Middlesex UB6 7HG



DALIVIT*

Presentation *Capsules:* Oval red, soft gelatine capsules containing oily yellow suspension.

Drops: Deep yellow liquid with a characteristic taste and odour.

Syrup: Pale yellow liquid with a characteristic taste and odour

Formula	Capsules	Drops	Syrup
Vitamin A	10,000 i.u.	5,000 i.u.	5,000 i.u.
Vitamin D	1,000 i.u.	400 i.u.	1,000 i.u.
Thiamine Hydrochloride BP	—	1 mg	2.5 mg
Thiamine Mononitrate USP	3 mg	—	—
Riboflavin BP	3 mg	0.4 mg	1 mg
Pyridoxine Hydrochloride BP	1 mg	0.5 mg	1 mg
Ascorbic Acid BP	75 mg	50 mg	25 mg
Nicotinamide BP	25 mg	5 mg	10 mg
Calcium pantothenate	5 mg	—	5 mg
	in each capsule	in each 0.6 ml	in each 5 ml

Actions and uses *Drops:* These are intended principally for administration to infants and very young children for the prevention and treatment of vitamin deficiency states and for the maintenance of normal health and growth in early childhood.

Capsules and syrup: For the prevention and treatment of vitamin deficiency in older children and adults. Indicated during pregnancy and lactation, in febrile and infective conditions or to provide essential vitamins for patients on restricted diets.

Dosage and administration *Adults:* 1 Dalivit Capsule or 15 ml Dalivit Syrup daily. In febrile conditions, in pregnancy and during lactation or in the presence of infection, requirements of vitamins are increased beyond the normal so 3 capsules or 30 ml syrup daily may be required.

Infants: Prophylaxis. Drops.

Up to 12 months: 0.3 ml daily.

Over 12 months: 0.6 ml daily.

In conditions of impaired absorption or frank vitamin deficiency, these doses may be increased at the discretion of the physician.

Contra-indications, warnings, etc Hypersensitivity to any of the active ingredients is a contra-indication. Excessive doses of vitamins A and D can lead to hypervitaminosis. When multivitamin preparations are prescribed allowance must be made for vitamins from other sources.

Pharmaceutical precautions *Capsules:* Store in a cool place.

Drops: Store below 8°C—refrigerate.

Syrup: Store in a cool place protected from light.

Legal category Capsules and Syrup P.
Drops GSL.

Package quantities *Capsules:* 100, 500.

Drops: 15 ml, 100 ml.

Syrup: 100 ml, 1 litre.

Further information Nil.

Product licence numbers

Capsules 0051/5018

Drops 0051/5016

Syrup 0051/5017

GONADOTRAPHON LH*

Presentation Gonadotrophon LH is presented as ampoules containing a sterile, white, freeze-dried plug of 500 i.u., 1,000 i.u. or 5,000 i.u. of Chorionic Gonadotrophin BP for injection in a Lactose BP base. All strengths are packed with 2 ml ampoules of solvent.

Actions and uses *In the male:* Delayed puberty, cryptorchidism, oligospermia or aspermia with inactive testes.

In the female: Induction of ovulation, menorrhagia due to persistent follicular phase, recurrent abortion.

Dosage and administration Intramuscular injection.

Delayed puberty: 500 i.u. twice weekly. *Cryptorchidism:* Treat before age of puberty. Not indicated for ectopic testis. Optimum age range for treatment is 7–10 years. 500 i.u. thrice weekly for 6–10 weeks depending upon response. Oligospermia or aspermia with inactive testes: 500 i.u. twice or thrice weekly for 12–16 weeks.

Induction of ovulation: In conjunction with Serum Gonadotrophin. Gonadotrophon FSH (Serum Gonadotrophin BP) 500 i.u. intramuscularly daily from 5th to 14th day of cycle followed by Gonadotrophon LH 500 i.u. daily from 15th to 24th day of cycle.

Menorrhagia due to persistent follicular phase: 1000 i.u. twice weekly for last 2 weeks of cycle. Recurrent abortion: 1000 i.u. to 2000 i.u. twice weekly from earliest evidence of pregnancy to 14th week of gestation.

Contra-indications, warnings, etc If pregnancy follows treatment with Gonadotrophon LH and FSH the likelihood of multiple births is greater than usual.

Pharmaceutical precautions Aqueous solutions of gonadotrophic hormones are unstable but the dry-filled ampoules will remain stable if stored at a temperature not exceeding 20°C.

Legal category POM.

Package quantities Box of 5 or 50 twin ampoules (powder and solvent) 500 i.u. and 1,000 i.u. Single ampoule and boxes of 5 (powder and solvent) 5,000 i.u.

Further information Nil.

Product licence numbers

500 i.u. 51/5026
1,000 i.u. 51/5027
5,000 i.u. 51/5028

HEPARIN INJECTION BP (PABYRN)

Presentation A sterile, pyrogen-free, clear, colourless solution for injection supplied in multidose vials containing Heparin Sodium BP (Mucous) in concentrations of 1,000, 5,000 or 25,000 i.u. per ml. Also available in single dose ampoules without preservative.

Actions and uses Heparin has an anticoagulant action and its principal use is in the prophylaxis and treatment of thrombo-embolic disorders. It is of particular value in the treatment of deep vein thrombosis following major surgery and is used routinely in extra corporeal circulation procedures involving heart-lung and renal dialysis machines.

Dosage and administration An initial intravenous injection of 12,500 units followed by 7,500–10,000 units at four hourly intervals as required. May also be administered by continuous infusion via Dextrose/Saline Solutions. The aim of treatment is to extend clotting time to about 15 minutes, which is two to three times the normal rate. In the prophylaxis and treatment of post-operative deep vein thrombosis, a subcutaneous dose of 5,000 i.u. two hours pre-operatively followed by 5,000 i.u. every 8–12 hours for 7–10 days.

Contra-indications, warnings, etc Heparin is contra-indicated in haemophilia, purpura and other haemorrhagic states. Also in bacterial endocarditis, gastric and duodenal ulcers, threatened abortion and advanced renal or hepatic disease.

Haemorrhage due to overdosage can often be controlled by discontinuing Heparin therapy. Severe bleeding may be reduced by administering 1 mg of protamine sulphate for each 100 units of Heparin to be neutralised. Hypersensitivity reactions are rare.

Pharmaceutical precautions Heparin injections should be stored in a cool place protected from light and should not be used after expiry date indicated. As Heparin loses potency in solutions with a pH less than 6 (e.g. Dextrose 5%) it should only be added to such solutions immediately prior to infusion. Heparin is incompatible in aqueous solutions with certain substances including antibiotics, antihistamines, phenothiazines, narcotic analgesics, hydrocortisone and hyaluronidase.

Legal category POM.

Package quantities 1 and 5 ml ampoules and 5 ml r/c vials containing 1,000, 5,000 or 25,000 i.u. per ml. All in packs of 10. Also ampoule containing 5,000 i.u. in 0.2 ml.

Further information Nil.

Product licence numbers

1,000 i.u./ml	0051/5069	} with preservative
5,000 i.u./ml	0051/5070	
25,000 i.u./ml	0051/5071	

0.2 ml ampoule		} without preservative
5,000 i.u./0.2 ml	0051/5071	
1 and 5 ml ampoules		
1,000 i.u./ml	0051/5044	
5,000 i.u./ml	0051/5144	

KETOVITE* TABLETS

Presentation Yellow tablets. Each Ketovite Tablet contains:

Thiamine hydrochloride	1.0 mg
Riboflavin	1.0 mg
Pyridoxine hydrochloride	0.33 mg
Nicotinamide	3.3 mg
Calcium pantothenate	1.16 mg
Ascorbic acid	16.6 mg
α -Tocopheryl acetate	5.0 mg
Inositol	50.0 mg
Biotin	0.17 mg
Folic acid	0.25 mg
Acetomenaphthone	0.5 mg

Action and uses The artificial nature of many therapeutic diets will inevitably mean that certain essential vitamins will not be available from food and these must, therefore, be provided in an acceptable alternative form. It is for this purpose that Ketovite Tablets have been devised. Ketovite Tablets do not contain any sucrose, glucose, fructose, lactose, starch, sodium or artificial colouring material and may be used in conjunction with Ketovite (Supplement) Liquid to provide complete vitamin supplementation in conditions such as galactosaemia, disaccharide intolerance, phenylketonuria and other disorders of carbohydrate or amino-acid metabolism involving the use of synthetic foods. Ketovite Tablets are also of value to supplement other restricted diets, such as those used in renal conditions and malabsorption states.

Note: This is not a substitute for Ketovite (Supplement) Liquid.

Dosage and administration As a complete vitamin supplement for infants, young children or adults on restricted or synthetic diets: 1 Ketovite Tablet three times a day *plus* 5 ml Ketovite (Supplement) Liquid daily.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Store in a cool dry place and use before the expiry date indicated.

Legal category POM.

Package quantities 100, 500.

Further information Nil.

Product licence number 0051/5079.

KETOVITE* (SUPPLEMENT) LIQUID

Presentation Pale pink liquid. Each 5 ml dose of Ketovite (Supplement) Liquid contains:

Vitamin A	2,500 units
Vitamin D	400 units
Choline chloride	150 mg
Cyanocobalamin	12.5 mcg

Action and uses The artificial nature of many therapeutic diets will inevitably mean that certain essential vitamins will not be available from food and these must, therefore, be provided in an acceptable alternative form.

It is for this purpose that Ketovite (Supplement) Liquid has been devised. Ketovite (Supplement) Liquid does not contain any sucrose, glucose, fructose, lactose, starch, sodium or artificial colouring material and may be used in conjunction with Ketovite Tablets to provide complete vitamin supplementation in conditions such as galactosaemia, disaccharide intolerance, phenylketonuria and other disorders of carbohydrate or amino-acid metabolism involving the use of synthetic foods. Ketovite is also of value to supplement other restricted diets, such as those used in renal conditions and malabsorption states.

Note: This is not a substitute for Ketovite Tablets.

Dosage and administration As a complete vitamin supplement for infants, young children or adults on restricted or synthetic diets: 5 ml Ketovite (Supplement) Liquid daily *plus* 1 Ketovite Tablet three times a day.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Store between 5°C and 15°C and use before expiry date shown on label. Dilute if required with distilled water and use the diluted preparation within seven days.

Legal category P.

Package quantities 100 ml, 500 ml.

Further information Nil.

Product licence number 0051/5080.

PABRINEX*

Presentation Pairs of amber ampoules of Vitamins B and C Injection BPC for intravenous and intramuscular injection:

I/V High Potency – 5 ml No. 1 + 5 ml No. 2 Printed Blue
I/M High Potency – 5 ml No. 1 + 2 ml No. 2 Printed Red
I/M Maintenance – 2 ml No. 1 + 2 ml No. 2 Printed Pink

Active ingredients:

Uses Rapid therapy of severe depletion or malabsorption of the water soluble vitamins B and C, particularly in alcoholism, after acute infections, post-operatively and in psychiatric states.

Also used to maintain levels of Vitamins B and C in patients on chronic intermittent haemodialysis.

Dosage and administration

Intravenous: The contents of each pair of ampoules (total 10 ml) are drawn up into a syringe to mix them just before use, then injected slowly into a vein. For drip injection dilute with normal saline. *Not for intramuscular use.*

Intramuscular: The contents of each pair of ampoules (total: 7 ml – High Potency, 4 ml – Maintenance) are drawn up into a syringe to mix them just before use, then injected slowly high into the gluteal muscles, 5 cm below the iliac crest. *Not for intravenous use.*

Adult dose: Pabrinex is indicated for rapid therapy of severe vitamin depletion or malabsorption reported to occur in the following conditions:

Coma or delirium from alcohol, narcotics or barbiturates; collapse following continuous narcosis. The contents of 2–3 pairs of ampoules Intravenous High Potency (Blue No 1 and No 2) injected at intervals of 8 hours or at the discretion of the physician.

Psychosis following narcosis or ECT; toxicity from acute infections. The contents of one pair of ampoules Intravenous High Potency (Blue No 1 and No 2) or Intramuscular High Potency (Red No 1 and No 2) twice daily for up to 7 days.

Psychiatric states due to continued ill-health, old age, post operative debility and chronic infections; stress conditions. The contents of one pair of ampoules Intramuscular Maintenance (Pink No 1 and No 2) twice daily until maximum improvement is observed and maintained.

Haemodialysis. The contents of one pair of ampoules Intravenous High Potency (Blue No 1 and No 2) every

	Intravenous		Intramuscular			
	High potency		High potency		Maintenance	
Colour code	Blue label		Red label		Pink label	
Composition	No 1	No 2	No 1	No 2	No 1	No 2
Thiamine Hydrochloride BP (Vitamin B ₁)	250 mg		250 mg		100 mg	
Riboflavin (as Phosphate Sodium BP) (Vitamin B ₂)	4 mg		4 mg		4 mg	
Pyridoxine Hydrochloride BP (Vitamin B ₆)	50 mg	160 mg	50 mg	160 mg	50 mg	160 mg
Niacinamide BP						
Ascorbic Acid BP (as Sodium Ascorbate) (Vitamin C)		500 mg		500 mg		500 mg
Anhydrous Dextrose BP		1 g†				
Benzyl Alcohol BP			140 mg*		80 mg*	
Volume per Ampoule	5 ml	5 ml	5 ml	2 ml	2 ml	2 ml
Dose Volume	10 ml		7 ml		4 ml	

(* provides 2% w/v in mixed ampoules)

(† provides 10% w/v in mixed ampoules)

two weeks diluted with saline and given at the end of the dialysis.

Children's dose: Pabrinex is rarely indicated for administration to children, but suitable doses are:

Under 6 years	– $\frac{1}{4}$ adult dose
6–10 years	– $\frac{1}{3}$ adult dose
10–14 years	– $\frac{1}{2}$ – $\frac{2}{3}$ adult dose
14 years and over	– adult dose

Contra-indications, warnings, etc Sensitivity to any of the vitamins present, though this is rarely encountered. Occasionally hypotension or mild paraesthesia may result from continued high doses of Thiamine (Vitamin B₁), but this may be counteracted by the simultaneous injection of 25 mg of d-Calcium Pantothenate.

Pharmaceutical precautions Store in a cool place and protect from light.

Legal category POM.

Package quantities Packs of 5 pairs and 10 pairs of ampoules.

Further information Nil.

Product licence numbers

I/V High Potency	51/5008
I/M High Potency	51/5005
I/M Maintenance	51/5006

PANCREX[®] V

Presentation *Pancrex V Powder:* (Pancreatin BP). A high potency buff coloured powder having not less than the following activity in each mg:

Free protease	1.4 BP units
Lipase	25 BP units
Amylase	30 BP units

Pancrex V Capsules: Ivory coloured opaque hard gelatine capsules imprinted 'Pancrex V' and company logo.

Containing Pancreatin BP and providing not less than the following activity per capsule:

Free protease	430 BP units
Lipase	8,000 BP units
Amylase	9,000 BP units

The capsules provide a simple and convenient method of dose measurement of the powder for administration to younger children.

Pancrex V Tablets: (Pancreatin Tablets BP). White sugar and enteric coated tablets each containing not less than the following activity:

Free protease	110 BP units
Lipase	1,900 BP units
Amylase	1,700 BP units

Pancrex V Forte Tablets: (Pancreatin Tablets BP). White sugar and enteric coated tablets each containing not less than the following activity:

Free protease	330 BP units
Lipase	5,600 BP units
Amylase	5,000 BP units

Pancrex Granules: (Pancreatin Granules BP). Enteric coated granules containing not less than the following activity in each gram:

Free protease	300 BP units
Lipase	5,000 BP units
Amylase	4,000 BP units

Action and uses To compensate for reduced intestinal enzyme activity in pancreatic deficiency states.

Indications: Fibrocystic disease of the pancreas, chronic pancreatitis and pancreatic steatorrhoea following pan-createctomy, vagotomy or gastrectomy.

Dosage and administration It is generally accepted that dosage may vary considerably according to the needs of the individual patient, but the following dosage scale provides a suitable basis for adjustment.

Pancrex V Powder: $\frac{1}{2}$ –2 g swallowed dry or mixed with a little water or milk, four times daily before meals.

Pancrex V Capsules: Infants: The contents of 1–2 capsules mixed with feeds.

Older children and adults: The contents of 2–3 capsules four times daily before meals, or sprinkled on food at mealtimes. They may also be swallowed.

Pancrex V Tablets: 5–15 tablets four times daily before meals.

Pancrex V Forte Tablets: 2–6 tablets four times daily before meals.

Pancrex Granules: 5–10 g, swallowed dry or mixed with a little water or milk, four times daily before meals.

Contra-indications, warnings, etc *Cautionary note:* In the case of newborn infants, a dose of from 0.25 to 0.5 g of Pancrex V may be indicated, and it is possible that with this dosage some irritation of the skin surrounding the mouth and the anus may occur. A barrier cream will effectively prevent such local irritation.

If Pancrex V powder is mixed with liquids or feeds the resulting mixture should not be allowed to stand for more than one hour prior to use.

Pharmaceutical precautions The preparations should be stored in a well-closed container in a cool place and used before the expiry date indicated on the label.

Legal category GSL.

Package quantities *Pancrex V Powder:* 100 g and 250 g.

Pancrex V Tablets: 100 and 500.

Pancrex V Forte Tablets: 100 and 500.

Pancrex V Capsules: 100 and 500.

Pancrex Granules: 100 g and 500 g.

Further information Nil.

Product licence numbers

Pancrex V Powder	0051/5004
Pancrex V Tablets	0051/5002
Pancrex V Forte Tablets	0051/5000
Pancrex V Capsules	0051/5043
Pancrex Granules	0051/5003

*Trade Mark

Parke, Davis & Company
Mitchell House
Southampton Road
Eastleigh
Hampshire SO5 5RY

PARKE-DAVIS

BENAFED*

Presentation Orange/red linctus. Each 5 ml contains

Diphenhydramine Hydrochloride PhEur	12.5 mg
Dextromethorphan Hydrobromide PhEur	15 mg
Pseudoephedrine Hydrochloride BP	30 mg
Ammonium Chloride PhEur	125 mg
Sodium Citrate PhEur	57 mg
Menthol BP	1 mg

Action Non-narcotic, antitussive, decongestant and expectorant to give comprehensive relief to the coughing patient.

Indications Benafed is indicated for the relief of cough and its congestive symptoms and in the treatment of hay fever and other allergic conditions affecting the upper respiratory tract.

Dosage and administration Oral.

Adults: One 5 ml spoonful every four to six hours.

Children: 4-12 years: Half to one 5 ml spoonful every six hours.

2-4 years: 1.25 ml every six hours.

Recommended diluent Syrup BP. When diluted use within 14 days of preparation.

Contra-indications, warnings, etc Contra-indicated in patients with known hypersensitivity to any of the active constituents and in those receiving monoamine oxidase inhibitors, or within 14 days of stopping such treatment. Renal dysfunction. Caution may be necessary in patients with cardiovascular disease, hyperthyroidism, and prostatic enlargement. This preparation may cause drowsiness. If affected the patient should not drive or operate machinery. Avoid alcoholic drink, as this product potentiates the effects of alcohol and other CNS depressants.

As with any other medicine, care should be taken in administration during pregnancy.

Treatment of overdose: Gastric lavage in the conscious patient and intensive supportive therapy when necessary, as with cases of overdose with antihistaminic drugs.

Pharmaceutical precautions Keep container tightly closed.

Recommended diluent Syrup BP. When diluted use within 14 days of preparation.

Legal category P.

Package quantities 500 ml and 2.25 litres.

Further information Nil.

Product licence number 0018/0071

BENYLIN* DECONGESTANT

Presentation A clear yellow syrup with a honey and lemon flavour.

Each 5 ml contains:

Diphenhydramine hydrochloride PhEur	14.0 mg
Pseudoephedrine hydrochloride BP	10.0 mg
Sodium citrate PhEur	57.0 mg
Menthol BP	1.1 mg

Action The antihistaminic action of diphenhydramine hydrochloride helps to provide relief from nasal stuffiness, sneezing and watering of the eyes; the antitussive action suppresses the cough reflex and the local anaesthetic action helps to ease sore throats.

Pseudoephedrine combats the congestive symptoms that frequently accompany the cough and reduces bronchial and nasal congestion.

Indications For relief of cough and its congestive symptoms; particularly suitable for coughs associated with colds.

Dosage and administration Oral.

Adults: Two 5 ml spoonfuls four times a day.

Children: 6-12 years: One 5 ml. spoonful four times a day.

1-5 years: Half a 5 ml spoonful four times a day.

Contra-indications, warnings, etc Contra-indicated in patients with known hypersensitivity to any of the active constituents and in those receiving monoamine oxidase inhibitors or having received them within the previous fourteen days. Caution may be necessary in patients with cardiovascular disease, hyperthyroidism, and prostatic enlargement.

This preparation may cause drowsiness. If affected, the patient should not drive or operate machinery. Avoid alcoholic drink, as this product potentiates the effect of alcohol and other CNS depressants.

As with any other medication care should be taken in administration during pregnancy.

Treatment of overdose: Gastric lavage in the conscious patient and intensive supportive therapy when necessary as with cases of overdose with antihistaminic drugs.

Pharmaceutical precautions Keep container tightly closed.

Recommended diluent: Syrup BP. When diluted use within 14 days of preparation.

Legal category P.

Package quantities 500 ml, 2.25 L.

Further information Nil.

Product licence number 0018/0110.

BENYLIN* EXPECTORANT

Presentation A clear red syrup. Each 5 ml contains

Diphenhydramine Hydrochloride PhEur	14 mg
Ammonium Chloride PhEur	135 mg

Sodium Citrate PhEur
Menthol BP

57 mg
1.1 mg

Action Benylin Expectorant gives comprehensive relief to the coughing patient since it combines the antihistaminic and anticholinergic actions of Benadryl* (Diphenhydramine Hydrochloride BP) with selected expectorant and demulcent agents. It makes the cough more productive by loosening tenacious bronchial mucus. It combats the congestive symptoms that frequently accompany the cough and reduces bronchial and nasal congestion. Benylin Expectorant contains no opiate drugs.

Indications For the relief of cough and its congestive symptoms. It also alleviates histamine-induced bronchoconstriction.

Dosage and administration Oral.

Adults: One or two 5 ml spoonfuls every two or three hours.

Children: 1-5 years: Half 5 ml spoonful every three or four hours.

6-12 years: One 5 ml spoonful every three or four hours.

Contra-indications, warnings, etc Known hypersensitivity to any of the active constituents. Renal dysfunction. May cause drowsiness. If affected, the patient should not drive or operate machinery. Avoid alcoholic drink.

As with any other medicine, care should be taken in administration during pregnancy.

Treatment of overdose: Gastric lavage in the conscious patient and intensive supportive therapy where necessary, as with cases of overdose of antihistaminic drugs.

Pharmaceutical precautions Keep container tightly closed.

Recommended diluent – Syrup BP. When diluted use within 14 days of preparation.

Legal category P.

Package quantities 125 ml, 250 ml and 2.25 litres.

Further information Nil.

Product licence number 0018/5090.

BENYLIN* WITH CODEINE

Presentation A clear red syrup. Each 5 ml contains:

Diphenhydramine Hydrochloride PhEur	14 mg
Codeine Phosphate PhEur	5.7 mg
Sodium Citrate PhEur	57 mg
Menthol PhEur	1.1 mg

Action Benylin with Codeine is an antitussive preparation designed specifically to control the dry irritating cough. It combines the antitussive, antihistaminic, local anaesthetic and anticholinergic effects of Benadryl* (Diphenhydramine Hydrochloride BP) with the antitussive action of codeine phosphate.

Indications Benylin with Codeine is indicated in the treatment of persistent dry irritating cough.

Dosage and administration Oral.

Adults: Two 5 ml spoonfuls every three or four hours.

Children: 1-5 years: Half 5 ml spoonful every three or four hours.

6-12 years: One 5 ml spoonful every three or four hours.

Contra-indications, warnings, etc Known hypersensitivity to any of the active constituents. May cause drowsiness. If affected, the patient should not drive or operate machinery. Avoid alcoholic drink.

As with any other medicine, care should be taken in administration during pregnancy. Codeine may be habit forming.

Treatment of overdose: Gastric lavage in the conscious patient and intensive supportive therapy where necessary, as with cases of overdose with antihistaminic drugs.

Pharmaceutical precautions Keep container tightly closed.

Recommended diluent – Syrup BP. When diluted use within 14 days of preparation.

Legal category P.

Package quantities 2.25 litres.

Further information Nil.

Product licence number 0018/0097

BENYLIN* PAEDIATRIC

Presentation A bright red syrup. Each 5 ml contains:

Diphenhydramine Hydrochloride PhEur	7 mg
Sodium Citrate PhEur	28.5 mg
Menthol BP	0.55 mg

Action Benylin Paediatric is formulated to give comprehensive relief to the coughing child since it combines the potent antihistaminic and anticholinergic actions of Benadryl* (Diphenhydramine Hydrochloride BP) with demulcent agents: to combat the congestive symptoms that frequently accompany the cough; and reduce bronchial and nasal congestion. Benylin Paediatric contains no opiate drugs.

Indications Benylin Paediatric is indicated for the relief of cough and its congestive symptoms, and in the treatment of hay fever and other allergic conditions affecting the upper respiratory tract. It is specially formulated for children.

Dosage and administration Oral.

Children: 1-5 years: One 5 ml spoonful every three hours.

6 years and over: Two 5 ml spoonfuls every three hours.

Contra-indications, warnings, etc Known hypersensitivity to any of the active constituents.

This preparation may cause drowsiness.

Treatment of overdose: Gastric lavage in the conscious patient and intensive supportive therapy where necessary, as with cases of overdose with antihistaminic drugs.

Pharmaceutical precautions Recommended diluent – Syrup BP. When diluted use within 14 days of preparation. Keep container tightly closed.

Legal category P.

Package quantities 125 ml and 2.25 litres.

Further information Nil.

Product licence number 0018/0067.

CHLOROMYCETIN* OPHTHALMIC PREPARATIONS

Presentation Eye drops, eye ointment.

Composition: Chloromycetin Redidrops* (Ophthalmic) 0.5% (Chloramphenicol Eye Drops BP):

Chloramphenicol Ph Eur	5 mg
Boric Acid Ph Eur	15 mg
Borax Ph Eur	3 mg
Phenylmercuric Acetate BPC 1973	0.02 mg
Purified water Ph Eur	qs to 1 ml

Chloromycetin Ophthalmic Ointment (Chloramphenicol Eye Ointment BP) contains 1% chloramphenicol in a petrolatum base.

Action Chloromycetin (Chloramphenicol Ph Eur) has a wide range of antibacterial activity and is effective against virtually all bacterial pathogens known to cause diseases of the eye. It penetrates the non-inflamed eye better than any other antibiotic regardless of the mode of administration, and resistance to it is slow to develop, moderate in degree and not necessarily permanent. Clinical studies have shown that preparations of Chloromycetin for local treatment of ocular conditions are well tolerated.

Indications Treatment of bacterial conjunctivitis caused by the organisms *Escherichia coli*, *Haemophilus influenzae*, *Staphylococcus aureus*, *Streptococcus haemolyticus*, *Morax-Axenfeld* and others.

Dosage and administration The recommended dosage for adults, children and infants of all age groups is 2 drops, or a small amount of ointment to be applied to the affected eye every three hours or more frequently if required: treatment should be continued for at least 48 hours after the eye appears normal.

Contra-indications, warnings, etc Chloromycetin Ophthalmic Preparations should not be administered to patients hypersensitive to chloramphenicol.

In severe infections the topical use of chloramphenicol should be supplemented by appropriate systemic treatment. The prolonged use of antibiotics may occasionally result in overgrowth of non-susceptible organisms, including fungi. If any new infection appears during treatment the antibiotic should be discontinued and appropriate measures taken. Chloramphenicol should be reserved for use only in infections for which it is specifically indicated.

Aplastic anaemia has been reported following topical use of chloramphenicol. Whilst the hazard is a rare one, it should be borne in mind when assessing the benefits expected from the use of this compound.

Treatment of overdosage: Not applicable.

Pharmaceutical precautions *Chloromycetin Redidrops:* Store between 2–8°C. Protect from light. Contents must be used within four weeks of being dispensed.

Chloromycetin Ophthalmic Ointment 1%: Store at a temperature not exceeding 30°C. Use within one month of opening.

Legal category POM.

Package quantities *Chloromycetin Redidrops:* 5 ml and 10 ml in polythene dropper bottle.

Chloromycetin Ophthalmic Ointment 1%: Collapsible tube of 4 g.

Further information Nil

Product licence numbers

Chloromycetin Redidrops	0018/0065
Chloromycetin Ophthalmic Ointment 1%	0018/5074

EPANUTIN* CAPSULES AND SUSPENSION

Presentation Epanutin Capsules (Phenytoin Capsules BP) contain 25 mg, 50 mg or 100 mg Phenytoin Sodium Ph Eur.

Epanutin Suspension (Phenytoin Mixture BPC 1973) contains 30 mg Phenytoin BPC 1973 in 5 ml.

Epanutin Capsules 25 mg: A white powder in a No. 4 hard gelatin capsule with a white opaque body and a purple opaque cap imprinted PARKE DAVIS. PD25

Epanutin Capsules 50 mg: A white powder in a No. 4 hard gelatin capsule with a white opaque body and a pale pink opaque cap imprinted PARKE DAVIS PD50

Epanutin Capsules 100 mg: A white powder in a No. 3 hard gelatin capsule with a white opaque body and orange cap imprinted PARKE DAVIS. PD100

Epanutin Suspension: Cherry-red suspension.

Action Anticonvulsant which appears to stabilise rather than raise the seizure threshold and prevent spread of seizure activity rather than abolish the primary focus of seizure discharge.

Indications Control of grand mal epilepsy, temporal lobe seizures and certain other convulsive states. Epanutin has also been employed in the treatment of migraine, trigeminal neuralgia and certain psychoses.

Dosage and administration *Epanutin Capsules:* Oral.

Adults: 100 mg two to four times daily before meals, with a maximum total of 600 mg a day.

Infants and children up to 3 years: The initial dose is up to 50 mg two or three times daily.

Children 4–6 years: The dosage may be increased above the infant dose.

Children 7–12 years: As for adults.

Each dose of Epanutin should be followed by at least $\frac{1}{2}$ tumblerful of water. In cases showing a tendency to nausea and a feeling of fullness of the stomach, the dose may be given with or following meals.

Epanutin Suspension: Oral.

Adults: 15 ml three times daily. Subsequent dosage should be adjusted according to the therapeutic response.

Children under 6 years: 5 ml twice daily increasing to 5 ml three or four times daily.

Children 6 years and over: As for adults.

These dosages are a guide only and the generally accepted principles of anticonvulsant treatment should be carried out, i.e. Epanutin Capsules or Suspension should be introduced in small dosage with gradual increments until control is achieved (or therapeutic blood levels reached, if facilities for estimation of these exist) or until toxic effects appear. If toxic effects do appear, the dose should be decreased, and if control is not achieved, the drug should be withdrawn gradually and an alternative anticonvulsant substituted. Maintenance of treatment should be the lowest dose of anticonvulsant consistent with control of seizures.

Contra-indications, warnings, etc Hypersensitivity to hydantoins.

There is some evidence that phenytoin may produce congenital abnormalities in the offspring of a small number of epileptic patients, therefore it should not be used as the first drug in pregnancy, especially early pregnancy, unless in the judgement of the physician the potential benefits outweigh the risk. Small quantities of phenytoin are excreted in breast milk.

If the patient has been receiving other anticonvulsants, such as phenobarbitone, the sudden withdrawal of the drugs may precipitate a series of attacks before Epanutin has been given in sufficient amounts to exercise control. This may be avoided by gradually replacing with Epanutin the anticonvulsant previously used.

During initial treatment, minor side-effects may include gastric distress, nausea, transient nervousness, weight loss, sleeplessness and a feeling of unsteadiness. Side-effects usually subside with continued use. Allergic phenomena such as polyarthropathy, fever, skin eruptions and hepatitis may occur. Eruptions usually subside upon discontinuance of therapy. Lupus erythematosus and erythema multiforme have occurred. Though mild and rarely an indication for stopping dosage, gingival hypertrophy, hirsutism and excessive motor activity are occasionally encountered in the younger age groups. Haematological disorders including megaloblastic anaemia, leucopenia, agranulocytosis, thrombocytopenia, ancytopenia and aplastic anaemia have been reported. The occasional occurrence of lymphadenopathy indicates the need to differentiate such a condition from that of lymph-gland pathology. Nystagmus in combination with diplopia and ataxia indicates that dosage should be reduced.

Phenytoin should be used with caution in the presence of liver dysfunction.

Certain drugs have been shown to elevate phenytoin plasma levels including antituberculous agents, dicoumarol anticoagulants, sulthiame, pheneturide, disulfiram, chloramphenicol, halothane, thyroid preparations and ioxazine. The levels of phenytoin are decreased by carbamazepine. The effect of phenytoin may be diminished by alcohol and altered by phenobarbitone. Phenytoin induced enzyme induction can enhance the metabolism of oral contraceptives and therefore may lead to a diminished contraceptive effect. Phenytoin may affect blood calcium and blood sugar metabolism and exanthemasone and metyrapone tests.

Treatment of overdosage: The mean lethal dose for adults is estimated to be 2-5 g. The cardinal initial symptoms are nystagmus, ataxia and dysarthria. The patient then becomes comatose, the pupils are unresponsive and hypotension occurs followed by respiratory depression and apnoea. Treatment is non-specific since there is no known antidote. First, the stomach should be emptied. If the gag reflex is absent, the airway should be supported. Oxygen, vasopressors and assisted ventilation may be necessary for central nervous system respiratory and cardiovascular depression. Total exchange transfusion has been utilised in the treatment of severe intoxication in children.

Pharmaceutical precautions Store at a temperature not exceeding 30°C.

Epanutin Suspension: Suitable diluent - Syrup BP. When diluted use within 14 days of preparation.

Legal category POM.

Package quantities Epanutin Capsules 100 mg are available in containers of 500 and 1,000.

Epanutin Capsules 50 mg and 25 mg are available in containers of 500.

Epanutin Suspension (30 mg per 5 ml) is available in bottles of 500 ml.

Further information Conventional doses of phenytoin will produce a therapeutically desirable serum level (between 10 and 20 micrograms/ml) only in a proportion of patients under treatment. Levels below 10 micrograms/ml may result in ineffective treatment, whilst it has been reported that with levels above 20 to 25 micrograms/ml toxic effects begin to appear.

The 25 mg Epanutin Capsule has been introduced because incremental doses of the drug should become progressively smaller as the serum concentration increases, since there is no linear relationship between dose and serum level - for example, an incremental dose of 50 mg may be enough to increase a serum level in a particular patient from 10 micrograms/ml to a toxic level.

Product licence numbers

Epanutin Capsules 25 mg	0018/0112
Epanutin Capsules 50 mg	0018/5079
Epanutin Capsules 100 mg	0018/5080
Epanutin Suspension	0018/5106

EPANUTIN* INFATABS*

Presentation Yellow, triangular, flat, chewable tablets with breaking line on one side and with a spearmint flavour. Each Infatab contains 50 mg Phenytoin BPC 1973.

Action Anticonvulsant which appears to stabilise rather than raise the seizure threshold and prevent spread of seizure activity rather than abolish the primary focus of seizure discharge.

Indications Control of grand mal epilepsy, temporal lobe seizures and certain other convulsant states.

Dosage and administration Oral - to be chewed.

Initially: Under 1 year: $\frac{1}{2}$ tablet twice daily.

1-6 years: $\frac{1}{2}$ tablet two to four times daily.

7-12 years: 1 tablet two to four times daily.

Adults: 2 tablets two to four times daily.

These dosages are a guide only and the generally accepted principles of anticonvulsant treatment should be carried out, i.e. Epanutin Infatabs should be introduced in small dosage with gradual increments until control is achieved (or therapeutic blood levels reached, if facilities for estimation of these exist) or until toxic effects appear. If toxic effects do appear, the dose should be decreased, and if control is not achieved, the drug should be withdrawn gradually and an alternative anticonvulsant substituted. Maintenance of treatment should be the lowest dose of anticonvulsant consistent with control of seizures.

Equal doses of Epanutin Infatabs and Capsules may not give rise to equivalent blood levels.

Contra-indications, warnings, etc Hypersensitivity to hydantoins.

There is some evidence that phenytoin may produce congenital abnormalities in the offspring of a small number of epileptic patients, therefore it should not be used as first drug during pregnancy, especially in early pregnancy, unless in the judgement of the physician, the

potential benefits outweigh the risks. Small quantities of phenytoin are excreted in breast milk.

If the patient has been receiving other anticonvulsants, the sudden withdrawal of the drugs may precipitate a series of seizures before Epanutin Infatabs have been given in sufficient amounts to exercise control. This may be avoided by replacing the anticonvulsant previously used gradually with Epanutin Infatabs. During initial treatment, minor side-effects may include gastric distress, nausea, transient nervousness, weight loss, sleeplessness and a feeling of unsteadiness. Side-effects usually subside with continued use. Allergic phenomena such as polyarthropathy, fever, skin eruptions and hepatitis may occur. Eruptions usually subside upon discontinuance of therapy. Lupus erythematosus and erythema multiforme have occurred. Though mild and rarely an indication for stopping dosage, gingival hypertrophy, hirsutism and excessive motor activity are occasionally encountered in the younger age groups. Haematological disorders including megaloblastic anaemia, leucopenia, agranulocytosis, thrombocytopenia, pancytopenia and aplastic anaemia have been reported. The occasional occurrence of lymphadenopathy indicates the need to differentiate such a condition from other lymph-gland pathology. Nystagmus in combination with diplopia and ataxia indicates that dosage should be reduced.

Phenytoin should be used with caution in the presence of liver dysfunction.

Certain drugs have been shown to elevate phenytoin plasma levels including anti-tuberculous agents, dicoumarol anticoagulants, sulthiame, pheneturide, disulfiram, chloramphenicol, halothane, thyroid preparations and viloxazine. The levels of phenytoin are decreased by carbamazepine. The effect of phenytoin may be diminished by alcohol and altered by phenobarbitone. Phenytoin induced enzyme induction can enhance the metabolism of oral contraceptives and therefore may lead to a diminished contraceptive effect. Phenytoin may affect blood calcium and blood sugar metabolism and dexamethasone and metyrapone tests.

Treatment of overdose: The mean lethal dose for adults is estimated to be 2-5 g. The cardinal initial symptoms are nystagmus, ataxia and dysarthria. The patient then becomes comatose, the pupils are unresponsive and hypotension occurs followed by respiratory depression and apnoea. Treatment is non-specific since there is no known antidote. First, the stomach should be emptied. If the gag reflex is absent, the airway should be supported. Oxygen, vasopressors and assisted ventilation may be necessary for central nervous system, respiratory and cardiovascular depression. Total exchange transfusion has been utilised in the treatment of severe intoxication in children.

Pharmaceutical precautions Store at a temperature not exceeding 30°C.

Legal category POM.

Package quantities Packs of 100 tablets

Further information Nil.

Product licence number 0018/0069.

EPANUTIN* WITH PHENOBARBITONE CAPSULES

Presentation Capsules containing 100 mg Phenytoin

Sodium Ph Eur and 50 mg Phenobarbitone Ph Eur, white powder in a No. 3 hard gelatin capsule with white opaque body and yellow cap, imprinted PARKE-DAVIS

Action Anticonvulsant. Phenytoin appears to stabilise rather than raise the seizure threshold and prevent spread of seizure activity rather than abolish the primary focus of seizure discharge.

Indications Control of grand mal epilepsy, temporal lobe seizures and certain other convulsive states.

Dosage and administration Oral.

Adults: 1-3 capsules daily according to therapeutic response.

Children: None.

Each dose of Epanutin with Phenobarbitone should be followed by at least $\frac{1}{2}$ tumblerful of water. In case showing a tendency to nausea and a feeling of fullness of the stomach, the dose may be given with or following meals.

These dosages are a guide only and the generally accepted principles of anticonvulsant treatment should be carried out, i.e. Epanutin with Phenobarbitone Capsules should be introduced in small dosage with gradual increments until control is achieved (or therapeutic blood levels reached, if facilities for estimation of these exist) or until toxic effects appear. If toxic effects do appear, the dose should be decreased, and if control is not achieved, the drugs should be withdrawn gradually and an alternative anticonvulsant substituted. Maintenance of treatment should be the lowest dose of anticonvulsant consistent with control of seizures.

Contra-indications, warnings, etc Hypersensitivity to hydantoins or barbiturates.

There is some evidence that phenytoin and phenobarbitone may produce congenital abnormalities in the offspring of a small number of epileptic patients, therefore they should not be used as first drugs during pregnancy, especially early pregnancy, unless in the judgement of the physician, potential benefits outweigh the risks. Small quantities of phenytoin and phenobarbitone are excreted in breast milk.

If the patient has been receiving other anticonvulsants, the sudden withdrawal of the drugs may precipitate a series of attacks before Epanutin with Phenobarbitone has been given in sufficient amounts to exercise control. This may be avoided by gradually replacing with Epanutin with Phenobarbitone the anticonvulsant previously used.

During initial treatment, minor side-effects from phenytoin may include gastric distress, nausea, transient nervousness, weight loss, sleeplessness and a feeling of unsteadiness. Side-effects usually subside with continued use. Allergic phenomena such as polyarthropathy, fever, skin eruptions and hepatitis may occur. Eruptions usually subside upon discontinuance of therapy. Lupus erythematosus and erythema multiforme have occurred. Though mild and rarely an indication for stopping dosage, gingival hypertrophy, hirsutism and excessive motor activity are occasionally encountered in the younger age groups. Haematological disorders including megaloblastic anaemia, leucopenia, agranulocytosis, thrombocytopenia, pancytopenia and aplastic anaemia have been reported. The occasional occurrence of lymphadenopathy indicates the need to differentiate such a condition from other lymph-gland pathology. Nystagmus in combination with diplopia and ataxia indicates that dosage should be reduced.

Epanutin with Phenobarbitone should be used with care in patients with impaired hepatic or renal function, and is contra-indicated in patients with acute intermittent porphyria.

Phenobarbitone causes drowsiness.

Certain drugs have been shown to elevate phenytoin plasma levels including antituberculous agents, dicoumarol anticoagulants, sulthiame, pheneturide, disulfiram, chloramphenicol, halothane, thyroid preparations and iloxazine. The levels of phenytoin are decreased by carbamazepine. The effect of phenytoin may be diminished by alcohol and altered by phenobarbitone. Anticonvulsant induced enzyme induction can enhance the metabolism of oral contraceptives and therefore may lead to a diminished contraceptive effect. Phenytoin may affect blood-calcium and blood sugar metabolism and lefamethasone and metyrapone tests.

Barbiturates will increase the effects of CNS depressants, e.g. alcohol, antihistamines.

Treatment of overdosage: The mean lethal dose of phenytoin for adults is estimated to be 2–5 g. The cardinal initial symptoms are nystagmus, ataxia and dysarthria. The patient then becomes comatose, the pupils are unresponsive and hypotension occurs followed by respiratory depression and apnoea. Treatment is non-specific since there is no known antidote. First, the stomach should be emptied. If the gag reflex is absent, the airway should be supported. Oxygen, vasopressors and assisted ventilation may be necessary for central nervous system, respiratory and cardiovascular depression. Total exchange transfusion has been utilised in the treatment of severe intoxication in children. Forced alkaline diuresis and charcoal haemoperfusion may be considered to hasten the removal of phenobarbitone.

Pharmaceutical precautions Store at a temperature not exceeding 30°C.

Legal category POM.

Package quantities Epanutin with Phenobarbitone capsules are available in containers of 500.

Further information Nil.

Product licence number 0018/5105.

PANUTIN* READY MIXED PARENTERAL

Representation Epanutin Ready Mixed Parenteral Phenytoin Injection BP) contains 250 mg Phenytoin sodium Ph Eur in each 5 ml ampoule.

Action Anticonvulsant which appears to stabilise rather than raise the seizure threshold and prevent spread of seizure activity rather than abolish the primary focus of seizure discharge.

Indications Epanutin Ready Mixed Parenteral is indicated for the control of status epilepticus and other persistent convulsive disorders: for the prophylactic control of seizures in neurosurgery. It is of use in the treatment of certain cardiac arrhythmias, especially when these are digitalis induced.

Dosage and administration *Use in status epilepticus:* **Adults:** By slow intravenous injection, at a rate not exceeding 50 mg per minute, 150–250 mg, followed if necessary, after 30 minutes, by 100–150 mg. Where it is impossible to immobilise an extremity, or veins are inaccessible, the intramuscular route may be used

initially. Great care should be taken to avoid the risk of breaking the injection needle.

Children: Dosage is usually determined according to weight, in proportion to the dosage for a 150 lb (70 kg) adult.

Use in neurosurgery: 2–4 ml (100–200 mg) intramuscularly three to four times daily during the period encompassing surgery and the post-operative phase.

Use in cardiac arrhythmias: 3.5–5 mg per kg of body weight intravenously initially, repeated once if necessary. The solution should be injected slowly intravenously and at a uniform rate which should not exceed 1 ml (50 mg) per minute.

Contra-indications, warnings, etc Hypersensitivity to hydantoin. Heart block. Intra-arterial administration must be avoided in view of the high pH of the preparation.

Fatalities due to cardiac arrest, ventricular fibrillation, tonic seizures and respiratory arrest have been reported following intravenous administration of phenytoin in cases with cardiac arrhythmias. Alterations of cardiac and respiratory function can be produced by too rapid administration of the drug intravenously. Complications may occur more readily in elderly and gravely ill patients. In all cases optimal dosage of Epanutin Ready Mixed Parenteral must be determined by trial. Dosage in excess of the minimum required to prevent convulsions is not recommended. Subcutaneous or perivascular injection should be avoided because of the highly alkaline nature of the solution, which may cause local tissue damage. Solutions of Epanutin Ready Mixed Parenteral should not be added to intravenous solutions because of the precipitation of the free acid.

There is some evidence that phenytoin may produce congenital abnormalities in the offspring of a small number of epileptic patients, therefore it should not be used as first drug during pregnancy, especially early pregnancy, unless in the judgement of the physician the potential benefits outweigh the risks. Small quantities of phenytoin are excreted in breast milk.

Caution: The use of Epanutin by the intravenous route should be considered an emergency procedure. Continuous electrocardiographic monitoring is recommended. As with the administration of any potent cardiac anti-arrhythmic drug, cardiac resuscitative equipment should be available.

Treatment of overdosage: The mean lethal dose in adults is estimated to be 2–5 g. The cardinal initial symptoms are nystagmus, ataxia and dysarthria. The patient then becomes comatose, pupils unresponsive and hypotension occurs followed by respiratory depression and apnoea. Treatment is non-specific since there is no known antidote. If the gag reflex is absent, the airway should be supported. Oxygen, vasopressors and assisted ventilation may be necessary for central nervous system, respiratory and cardiovascular depression. Total exchange transfusion has been utilised in the treatment of severe intoxication in children.

Pharmaceutical precautions Store at a temperature not exceeding 25°C. Protect from light. The product should not be used if a precipitate or haziness develops in the solution in the ampoule. Epanutin Ready Mixed Parenteral should not be added to intravenous infusion fluids because of precipitation of the acid.

Legal category POM.

Package quantities 10 × 5 ml ampoules.

Further information Nil.

Product licence number 0018/0070.

LOESTRIN* 20

Presentation A pale blue-grey film-coated tablet. Each tablet contains Norethisterone Acetate BP 1 mg and Ethinyloestradiol Ph Eur 0.02 mg.

Action Loestrin achieves contraceptive effect primarily by inhibition of ovulation through gonadotrophin suppression. It is possible that other sites of action such as changes in cervical mucus and in the endometrium may contribute to the efficacy of combined oral contraceptives.

Indications Control of conception.

Dosage and administration *Oral:* One Loestrin tablet should be taken daily for three weeks, starting on the fifth day of menstrual bleeding, and then an interval of one week allowed before commencing the second course of tablets. In the first cycle only, it is advisable to use another method of contraception for the first 14 days in addition to taking the tablets. Second and subsequent courses should be taken for three weeks with one week without tablets between courses. Thus each new course of tablets is always started on the same day of the week. It is important that the tablets are taken as directed. Tablets should be taken without regard to menstrual bleeding except in the initial cycle.

If a tablet is not taken at the usual time, it must be taken within the next 12 hours. If the delay exceeds 12 hours the course should be continued by taking the tablets in the pack at their proper times and leaving the missed tablet(s). Additional contraceptive methods should be used until the next withdrawal bleed.

Vomiting and/or diarrhoea may reduce the effectiveness of the pill. If this occurs extra contraceptive measures should be taken for the rest of the cycle.

It has been suggested that certain drugs may produce increased metabolism of oral contraceptive steroids. Patients receiving additional drugs, including phenobarbitone, phenytoin and some antibiotics, might be advised to use non-hormonal additional methods of contraception for the rest of the cycle.

Post-partum: Oral contraception is usually started as soon as spontaneous menstruation has resumed after childbirth. However, oral contraception can be started within 7–12 days of a vaginal delivery, provided that the patient is ambulant and there are no puerperal complications. If medication is started within 12 days of delivery, additional contraceptive precautions are unnecessary. After a first trimester abortion, oral contraceptives can normally be started immediately.

Children: None.

Contra-indications, warnings, etc

Contra-indications: Thromboembolic disorders, or a past history of these conditions; sickle cell anaemia; known or suspected disorders of lipid metabolism; markedly impaired liver function; known or suspected carcinoma of the breast; known or suspected oestrogen dependent neoplasms; undiagnosed abnormal vaginal bleeding. Loestrin should not be given during pregnancy, or to patients with a history of severe pruritis during pregnancy or of herpes of pregnancy. Loestrin should not be given

to patients with a history of otosclerosis, idiopathic jaundice; Dubin-Johnson or Roter syndromes or an significant liver disease.

Warnings: The use of oral contraceptives has been shown to be associated with an increased risk of thromboembolic disorders. The physician should be alert to the earliest manifestations of these disorders, (thrombophlebitis, cerebrovascular disorders, pulmonary embolism, and retinal thrombosis). Should any of these occur or be suspected, Loestrin should be discontinued immediately.

Certain factors may predispose to the development of thrombosis, e.g. smoking, obesity, age, the presence of varicose veins, cardiovascular disease, diabetes and migraine. The suitability of combined oral contraceptive for patients with any of these conditions should be discussed with the patient before a final decision is taken.

The risk of arterial thrombosis associated with combined oral contraceptives increases with age, and the risk is aggravated by cigarette smoking. The use of combined oral contraceptives by women in the older age group, especially those who are cigarette smokers should therefore be discouraged, and alternative methods advised.

Very rarely, hepatic tumours have been reported in users of combined oral contraceptives, generally for a protracted period of time. A hepatic tumour should be considered in the differential diagnosis when upper abdominal pain, enlarged liver or signs of intra-abdominal haemorrhage occur.

Medication should be discontinued pending examination if there is a sudden onset of proptosis, diplopia or migraine.

Patients with a history of depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree.

Since the safety of Loestrin in pregnancy has not been demonstrated, it is recommended that for any patient who has missed a period, the absence of pregnancy should be established before continuing the contraceptive regimen.

Combined oral contraceptives should be stopped at least six weeks before elective surgery and during immobilisation, e.g. after accidents etc.

Loestrin should be discontinued if the patient becomes jaundiced or has a significant rise in blood pressure.

Precautions: The pre-treatment and periodic physical examination should include special reference to breast and pelvic organs, including Papanicolaou smear since oestrogens have been known to produce tumours, some of them malignant in five species of subprimate animals.

Oestrogen-progestogen preparations should be used with caution in patients with a history of hypertension. Some women experience an increase in blood pressure following administration of contraceptive steroids. Pregnancy should be excluded before starting treatment.

Because these agents may cause some degree of fluid retention, patients with conditions which might be influenced by this such as epilepsy, migraine, asthma and cardiac or renal dysfunction, should be carefully observed.

A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Loestrin.

Under the influence of oestrogen-progestogen prep-

rations, pre-existing uterine fibroid myoma may increase in size.

The following conditions also require careful consideration: multiple sclerosis, porphyria, tetany, disturbed liver function, gallstones, cardiovascular disease, renal disease, chloasma, the wearing of contact lenses or any disease that is prone to worsen during pregnancy. The deterioration or first appearance of any of these conditions may indicate that the oral contraceptive should be stopped.

Loestrin may mask the onset of the climacteric.

The following laboratory results may be altered by the use of oral contraceptives: hepatic function (increased urobilinogen retention and other tests); thyroid function (thyroid-binding globulin, T3, T4 serum levels); haematological tests (increase in prothrombin factors II, VIII, IX, and X; decreased antithrombin; increased adrenalin-induced platelet aggregation); measurement of pregnanediol excretion (reduced). Therefore, if such tests are abnormal in a patient taking Loestrin, it is recommended that they be repeated after Loestrin has been withdrawn for two months.

The pathologist should be advised of the administration of Loestrin when relevant specimens are submitted.

Any possible influence of prolonged administration of Loestrin on pituitary, ovarian, adrenal, hepatic and uterine functions is unknown at present.

A small fraction of the hormonal agents in oral contraceptives have been identified in the milk of mothers receiving these drugs. The long range effect to the nursing infant is at present unknown.

Adverse effects: The following adverse effects which have been reported in patients receiving oral contraceptives are believed to be drug-related.

Nausea, vomiting, gastro-intestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhoea during and after treatment, oedema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight, cervical erosion and changes in cervical secretion, suppression of lactation when given immediately post-partum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure, depression, and thromboembolic disorders.

Although the following adverse effects have been reported in women taking oral contraceptives, an association has been neither confirmed nor refuted: prolonged amenorrhoea after discontinuing oral contraceptives, pre-menstrual like syndrome, headache, nervousness, dizziness, fatigue, cataract, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, haemorrhagic eruption and itching.

In most women the menstrual flow is reduced and occasionally may be missed altogether. This reduced flow is not normally indicative of pregnancy, particularly if the tablets have been taken correctly, but pregnancy should be ruled out before a new course of tablets is started.

Breakthrough bleeding happens more often in the first two or three cycles after starting the tablets. The patient should continue taking the tablets according to the schedule if breakthrough bleeding occurs. Probably it will amount to no more than spotting and will not last more than a day or two. If breakthrough bleeding is experienced after the third cycle, the patient should consult her physician.

Treatment of overdosage: The usual effects in children are nausea, and drowsiness. Slight vaginal bleeding

occasionally occurs in girls. In view of the low toxicity following overdosage with oral contraceptives, it is suggested that treatment should be conservative.

Clinical discussion: In view of the reports of thromboembolism following the use of oral contraceptives, the trend in prescribing has been towards avoiding formulations with high oestrogen content. Parke-Davis have developed this low dose formulation in which the ethinylloestradiol content is only 20 mcg in the expectation that the dosage may be less likely to give rise to thromboembolic disorders. Obviously it may take many years to establish this hypothesis.

Pharmaceutical precautions No special storage precautions.

Legal category POM.

Package quantities Available in packs of 21 tablets.

Further information Nil.

Product licence number 0018/0086.

PONSTAN® Capsules

(Mefenamic Acid Capsules BP)

PONSTAN® Paediatric Suspension

(Mefenamic Acid Suspension 50 mg/5 ml)

Presentation *Capsules:* An off-white powder in a No. 1 hard gelatin capsule with an ivory opaque body and aqua-blue opaque cap. Each capsule contains Mefenamic Acid BP 250 mg.

Paediatric Suspension: An off-white suspension, with a typical aroma and taste. Each 5 ml suspension contains Mefenamic Acid BP 50 mg.

Action Mefenamic acid is an analgesic with anti-inflammatory properties and a demonstrable antipyretic effect. It has also been shown to inhibit prostaglandin activity.

Indications 1. For the relief of mild to moderate pain including muscular, traumatic and dental pain, headaches of most aetiology, post operative and post partum pain; pyrexia in children.

2. For the relief of mild to moderate pain in rheumatoid arthritis (including Still's Disease) and osteoarthritis.

3. Menorrhagia due to dysfunctional causes and presence of an IUD when other pelvic pathology has been ruled out.

Dosage and administration Oral.

Adults: 2 capsules (500 mg) three times daily.

In menorrhagia to be administered on the first day of excessive bleeding and continued according to the judgement of the physician.

Children: It is recommended that children under 12 years of age should be given Ponstan Paediatric Suspension (50 mg/5 ml) in the following dosage regime.

Infants over 6 months – 25 mg/kg of body weight daily in divided doses, or

6 months–1 year – one 5 ml spoonful.

2 years–4 years – two 5 ml spoonfuls.

5 years–8 years – three 5 ml spoonfuls.

9 years–12 years – four 5 ml spoonfuls.

Dose may be repeated as necessary, up to three times daily.

Apart from the treatment of Still's Disease, therapy should not be continued for longer than seven days in children.

Contra-indications, warnings, etc Mefenamic acid is contra-indicated in inflammatory bowel disease and in patients suffering from peptic and/or intestinal ulceration, and in patients with renal or hepatic impairment.

Precautions: Safety in pregnancy has not been established. In patients suffering from dehydration and renal disease, particularly the elderly. Concurrent therapy with other plasma protein binding drugs may necessitate a modification in dosage. In the case of anticoagulants the dose of the anticoagulant may need to be reduced.

In menorrhagia lack of response should alert the physician to investigate other causes.

Warnings and adverse effects: Diarrhoea occasionally occurs following usual analgesic dosage of mefenamic acid and has been reported to have occurred within 24 hours of starting treatment. If diarrhoea occurs, the medication should be discontinued immediately. The patient so affected is usually henceforth unable to tolerate the drug without recurrence of diarrhoea.

Skin rashes have been observed following the administration of mefenamic acid and occurrence of a rash is a definite indication to withdraw medication.

As with other prostaglandin inhibitors allergic glomerulonephritis has occurred occasionally: non-oliguric renal failure has been reported on a few occasions in elderly patients with dehydration usually from diarrhoea. It has been suggested that the recovery is more rapid and complete than with other forms of analgesic induced renal impairment.

Rarely, thrombocytopenia has been reported with mefenamic acid.

In some cases reversible haemolytic anaemia has occurred. Temporary lowering of the white blood cell count which may have been due to mefenamic acid has been reported. Blood studies should therefore be carried out during long-term administration.

Bronchospasm may be precipitated in patients suffering from, or with a previous history of, bronchial asthma or allergic disease. Patients on prolonged therapy should also be kept under surveillance with particular attention to liver dysfunction. Should this appear it is an indication to discontinue therapy.

Drowsiness and dizziness have rarely been reported.

Note: A positive reaction in certain tests for bile in the urine of patients receiving mefenamic acid has been demonstrated to be due to the presence of the drug and its metabolites and not to the presence of bile.

Treatment of overdosage: Gastric lavage in the conscious patient and intensive supportive therapy where necessary. Activated charcoal has been shown to be a powerful adsorbent for mefenamic acid and its metabolites. Studies in experimental animals showed that a 5 to 1 ratio of charcoal to mefenamic acid resulted in considerable suppression of absorption of the drug.

Pharmaceutical precautions Store at a temperature not exceeding 30°C. Recommended diluent for Suspension – Syrup BP. When diluted use within 14 days of preparation.

Legal category POM.

Package quantities *Capsules:* Available in packs of 100 and 500.

Suspension: Available in packs of 125 ml.

Further information Nil.

Product licence numbers

Ponstan Capsules 0018/0094R

Ponstan Paediatric Suspension 0018/5025R

PONSTAN FORTE*

Presentation Yellow film-coated ovoid tablet.

Composition: Each tablet contains Mefenamic Acid BF 500 mg.

Action Mefenamic acid is an analgesic with anti-inflammatory properties. It has also been shown to inhibit prostaglandin activity.

Indications 1. For the relief of mild to moderate pain in rheumatoid arthritis (including Still's Disease) and osteoarthritis.

2. For the relief of mild to moderate pain including muscular, traumatic and dental pain, headaches of most aetiology, post-operative and post-partum pain.

3. Menorrhagia due to dysfunctional causes and presence of an IUD when other pelvic pathology has been ruled out.

Dosage and administration Oral.

Adults: 1 tablet (500 mg) three times daily.

In menorrhagia to be administered on the first day of excessive bleeding and continued according to the judgement of the physician.

Children: It is recommended that children under 12 years of age should be given Ponstan Paediatric Suspension (see Ponstan data sheet).

Contra-indications, warnings, etc Mefenamic acid is contra-indicated in inflammatory bowel disease and in patients suffering from peptic and/or intestinal ulceration, and in patients with renal or hepatic impairment.

Precautions: Safety in pregnancy has not been established. In patients suffering from dehydration and renal disease, particularly the elderly. Concurrent therapy with other plasma protein binding drugs may necessitate a modification in dosage. In the case of anticoagulants the dose of the anticoagulant may need to be reduced. In menorrhagia, lack of response should alert the physician to investigate other causes.

Warnings and adverse effects: Diarrhoea occasionally occurs following usual analgesic dosage of mefenamic acid and has been reported to have occurred within 24 hours of starting treatment. If diarrhoea occurs, the medication should be discontinued immediately. The patient so affected is usually henceforth unable to tolerate the drug without recurrence of diarrhoea.

Skin rashes have been observed following the administration of mefenamic acid and the occurrence of a rash is a definite indication to withdraw medication.

As with other prostaglandin inhibitors allergic glomerulonephritis has occurred occasionally: non-oliguric renal failure has been reported on a few occasions in elderly patients with dehydration usually from diarrhoea. It has been suggested that the recovery is more rapid and complete than with other forms of analgesic induced renal impairment.

Rarely, thrombocytopenia has been reported with mefenamic acid.

In some cases reversible haemolytic anaemia has occurred. Temporary lowering of the white blood cell count which may have been due to mefenamic acid has been reported. Blood studies should therefore be carried out during long-term administration.

Bronchospasm may be precipitated in patients suffering from, or with a previous history of, bronchial asthma or allergic disease.

Patients on prolonged therapy should also be kept under surveillance with particular attention to liver

dysfunction. Should this appear it is an indication to discontinue therapy.

Drowsiness and dizziness have rarely been reported.

Note: A positive reaction in certain tests for bile in the urine of patients receiving mefenamic acid has been demonstrated to be due to the presence of the drug and its metabolites and not to the presence of bile.

Treatment of overdose: Gastric lavage in the conscious patient and intensive supportive therapy where necessary. Activated charcoal has been shown to be a powerful adsorbent for mefenamic acid and its metabolites. Studies in experimental animals showed that a 5 to 1 ratio of charcoal to mefenamic acid resulted in considerable suppression of absorption of the drug.

Pharmaceutical precautions No special storage requirements.

Legal category POM.

Package quantities Available in packs of 50 and 100.

Further information Nil.

Product licence number 0018/0095R.

VIRA-A* ▼

Presentation An ophthalmic ointment.

Composition: Vira-A (Vidarabine) Ophthalmic Ointment contains: Vidarabine (9- β -D-arabinofuranosyladenine) 3% in a sterile, inert, petrolatum base.

Action Vira-A is a purine nucleoside which possesses antiviral activity. Vira-A possesses virostatic activity against the DNA family of viruses including herpes simplex (types I and II), varicella, vaccinia, and cytomegalovirus in both tissue culture and experimental animal infections.

Vira-A is rapidly metabolised to arabinosyl-hypoxanthine (Ara-Hx), the principal metabolite. Ara-Hx also possesses antiviral activity but it is significantly less than that of the parent compound. Following topical ocular administration in humans, trace amounts of both Vira-A and Ara-Hx can be detected in the aqueous humour only if the cornea is severely defective. If the cornea is intact, only trace amounts of Ara-Hx can be recovered from the aqueous humour.

Systemic absorption of Vira-A should not occur following ocular administration and swallowing tears from the lacrimal duct. In laboratory animals, Vira-A is rapidly deaminated in the gastro-intestinal tract to Ara-Hx. Vira-A interferes with corneal wound healing less than other forms of antiviral ocular chemotherapy such as idoxuridine.

Indications Vira-A Ophthalmic Ointment is indicated for the treatment of herpes keratoconjunctivitis manifested by dendritic keratitis or geographic corneal ulcers. The drug is effective against both fresh corneal lesions and those which have not responded to idoxuridine. Vira-A is also indicated in patients who have developed toxic or allergic reactions to idoxuridine. The diagnosis is established by finding the typical dendritic or geographic lesions on slit-lamp examination. Generally, an average of seven days' continuous therapy is required to achieve corneal re-epithelialisation of previously untreated lesions. Approximately 90% of treated eyes will re-epithelialise by the end of three weeks' therapy. Lesions which have not healed previously on idoxuridine require an average of 11 days to re-epithelialise. Approximately

75% of patients with idoxuridine-refractory lesions will heal by the end of four weeks of Vira-A therapy. Continuation of therapy for an additional seven days after corneal re-epithelialisation is recommended to prevent relapses of the infection.

Vira-A is less effective against stromal keratitis and uveitis as compared to epithelial disease secondary to the herpes virus.

Vira-A is not effective against RNA-virus and adenoviral ocular infections. It is also not effective against bacterial infections of the cornea or non-viral ulcers such as trophic or disciform keratitis.

Dosage The proper dose is to extrude one half inch of the ointment into the conjunctival sac five times daily until corneal re-epithelialisation has occurred. Treatment may then be continued at a reduced frequency, such as twice daily, for an additional seven days.

Contra-indications, warnings, etc Vira-A Ophthalmic Ointment is contra-indicated in patients who develop intolerance to it. The possibility of development of viral resistance to vidarabine cannot be ruled out. If there is no response after seven days' treatment, other forms of therapy should be considered.

Precautions: The diagnosis of herpes keratoconjunctivitis should be established clinically prior to prescribing Vira-A.

Vira-A parenterally is teratogenic in rats and mice. Typically, 10% Vira-A ointment applied to 10% of the body surface of rabbits during organogenesis induced foetal abnormalities. When 10% Vira-A ointment was applied to 2% to 3% of the body surface of rabbits, no foetal abnormalities were found. This dose greatly exceeds the total recommended human dose. Since a risk of producing foetal damage is present if Vira-A is administered to pregnant women, it should be used in women who are or may become pregnant only when it is clearly needed and the anticipated benefit to the patient outweighs this potential risk to the foetus.

It is not known whether Vira-A is secreted in human milk. As a general rule, nursing should not be undertaken while a patient is under treatment since many drugs are excreted in human milk. Patients should be forewarned that Vira-A, like any ophthalmic ointment, may produce a temporary visual haze.

Side-effects: Lacrimation, foreign body sensation, conjunctival injection, burning, irritation, superficial punctate keratitis, pain, photophobia, punctal occlusion, and sensitivity have been reported. The following have also been reported but appear disease-related: uveitis, stromal oedema, secondary glaucoma, trophic defects, corneal vascularisation, and hyphaemia.

Treatment of overdose: Acute massive overdose by oral ingestion of the ophthalmic ointment has not occurred. However, the rapid deamination to arabinosyl-hypoxanthine should preclude any serious consequences. The oral LD₅₀ for pure Vira-A is greater than 5,020 mg/kg in mice and rats. Thus, no untoward effects should result from ingestion of the entire contents of a tube (105 mg).

Ocular overdose is unlikely because any excess is quickly expelled from the conjunctival sac. Too frequent administration should be avoided.

Pharmaceutical precautions Store at a temperature not exceeding 30°C.

Legal category POM.

Package quantities Available in tubes of 3.5 g.

Further information Nil.

Product licence number 0018/0072.

VIRA-A* PARENTERAL ▼

Presentation An antiviral drug for intravenous administration only.

Composition: Vira-A (ara-A, vidarabine, adenine arabinoside) is a white crystalline solid with the empirical formula: $C_{10}H_{13}N_5O_4H_2O$. The molecular weight is 285.2; the solubility is 0.45 mg/ml at 25°C; and the melting point ranges from 260° to 270°C. The chemical name is 9-β-D-arabinofuranosyladenine.

Each ml of suspension contains 200 mg of vidarabine monohydrate equivalent to 187.4 mg of vidarabine. Each millilitre contains Pheneride* (benzethonium chloride), not more than 0.1 mg, as a preservative; disodium hydrogen phosphate, 0.957 mg, and sodium dihydrogen phosphate, 4.138 mg, as buffering agents. Hydrochloric acid may have been added to adjust pH.

Uses **Action:** Vira-A is a purine nucleoside obtained from fermentation cultures of *Streptomyces antibioticus*. Vira-A possesses *in vitro* and *in vivo* antiviral activity against herpes simplex types 1 and 2, varicella-zoster, and vaccinia viruses.

The antiviral mechanism of action has not yet been established. Vira-A appears to interfere with the early steps of viral DNA synthesis. Vira-A is rapidly deaminated to arabinosylhypoxanthine (Ara-Hx), the principal metabolite. Ara-Hx also possesses *in vitro* antiviral activity but this activity is significantly less than Vira-A.

Following IV administration, Vira-A is rapidly distributed into tissues and metabolised into Ara-Hx, resulting in low plasma levels of the parent compound. The Ara-Hx plasma levels reflect the rate of infusion, showing no accumulation with time. The mean half-life is 3.3 hours. Excretion is principally via the kidneys. Urinary excretion is constant over 24 hours. Forty-one to 53% of the daily dosage is recovered in the urine as Ara-Hx.

Indications and Usage: Varicella-zoster (herpes-zoster) infection: Vira-A is indicated in the treatment of varicella-zoster infections in the immunosuppressed patient, either localised or disseminated, and chickenpox in the immunosuppressed or immunocompromised patient. These infections are diagnosed by the typical clinical appearance. To be effective, Vira-A therapy should be initiated within six days of the onset of the disease, when new lesions are forming. The recommended dosage is 10 mg/kg/day intravenously for at least five days. Vira-A does not inhibit the rate of lesion crusting and scabbing.

Vira-A should only be administered to patients with serious varicella-zoster infections where the benefits clearly outweigh the risks.

Vira-A is not effective against RNA viral or adenoviral infections. It is also not effective against bacterial or fungal infections. There is no clinical data to indicate efficacy against cytomegalovirus, vaccinia, or variola infections.

Dosage and administration Important – the contents of the vial must be diluted prior to administration.

Method of Preparation: Each vial contains 200 mg of Vira-A per ml of suspension. The solubility of Vira-A in intravenous infusion fluids is limited. Each one mg of Vira-A requires 2.22 ml of intravenous infusion fluid for complete solubilisation. Therefore, each one litre of

intravenous infusion fluid will solubilise a maximum of 450 mg of Vira-A.

The following intravenous infusion fluids have been evaluated as being compatible with Vira-A Parenteral: 5% Dextrose Injection, 5% Dextrose and 0.33% Sodium Chloride Injection, 5% Dextrose and 0.45% Sodium Chloride Injection, 5% Dextrose and 0.9% Sodium Chloride Injection, Lactated Ringers Injection.

Vira-A has been shown to be pharmaceutically compatible with ampicillin, gentamicin and chloramphenicol.

Prepare the Vira-A solution for intravenous administration by aseptically transferring the proper dose of Vira-A into an appropriate intravenous infusion fluid. Shake the Vira-A vial well to obtain a homogeneous suspension before measuring and transferring. The intravenous infusion fluid used to prepare the Vira-A solution may be prewarmed to 35° to 40°C (95° to 100°F) to facilitate dissolution of the drug following its transference. Depending on the dose to be given, more than one litre of intravenous infusion fluid may be required. Thoroughly agitate the prepared mixture until *completely* clear. Complete dissolution of the drug, as indicated by a completely clear solution, is ascertained by careful visual inspection. Final filtration with an in-line membrane filter (0.45 µ or smaller) is recommended.

Once in solution, the drug has been found to be chemically stable at room temperature (below 86°F) for at least two weeks. However, as with all intravenous mixtures dilution should be made just prior to administration. Subsequent agitation, shaking, or inversion of the bottle is unnecessary once the drug is completely in solution.

Dosage: Chickenpox and localised or disseminated varicella-zoster - 10 mg/kg/day for at least five days.

Administration: Using aseptic technique, slowly infuse the total daily dose by intravenous infusion (prepared as discussed above) at a constant rate over a 12- to 24-hour period.

Rapid or bolus injections must be avoided.

Contra-indications, warnings, etc Vira-A is contra-indicated in patients who develop intolerance to it.

Vira-A must not be administered by the intramuscular or subcutaneous route due to the low solubility and poor absorption.

Precautions: Patients with impaired kidney function, such as following renal transplant, may have a slower rate of renal excretion of Ara-Hx. Therefore, the dosage of Vira-A may need to be adjusted according to the severity of impairment.

The volume of intravenous fluids necessary requires special care when administering Vira-A to patients susceptible to fluid overloading or cerebral oedema. Examples are patients with CNS infections and impaired renal function.

A platelet count and complete blood count are recommended during Vira-A administration since haemoglobin, haematocrit, white blood cells, and platelets may be depressed during therapy.

Because Vira-A is virostatic, some degree of immunocompetence must be present in order to achieve clinical response.

Usage in Pregnancy: Vira-A given parenterally is teratogenic in rats and rabbits.

Dosages of 5 mg/kg or higher given intramuscularly to pregnant rabbits during organogenesis induced foetal abnormalities. Dosages of 3 mg/kg or less did not induce teratogenic changes in pregnant rabbits. Vira-A doses

ranging from 30 to 250 mg/kg were given intramuscularly to pregnant rats during organogenesis; signs of maternal toxicity were induced at dosages of 100 mg/kg or higher and frank foetal abnormalities were found at dosages of 150 to 250 mg/kg.

A safe dose for the human embryo or foetus has not been established. Consequently, Vira-A should be used in pregnant patients only for life-threatening illnesses where the possible benefits to be derived outweigh the potential risks involved.

It is not known whether Vira-A is excreted in human milk. As a general rule, nursing should not be undertaken while a patient is under treatment because many drugs are excreted in human milk. If Vira-A is present in breast milk, it is unlikely that nursing infants would absorb appreciable amounts of drug because Vira-A is rapidly deaminated in the gastrointestinal tract.

Side-Effects: The principal side effects involve the gastrointestinal tract: anorexia, nausea, vomiting, and diarrhoea. In controlled and uncontrolled studies, the incidence of anorexia, nausea, vomiting, and/or diarrhoea was 14% in a dosage range of 10 to 15 mg/kg/day. These reactions are mild to moderate and seldom require termination of Vira-A.

CNS disturbances have been occasionally reported at therapeutic dosages. These are: tremor (1.8%), dizziness, hallucinations, confusion, psychosis, and ataxia.

Haematological clinical laboratory changes noted in controlled and uncontrolled studies were, a decrease in haemoglobin or haematocrit (16.5%), white blood cell count (6.8%), and platelet count (6.9%). SGOT elevations were observed in 6.6%. Other changes occasionally observed were decreases in reticulocyte count and elevated bilirubin.

Other symptoms reported were: weight loss, malaise, pruritus, rash, haematemesis, and pain at injection site.

Treatment of overdose: Acute massive overdose of the intravenous form has not been reported. Acute water overloading would pose a greater threat to the patient than Vira-A, due to its low solubility. Dosages of Vira-A two to three times the antiviral dosages can produce haematopoietic depression, principally thrombocytopenia. If a massive overdose of the intravenous form occurs, haematological, liver, and renal functions should be observed.

Acute massive oral ingestion should not be toxic because drug absorption from the gastrointestinal tract is minimal. The oral LD₅₀ for Vira-A is greater than 5,020 mg/kg in mice and rats.

Pharmaceutical precautions Store in a cool place, below 30°C (86°F). Protect from freezing. Shake well before diluting.

Legal category POM.

Package quantities Vials of 5 ml containing 200 mg/ml vidarabine monohydrate in the form of a sterile suspension. 10 × 5 ml vials per pack.

Further information Nil.

Product licence number 0018/0073.

VI-SIBLIN*

Presentation Brown Granules. Ispaghula Husks BP (obtained from *Plantago ovata*) 66.0%.

Action Plantago absorbs and retains 30 times its own volume of water and is therefore used as a bulk laxative.

Indications For the treatment of chronic constipation.

Dosage and administration Oral.

Adults: Two 5 ml spoonfuls with a glassful of water one or more times daily.

Children: None.

Contra-indications, warnings, etc Intestinal obstruction has been reported after the administration of bulk-forming agents. Patients who have difficulty swallowing should be warned not to take these preparations dry, and generous quantities of water should accompany the administration.

Treatment of overdose: None.

Pharmaceutical precautions No special storage precautions.

Legal category GSL.

Package quantities Available in packs containing 250 g.

Further information Nil.

Product licence number 0018/5063.

ZARONTIN*

Presentation Zarontin Syrup (Ethosuximide Elixir BP) is a clear red, raspberry-flavoured syrup. Each 5 ml contains Ethosuximide BP 250 mg.

Zarontin Capsules (Ethosuximide Capsules BP) are orange, 8 mm, oblong soft gelatin capsules containing a clear liquid and printed 'P-D' in ivory ink. Each capsule contains Ethosuximide BP 250 mg.

Action Ethosuximide suppresses the paroxysmal spike and wave pattern common to petit mal seizures. The frequency of epileptiform attacks is reduced, apparently by depression of the motor cortex and elevation of the threshold of the central nervous system to convulsive stimuli. Compared with other succinimide anticonvulsants, ethosuximide is more specific for pure petit mal.

Indications Primarily useful in petit mal epilepsy. When grand mal and other forms of epilepsy co-exist with petit mal, Zarontin may be administered in combination with other anticonvulsants such as phenobarbitone, Epanutin* (Phenytoin Sodium Ph Eur) and primidone.

Dosage and administration Oral.

Adults and children over 6 years: initially 2 capsules or two 5 ml spoonfuls daily and adjusted thereafter to the patient's needs; daily dosage should be increased by small increments, for example, by 1 capsule or 5 ml every four to seven days, until control is achieved with minimal side-effects; although 4–6 capsules or 20–30 ml daily in divided doses often produce control of seizures, 7–8 capsules or 35–40 ml daily is not an unusual requirement.

Children and infants under 6 years: The initial dose is 5 ml daily which is adjusted by small increments until control is achieved with minimal side-effects.

Contra-indications, warnings, etc Hypersensitivity to succinimides.

There is some evidence that the succinimides may produce congenital abnormalities in the offspring of a small number of epileptic patients, and therefore they should only be used in pregnancy if in the judgement of

the physician the potential benefits outweigh the risk. Ethosuximide may be excreted in breast milk. Zaronitin should be used with caution in patients with impaired hepatic or renal function.

Mild side-effects, which are usually transient, may occur initially. These include apathy, drowsiness, depression, mild euphoria, headache, ataxia, dizziness, anorexia, gastric upset, nausea and vomiting. Psychotic states thought to be induced or exacerbated by anticonvulsant therapy have been reported. Skin rashes have been seen in a few patients. Haematological reactions to ethosuximide appear to be uncommon. Cases of leucopenia, agranulocytosis and aplastic anaemia have been reported. The extent to which ethosuximide is implicated in these reactions is yet to be determined. Monocytosis, leucocytosis and transitory mild eosinophilia have also been noted. In most cases of leucopenia, the blood picture has been restored to normal on reduction of the dosage or discontinuation of the drug. Where leucopenia has occurred with other drugs, the polymorph count has in some cases increased steadily after starting treatment with ethosuximide and discontinuing previous medication. If the patient has been receiving other anticonvulsants the sudden withdrawal of the drugs may precipitate a series of attacks before Zaronitin has been given in sufficient amounts to exercise control. This may

be avoided by gradually replacing with Zaronitin the anticonvulsant previously used.

Treatment of overdosage: If less than 2 g have been taken, fluids should be given by mouth. If a larger dose has been taken the stomach should be emptied, respiration maintained and any other symptoms treated accordingly.

Pharmaceutical precautions *Capsules:* Store at a temperature not exceeding 30°C.

Syrup: Store at a temperature not exceeding 25°C.

Recommended diluent – Syrup BP. When diluted use within 14 days of preparation.

Legal category POM.

Package quantities *Capsules 250 mg:* 50 and 500.
Syrup: 250 ml.

Further information Nil.

Product licence numbers

Zaronitin Syrup	0018/5040
Zaronitin Capsules	0018/0078

*Trade Mark



ALEXAN* INJECTABLE SOLUTION ▼

Presentation Alexan (cytarabine) is available as an isotonic solution in ampoules ready for injection. Ampoules contain either 2 ml or 5 ml of a solution of 20 mg/ml cytarabine.

Uses Alexan is a cytostatic agent for induction of clinical remission and/or maintenance therapy in patients with:

Acute myeloid leukaemia
Acute non-lymphoblastic leukaemias
Acute lymphoblastic leukaemias
Blast crises of chronic myeloid leukaemia
Diffuse histiocytic lymphomas (non Hodgkin's lymphomas of high malignancy)

Dosage and administration Alexan is administered by continuous intravenous infusion, intravenous injection, intrathecal injection, intramuscular or subcutaneous injection. Due to the short half-life of cytarabine, use of a rapid i.v. injection will result, in most patients, in a plasma concentration below the minimal therapeutic level in less than one hour. If it is desirable to give a rapid i.v. injection then it is necessary to divide the daily recommended dosage into two or more administrations at equal time intervals.

To prepare an infusion solution, Alexan can be added to physiological saline or 5% aqueous glucose.

Continuous infusions have ranged from 8–12 hours to 120–168 hours. In comparison with single i.v. injections, continuous infusions of the same dosage show more pronounced side effects on the gastrointestinal tract. Intrathecal, lumbar or intraventricular administration of Alexan can be carried out with the original solution. It is recommended that 5–8 ml of cerebrospinal fluid (CSF) be drawn up, mixed with the injection solution in the syringe and slowly re-injected. Systemic toxicity is not to be expected using this route of administration.

Intramuscular and subcutaneous injections are usually only used in maintenance therapy. Intra-cutaneous injections should be avoided due to the risk of oedema.

Effective cytotoxic plasma levels may be expected to lie in the range 0.01–0.15 mcg/ml.

The dosage required should be as exact as possible for each individual and is best calculated according to body surface area. Unless otherwise indicated in special combinations Alexan should be used in the following doses:

Remission Induction Therapy:

Acute leukaemias: 100–200 mg/m²/day or 3–6 mg/kg/day

Current medical practice recommends 100 mg/m² twice daily when rapid intravenous injection is used. However, when continuous infusion is employed 100 mg/m²/day is recommended as a starting dose. The duration will depend on clinical and morphological (bone marrow) findings.

Either Treat the patient for up to seven days and allow 7–14 days treatment free to allow the bone marrow to recover before applying consolidation cycles (often of reduced duration of treatment) until remission or toxicity occurs.

or Continue to treat the patient until the appearance of bone marrow hypoplasia which may be considered a tolerance limit. Before repeating the therapy cycle (often of reduced duration) a treatment free period of at least 14 days should elapse or until the bone marrow has recovered. For remission induction therapy patients should be supervised in a centre with laboratory and supportive resources sufficient to monitor drug tolerance and protect and maintain a patient compromised by drug toxicity.

Remission Maintenance: Leukaemias: 75–100 mg/m²/day or 1.5–3 mg/kg/day for five consecutive days once a month or one day each week. CNS leukaemias: 10–30 mg/m² three times weekly intrathecally. Lymphomas: These conditions are normally treated with a suitable combination of agents.

Contra-indications, warnings, etc

Contra-indications: Patients who already have bone marrow suppression should be excluded from treatment with Alexan unless the clinician considers such a course vital in the patient's interest.

Warnings: Hyperuricaemic prophylaxis is an absolute requirement, particularly in patients with high blast counts with acute monoblastic leukaemia or with large tumour masses. The clinician should monitor the patient's blood uric acid level and be prepared to use such supportive and pharmacological measures as might be necessary to control this problem. Because of the possible teratogenic effect of cytarabine on male and female germ cells adequate conception control should be established during, and for a sufficient period after, treatment.

To minimise the risks associated with remission induction therapy (granulocytopenia and associated infection, haemorrhage secondary to thrombocytopenia) Alexan should only be used in centres where adequate supportive therapy is available. Cytarabine has also been reported to cause chromosome breaks in human leucocytes in vitro. It inhibits DNA synthesis in mammalian cell cultures. These factors should be considered in long term administration.

Use in Pregnancy: Alexan is known to be teratogenic in some animal species and should be used in women who are or who may become pregnant only after due consideration of the benefit/risk potential.

The use of Alexan in nursing mothers is not recommended.

Precautions: Alexan is a potent bone marrow suppressant. During induction therapy patients should be closely supervised and leucocyte and platelet counts performed daily. Remission maintenance may be carried out under

out-patient conditions but effects on the blood picture and bone marrow must be carefully monitored. If the platelet count falls below 50,000/cu.mm. or the leucocyte count falls below 1,000/cu.mm. suspension or modification of therapy should be considered. The blood count may continue to fall following discontinuation of Alexan. Treatment may be recommenced if indicated, when bone marrow recovery is confirmed by bone marrow biopsy.

Haemopoietic, renal and hepatic function should be regularly monitored.

Side Effects: With high dosage continuous infusion (more than 200 mg/m²/day) over 5–7 days the gastrointestinal complications are more pronounced and can exceptionally lead to paralytic ileus.

The following may also occur during treatment with Alexan: bone marrow suppression (such as thrombocytopenia, leucopenia, anaemia), megaloblastosis, immunosuppression, nausea, vomiting, diarrhoea, oral inflammation or ulceration, fever, pneumonia, anorexia, hepatic dysfunction.

Pharmaceutical precautions Store below 15°C.

Legal category POM.

Package quantities Alexan is a solution (20 mg/ml) ready prepared for use.

It is packed as:

2 ml ampoule (40 mg cytarabine) in packs of 10.
5 ml ampoule (100 mg cytarabine) in packs of 10.

Further information There is extensive literature available on the effectiveness of cytarabine both alone and in combination with other agents in the treatment of conditions for which it is indicated.

Product licence number 0057/0190.

ATARAX*

Presentation Atarax brand of hydroxyzine hydrochloride is available as:

10 mg sugar-coated tablets, coloured orange and coded on one side with 'Pfizer'.

25 mg sugar-coated tablets, coloured green and coded on one side with 'Pfizer'.

Syrup 10 mg/5 ml clear, flavoured with sugar, peppermint, spearmint and caramel.

Uses **Actions:** Atarax is rapidly absorbed from the gastro-intestinal tract and its effects are usually noted within 15 to 30 minutes after oral administration.

Atarax is unrelated chemically to phenothiazine, reserpine and meprobamate. Atarax has demonstrated its clinical effectiveness in the management of neuroses and emotional disturbances manifested by anxiety, tension, agitation, apprehension or confusion.

Atarax has been shown clinically to be a rapid-acting true ataractic with a wide margin of safety. It induces a calming effect in anxious, tense, psychoneurotic adults and also in anxious, hyperkinetic children without impairing mental alertness. It is not a cortical depressant,

but its action may be due to a suppression of activity in certain key regions of the subcortical area of the central nervous system.

Primary skeletal muscle relaxation has been demonstrated experimentally. Secondary skeletal muscle relaxation due to ataraxia should be regarded as additive to this primary effect.

Atarax has been shown experimentally to have antispasmodic properties, apparently mediated through interference with the mechanism that responds to spasmogenic agents such as serotonin, acetylcholine and histamine. Antihistamine effects have been demonstrated experimentally and confirmed clinically.

An antiemetic effect, both by the apomorphine test and the veriloid test, has been demonstrated.

Indications: Atarax is indicated in the management of anxiety, tension and psychomotor agitation in conditions of emotional stress.

Atarax is also useful in alleviating the manifestations of anxiety and tension in situations in which the causative stress is temporary, as in the preparation for dental and other minor surgical procedures and in acute emotional problems. It has also been recommended for the management of anxiety associated with organic disturbances such as digestive disorders, dermatoses, senility, the menopausal syndrome and behaviour problems in children. In addition, it has been recommended as adjunctive therapy in alcoholism, and allergic conditions with strong emotional overlay, as in asthma, chronic urticaria and pruritus.

The efficacy of Atarax as adjunctive pre- and post-operative sedative medication has also been well established, especially as regards its ability to allay anxiety, control emesis and reduce the amount of narcotic required. Neither atropine nor the cardiac glycosides are affected by Atarax.

Dosage and administration Dosage varies with individual requirements and ranges from 25 mg t.i.d. to 100 mg q.i.d. The usual children's dose is as follows:

Under 6 years: 30–50 mg daily in divided doses.

Over 6 years: 50–100 mg daily in divided doses.

As with all potent medications, the dosage should be adjusted according to the patient's response to therapy.

Contra-indications, warnings, etc

Contra-indications: Atarax is contra-indicated in patients who have shown a previous hypersensitivity to it.

Warnings: Atarax may potentiate the action of central nervous system depressants. If central nervous system depressants and Atarax are used concurrently, then dosage should be reduced.

Side-effects: No serious side-effects have been reported and confirmed in the administration of Atarax to date. Therapeutic doses of Atarax seldom produce impairment of mental alertness. However, drowsiness may occur; if so, it is usually transitory and may disappear in a few days of continued therapy or upon reduction of the dose. Dryness of the mouth may be encountered at higher doses.

Extensive clinical use has substantiated the absence of toxic effects on the blood or liver when administered in the recommended doses for over four years of uninterrupted therapy. The absence of adverse effects has been further demonstrated in experimental studies in which excessively high doses were administered.

Involuntary motor activity, including rare instances of tremor and convulsions, has been reported, usually with doses considerably higher than those recommended. Continuous therapy with over 1 g per day has been employed in some patients without these effects having been encountered. Pharmacological and clinical studies indicate that Atarax in therapeutic dosage does not increase gastric secretion or acidity and in most cases provides mild antisecretory benefits.

Use in pregnancy: Atarax, when administered to the pregnant mouse, rat and rabbit, induced foetal abnormalities in the rat at doses substantially above the human therapeutic range. Clinical data in human beings are inadequate to establish safety in early pregnancy. Until such data are available, Atarax should be used in pregnancy only when in the judgement of the physician the expected benefits outweigh the potential hazards to the mother and the foetus.

Overdosage: Gastric lavage. Sedation with paraldehyde or sodium phenobarbitone intramuscularly if marked CNS irritation.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities *Tablets 10 mg:* Packs of 100.
Tablets 25 mg: Packs of 100.
Syrup: Bottle of 150 ml.

Further information Nil.

Product licence numbers

Tablets 10 mg 0057/5003
Tablets 25 mg 0057/5004
Syrup 0057/5005

DELTACORTRIL* 'ENTERIC'

Presentation Deltacortril 'Enteric' tablets 2.5 mg uniformly brown in colour and coded 'Pfizer'.

Deltacortril 'Enteric' tablets 5 mg uniformly red in colour and coded 'Pfizer'.

Deltacortril is the synthetic crystalline steroid prednisolone.

Deltacortril 'Enteric' offers prednisolone in a specially balanced enteric coating which keeps the steroid from contact with the stomach and allows the tablet to disintegrate immediately on entering the jejunum.

Uses **Actions:** Naturally occurring glucocorticoids (hydrocortisone and cortisone) which possess salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. Their synthetic analogues are primarily used for their potent anti-inflammatory effects in disorders of many organ systems.

Deltacortril (prednisolone) is a synthetic steroid with powerful anti-inflammatory hormonal and metabolic effects similar to those of hydrocortisone. Deltacortril (prednisolone) has four times the glucocorticoid potency of hydrocortisone, with a lesser tendency to cause sodium retention.

Glucocorticoids cause profound and varied metabolic effects. In addition, they modify immune responses of the body to diverse stimuli.

Indications: **Endocrine disorders:** Primary or secondary adrenocortical insufficiency. (Hydrocortisone or cortisone is the drug of choice; synthetic analogues may be

used in conjunction with mineralocorticoids where applicable; in infancy mineralocorticoid supplementation is of particular importance.)

Congenital adrenal hyperplasia.

Non-suppurative thyroiditis.

Hypercalcaemia associated with cancer.

Rheumatic disorders: As adjunctive therapy for short-term administration (during an acute episode or exacerbation) in:

Psoriatic arthritis.

Rheumatoid arthritis (selected cases may require low-dose maintenance).

Acute gouty arthritis.

Ankylosing spondylitis.

Acute and subacute bursitis.

Juvenile rheumatoid arthritis.

Collagen diseases: Systemic lupus erythematosus.

Dermatomyositis.

Periarteritis nodosa.

Systemic sclerosis.

Acute rheumatic carditis.

Dermatological diseases: Pemphigus.

Bullous dermatitis herpetiformis.

Severe erythema multiforme (Stevens-Johnson syndrome).

Exfoliative dermatitis.

Mycosis fungoides.

Severe psoriasis.

Allergic states: Control of severe or incapacitating allergic conditions refractory to adequate trials of conventional treatment.

Seasonal or perennial allergic rhinitis.

Bronchial asthma.

Contact dermatitis.

Atopic dermatitis.

Serum sickness.

Angio-neurotic oedema.

Urticaria.

Ophthalmic diseases: Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as:

Allergic conjunctivitis.

Keratitis.

Allergic corneal marginal ulcers.

Herpes zoster ophthalmicus.

Iritis and iridocyclitis.

Chorioretinitis.

Anterior segment inflammation.

Diffuse posterior uveitis and choroiditis.

Optic neuritis.

Sympathetic ophthalmia.

Respiratory diseases: Symptomatic sarcoidosis.

Loeffler's syndrome not manageable by other means.

Fulminating or disseminated pulmonary tuberculosis when accompanied by appropriate antituberculous chemotherapy.

Berylliosis.

Pulmonary emphysema where bronchospasm or bronchial oedema plays a significant role.

Diffuse interstitial pulmonary fibrosis (Hamman-Rich syndrome).

Haematological disorders: Autoimmune haemolytic anaemia.

Idiopathic and secondary thrombocytopenia in adults.

Erythroblastopenia (RBC anaemia).

Congenital (erythroid) hypoplastic anaemia.

Gastro-intestinal diseases: To assist the patient during a critical period of disease in:

- Ulcerative colitis.
- Regional ileitis.

Neoplastic diseases: For palliative management of:

- Leukaemias and lymphomas in adults.
- Acute leukaemia of childhood.

Oedematous states: To induce a diuresis or remission of proteinuria in nephrotic syndrome, without uraemia, of the idiopathic type or that due to lupus erythematosus.

In conjunction with diuretic agents, to induce a diuresis in cirrhosis of the liver with refractory ascites.

Miscellaneous: Tuberculous meningitis with subarachnoid block or impending block when accompanied by appropriate antituberculous chemotherapy.

Dosage and administration The initial dosage of Deltacortril 'Enteric' tablets may vary from 5–60 mg daily depending on the specific disease entity being treated. In situations of less severity, lower doses will generally suffice while in selected patients higher initial doses may be required. The initial dosage should be maintained or adjusted until a satisfactory response is noted. If after a reasonable period of time there is a lack of satisfactory clinical response, Deltacortril 'Enteric' tablets should be discontinued and the patient transferred to other appropriate therapy. It should be emphasised that dosage requirements are variable and must be individualised on the basis of the disease under treatment and the response of the patient. After a favourable response is noted, the proper maintenance dosage should be determined by decreasing the initial drug dosage in small amounts at appropriate time intervals until the lowest dosage which will maintain an adequate clinical response is reached. Constant monitoring is needed in regard to drug dosage. Included in the situations which may make dosage adjustments necessary are changes in clinical status secondary to remissions or exacerbations in the disease process, the patient's individual drug responsiveness and the effect of patient exposure to stressful situations not directly related to the disease entity under treatment. In this latter situation, it may be necessary to increase the dosage of Deltacortril 'Enteric' tablets for a period of time consistent with the condition of the patient. If after long-term therapy the drug is to be stopped, it is recommended that it be withdrawn gradually rather than abruptly.

Contra-indications, warnings, etc

Contra-indications: Systemic fungal infections.

Warnings: Deltacortril should be used with great caution in the presence of a diminished cardiac reserve or congestive heart failure, diabetes mellitus, infectious diseases, chronic renal failure, uraemia and in elderly persons.

Patients on corticosteroid therapy subjected to unusual stress require increased dosage before, during and after the stressful situation.

Corticosteroids may mask some signs of infection and new infections may appear during their use. There may be decreased resistance and inability to localise infection when corticosteroids are used.

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, salt and water retention and increased excretion of potassium. These effects are less likely to occur with the synthetic derivatives except when used in large doses. Dietary salt

restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

While on corticosteroid therapy, patients should not be vaccinated against smallpox. Other immunisation procedures should not be undertaken in patients who are on corticosteroids, especially on high dose, because of possible hazards of neurological complications and a lack of antibody response.

The use of Deltacortril in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate antituberculous regimen.

Use in pregnancy: Since adequate human reproduction studies of corticosteroids are not available, the use of these drugs in pregnancy, nursing mothers or women of childbearing potential requires that the possible benefits of the drug be weighed against the potential hazards to the mother and foetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Precautions: Drug-induced secondary adrenocortical insufficiency may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy, therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis.

Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.

The lowest possible dose of corticosteroid should be used to control the condition under treatment, and when reduction in dosage is possible, the reduction should be gradual.

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes and severe depression, to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinaemia.

Steroids should be used with caution in non-specific ulcerative colitis, if there is a probability of impending perforation, abscess or other pyogenic infection and also in diverticulitis, fresh intestinal anastomoses, active or latent peptic ulcer, renal insufficiency, hypertension, osteoporosis and myasthenia gravis.

Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.

Adverse reactions: The following reactions have been reported with the use of corticosteroids:

Fluid and electrolyte disturbances:

- Sodium retention.
- Fluid retention.
- Congestive heart failure in susceptible patients.
- Potassium loss.
- Hypokalaemic alkalosis.
- Hypertension.

Musculoskeletal: Muscle weakness.

- Steroid myopathy.
- Loss of muscle mass.
- Osteoporosis.
- Vertebral compression fractures.
- Aseptic necrosis of femoral and humeral heads.
- Pathological fracture of long bones.

Gastro-intestinal: Peptic ulcer with possible subsequent perforation and haemorrhage.

- Pancreatitis.
- Abdominal distension.
- Ulcerative oesophagitis.

Dermatological: Hirsutism.

- Impaired wound healing.
- Thin fragile skin.
- Petechiae and ecchymoses.
- Facial erythema.
- Increased sweating.
- May suppress reactions to skin tests.

Neurological: Convulsions.

Increased intracranial pressure with papilloedema (pseudo-tumour cerebri) usually after cessation/reduction of treatment.

- Vertigo.
- Headache.

Endocrine: Menstrual irregularities.

Development of Cushingoid state.
Suppression of growth in children.
Secondary adrenocortical and pituitary unresponsive-ness, particularly in times of stress, as in trauma, surgery or illness.

- Decreased carbohydrate tolerance.
- Manifestations of latent diabetes mellitus.
- Increased requirements for insulin or oral hypoglycaemic agents in diabetics.

Ophthalmic: Posterior subcapsular cataracts.

- Increased intraocular pressure.
- Glaucoma.
- Exophthalmos.

Metabolic: Negative nitrogen balance due to protein catabolism.

Overdose: Treat symptomatically with attention to serum electrolytes.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Deltacortril 'Enteric' tablets 2.5 mg and 5 mg, Packs of 100 and 500.

Further information Nil.

Product licence numbers

- 2.5 mg tablets 0057/5012
- 5 mg tablets 0057/0128

DIABINESE®

Presentation Diabinese brand of chlorpropamide is available as a white scored tablet in two different strengths:

- Diabinese 100 mg tablet ($\frac{3}{32}$ " diameter) coded DIA/100 on the one side and 'Pfizer' on the other.
- Diabinese 250 mg tablet ($\frac{3}{8}$ " diameter) coded DIA/250 on the one side and 'Pfizer' on the other.

Diabinese is classified as an arylsulphonylurea.

Uses Actions: Diabinese is absorbed rapidly from the gastro-intestinal tract. Within one hour after a single oral dose, it is readily detectable in the blood, and the level reaches a maximum within two to four hours. It is slowly excreted in the urine, for the most part as unchanged Diabinese. The biological half-life of Diabinese averages about 36 hours. Within 96 hours, 80–90% of a single oral dose is excreted in the urine. However, long-term administration of therapeutic doses does not result in undue accumulation in the blood, since absorption and excretion rates become stabilised in about five to seven days after the initiation of therapy.

Diabinese exerts a hypoglycaemic effect in normal humans within one hour, becoming maximal at three to six hours and persisting for at least 24 hours. The potency of Diabinese is approximately six times that of tolbutamide. Some experimental results suggest that its increased effectiveness may be the result of slower excretion and absence of significant deactivation.

The mode of action of Diabinese is believed to be that of stimulation of synthesis and release of endogenous insulin.

There is now evidence that improvement in pancreatic beta cell function, with consequent improvement in glucose tolerance, may occur with prolonged administration of Diabinese. Accordingly, in individuals with asymptomatic diabetes mellitus, principally manifested by an abnormal glucose tolerance, continuous use of Diabinese may result in 'normalisation' of their tolerance to glucose.

Diabinese does not interfere with the usual tests to detect albumin in the urine.

Indications: Diabinese is an oral hypoglycaemic agent. The precise mechanism of action is not completely understood but it is not an oral insulin.

Diabinese is a potent, active, oral hypoglycaemic agent indicated for the treatment of selected diabetic patients. It is generally used alone to control the mild to moderately severe maturity-onset, stable diabetic. While Diabinese is a sulphonamide derivative, it is devoid of antibacterial activity.

Diabinese is indicated in uncomplicated diabetes mellitus of the stable, mild or moderately severe, non-ketotic, maturity-onset type, which cannot be completely controlled by diet alone. It can often be used in patients of this type in place of insulin.

It may also prove effective in controlling certain patients who have shown an inadequate response or true primary or secondary failure to other sulphonylurea agents. In patients requiring high doses or frequent administration of another oral agent, control may be facilitated through its use.

Patient selection: The most likely patient for therapy is one in whom diabetes is of the maturity-onset type, stable, and not controllable by dietary regulation alone. A past history of diabetic coma does not necessarily preclude successful therapeutic control with Diabinese. A trial period may be indicated in certain patients who might be expected to respond to this type of medication, but who failed in initial trials with, or after having been on other oral sulphonylurea agents, or in patients whose diabetic control on such agents has not been satisfactory. Diabinese may prove effective and provide improved control of the diabetes. The final evaluation of response in patients who qualify as candidates for Diabinese is a therapeutic trial for a period of at least seven days. During the trial period, the absence of ketonuria together with a satisfactory reduction of glycosuria and hypergly-

caemia, or maintenance of previously satisfactory control, indicates that the patient is responsive and amenable to control with the drug. However, the development of ketonuria within 24 hours after withdrawal of insulin usually will be indicative of a poor response. The patient is considered non-responsive if he fails to achieve satisfactory lowering of blood sugar levels or fails to obtain objective or subjective clinical improvement and if he develops ketonuria or glycosuria. Insulin is indicated for the therapy of such patients.

Concurrent Diabinese – Biguanide therapy: The concurrent use of Diabinese with biguanide (phenformin, metformin) is indicated in the treatment of uncomplicated diabetes mellitus of the stable, non-ketotic, maturity-onset or adult type, which cannot be controlled by diet alone, by diet and insulin, or by diet and sulphonylurea agents. The appropriate biguanide data sheet should be consulted for complete details of patient selection, indications, warnings, and dose.

Diabinese in diabetes insipidus: Limited studies to date have shown that Diabinese is also useful in the treatment of idiopathic diabetes insipidus. In using Diabinese for this purpose, the physician must remain constantly aware of the possible occurrence of hypoglycaemic reactions in such individuals, particularly when unrelated illness, or other causes, reduce food intake. When Diabinese must be temporarily discontinued in such cases, therapy with antidiuretic hormone should be substituted.

In the treatment of diabetes insipidus, daily dosage has been in the range of 100–500 mg daily for older children and adults. Because of the risk of hypoglycaemia that can develop in these individuals, it is desirable to start therapy at the lower range, gradually adjusting the dose as indicated. Patients, and particularly the parents of children who are patients, should be warned of the possibility and treatment of hypoglycaemic reactions, especially during inter-current infections or other periods of impaired food intake. In such circumstances, Diabinese therapy should be promptly discontinued and the patient's physician contacted. When physicians are considering Diabinese for the treatment of diabetes insipidus, it is essential that they read this Data Sheet completely and particularly those paragraphs relating to Precautions and Adverse Reactions.

Dosage and administration The total daily dosage is generally taken as a single dose each morning with breakfast. A loading or priming dose is not necessary and should not be used. The occasional case of gastrointestinal intolerance may be relieved by dividing the daily dosage.

Initial therapy: The mild to moderately severe, middle-aged, stable diabetic patient should be started on 250 mg daily. Because the geriatric diabetic patient appears to be more sensitive to the hypoglycaemic effect of sulphonylurea drugs, older patients should be started on smaller amounts of Diabinese, in the range of 100–125 mg daily.

No transition period is necessary when transferring patients from other oral hypoglycaemic agents to Diabinese. The other agent may be discontinued abruptly and Diabinese started at once. In prescribing Diabinese, due consideration must be given to its greater potency.

The large majority of mild to moderately severe middle-aged, stable diabetic patients receiving insulin can be placed directly on the oral drug and their insulin abruptly discontinued. For patients requiring more than 40 units of insulin daily, therapy with Diabinese may be initiated

with a 50% reduction in insulin for the first few days, with subsequent further reductions dependent upon the response.

During the insulin withdrawal period, the patient should test his urine for sugar and ketone bodies at least three times daily and report the results frequently to his physician. If they are abnormal, the physician should be notified immediately. In some cases, it may be advisable to consider hospitalisation during the transition period.

Five to seven days after the initial therapy, the blood level of Diabinese reaches a plateau. Dosage may subsequently be adjusted upward or downward by increments of not more than 50–125 mg at intervals of three to five days to obtain optimal control. More frequent adjustments are usually undesirable.

Maintenance therapy: Most moderately severe, middle-aged stable diabetic patients are controlled by approximately 250 mg daily. Many investigators have found that some milder diabetics do well on daily doses of 100–125 mg or less. Many of the more severe diabetics may require 500 mg daily for adequate control. Patients who do not respond completely to 500 mg daily will usually not respond to higher doses. Maintenance doses above 500 mg should be avoided.

Diabinese/Phenformin dosage: The dosage of Diabinese should be maintained at or increased to 500 mg. If control is still inadequate, phenformin may be added in accordance with the dosage recommendation appearing in the phenformin data sheet. In no case should the daily dose of phenformin exceed 100 mg.

If adequate control is obtained without side-effects, reduction in dosage of both Diabinese and phenformin should be undertaken slowly (reducing the dosage of one drug at a time) in an attempt to maintain control with the least possible medication.

Diabinese/Metformin dosage: The dosage of Diabinese should be maintained at or increased to 500 mg. If control is still inadequate, metformin may be added at a dosage of 0.5 g b.i.d., increasing by 0.5 to 1.0 g every one to two weeks to a maximum of 3 g daily.

If adequate control is obtained without side-effects, reduction in dosage of both Diabinese and metformin should be undertaken slowly (reducing the dosage of one drug at a time) in an attempt to maintain control with the least possible medication.

Contra-indications, warnings, etc Use of Diabinese is not indicated in patients having:

Juvenile or growth-onset diabetes mellitus.

Severe or unstable 'brittle' diabetes.

Diabetes complicated by ketosis and acidosis, diabetic coma, major surgery, severe infection, or severe trauma.

Diabinese is contra-indicated in patients with serious impairment of hepatic, renal or thyroid function.

Use in pregnancy: Diabinese is contra-indicated during pregnancy. Safe conditions for the use of Diabinese in pregnancy have not been established and serious consideration should be given to the potential hazard of its use in women of childbearing age who may become pregnant.

Precautions: Since animal studies suggest that the action of barbiturates may be prolonged by therapy with Diabinese, barbiturates should be employed with caution. Similarly, studies showing an exaggerated hypoglycaemic effect of Diabinese in adrenalectomised animals suggest cautious use in patients with Addison's disease. In some patients, a disulfiram-like reaction may be produced by the ingestion of alcohol.

Caution should be exercised when antibacterial sulphonamides, phenylbutazone, salicylates, probenecid, dicoumarol, or MAO inhibitors are administered concomitantly with Diabinese as hypoglycaemia resultant from either potentiation or accumulation of sulphonylureas has been reported.

During the first six weeks of therapy, the physician should be in contact with the patient at least once a week. During this initial period, the patient must be observed for evidence of occasional drug reactions as described in the Adverse Reactions section. Because of the possibility of the following manifestations of hypersensitivity the patient should be instructed to report immediately to his physician if he does not feel as well as usual, or notes any pruritus, rash, jaundice, dark urine, light coloured stools, low-grade fever, sore throat or diarrhoea. As with all drugs, careful attention must be given to weigh the therapeutic advantages against the nature and incidence of side-effects.

During the period of transition to Diabinese, the patient's urine should be tested for sugar and acetone at least three times daily and the results reviewed by the physician at least once a week. Frequent laboratory determinations of liver function should also be seriously considered. Although transient minor alterations, particularly of cephalin flocculation, thymol turbidity, and serum alkaline phosphatase levels are not unusual and are probably of no clinical significance, a progressive rise in the alkaline phosphatase value should alert the physician to the possibility of incipient biliary stasis and jaundice and chlorpropamide therapy should be promptly discontinued. After the initial six weeks of therapy, subsequent patient-physician contacts may be at less frequent intervals, the exact frequency dependent on the judgement of the physician.

The drug should be used as an adjunct to, not a substitute for, dietary regulation, for this remains the primary consideration of diabetic management. It does not alter the need to educate the patient to such standard prophylactic and therapeutic measures as weight and exercise control, proper hygiene, and prompt care of intercurrent infection.

Alcohol and decreased diet may lead to hypoglycaemia, ketosis, coma, and death. Thiazides, on the other hand, have been shown to suppress insulin secretion and therefore will contribute to hyperglycaemia.

Warnings: Diabinese should not be used in juvenile diabetes or in diabetes complicated by acidosis, coma, severe infection, major surgical procedures or severe trauma. Here, insulin is indispensable.

Although Diabinese given alone has controlled some patients with mild maturity-onset diabetes of the stable type during the stress of mild infection or minor surgery, insulin therapy is generally essential during intercurrent complications (for example, ketoacidosis, severe trauma, major surgical procedures, severe infections, severe diarrhoea, nausea and vomiting, etc.). The severity of the diabetes, the nature of the complication, and availability of laboratory facilities determine whether therapy with Diabinese can be continued or should be withdrawn while insulin is being used.

In case of accidental ingestion by children, due note should be taken of the fact that three to five days are required for complete elimination of Diabinese from the body, and the patient should be kept under close observation for this period of time despite apparent recovery.

Since insulin still remains the standard therapy for patients during periods of stress or complication, the

patient on Diabinese must be instructed in the use of insulin. The patient must also be alerted to the early detection and prompt treatment of hypoglycaemia since this complication, although less frequent, may develop on sulphonylurea therapy as well as on insulin therapy.

During the initial period of therapy with Diabinese, hypoglycaemic reactions may occasionally occur, particularly during the transition from insulin to oral drug. Hypoglycaemia within 24 hours after withdrawal of the intermediate or long-acting types of insulin will usually prove to be the result of insulin carry-over and not primarily due to the effect of Diabinese.

Adverse reactions: The majority of side-effects have been dose-related, transient, and have responded to dose reduction or withdrawal of the medication. However, clinical experience thus far has shown that, as with other sulphonylureas, some side-effects associated with hypersensitivity may be severe and deaths have been reported in some instances.

Certain untoward reactions associated with idiosyncrasy or hypersensitivity have occurred, including jaundice, skin eruptions rarely progressing to erythema multiforme and exfoliative dermatitis, and probably depression of formed elements of the blood, show no direct relationship to the size of the dose. They occur characteristically during the first six weeks of therapy. With a few exceptions, these manifestations have been mild and readily reversible on the withdrawal of the drug.

The more severe manifestations may require other therapeutic measures, including corticosteroid therapy. Diabinese should be discontinued promptly when the development of sensitivity is suspected.

Jaundice has been reported and is usually promptly reversible on discontinuance of therapy. On the basis of considerable histopathological evidence, the jaundice is cholangiolitic and results primarily from intracanalicular biliary stasis rather than hepatocellular degeneration. The alkaline phosphatase which frequently shows serial and progressive elevation in these patients is of particular diagnostic value. The occurrence of progressive elevation should suggest the possibility of incipient jaundice and constitutes an indication for withdrawal of the drug.

In contrast, transient alterations of certain liver function tests seen occasionally following institution of sulphonylurea therapy, appear to be of no clinical significance.

Skin rash may be either the only manifestation of sensitivity, or occur in association with jaundice, frequently preceding it. Low grade fever and eosinophilia may also occur in association with, or preceding the development of, clinical jaundice. Rarely, severe diarrhoea, sometimes accompanied by bleeding into the lower bowel and due to non-specific proctocolitis, has been associated with other hypersensitivity manifestations, particularly jaundice, skin rash or both. The occurrence, singly or together, of any of these hypersensitivity manifestations, should constitute an indication for prompt termination of the drug and such other therapeutic measures as are dictated by the circumstances should be instituted.

Leucopenia, thrombocytopenia, and mild anaemia which occur occasionally, are generally benign and revert to normal, following cessation of the drug. Leucopenia of mild degree, and not associated with a shift in the differential count, may be transient and frequently reverts to normal even while the drug is continued.

Cases of aplastic anaemia and agranulocytosis, generally similar to blood dyscrasias associated with other

sulphonylureas have been reported. Lymphocytosis appears to be of no clinical significance.

Dose-related side-effects previously mentioned are generally transient and not of a serious nature and would include anorexia, nausea, vomiting and epigastric discomfort as evidence of gastro-intestinal intolerance, and various vague neurological symptoms, particularly weakness and paresthesiae. These manifestations are generally a direct function of dosage and were reported much more frequently during the early clinical history of the drug when some clinicians employed relatively high doses. These side-effects are reversible on reduction of the daily dosage, or if necessary, by withdrawal of the medication.

Administration of the total daily drug requirement in two doses rather than one is sometimes an effective measure for alleviating symptoms of gastro-intestinal intolerance.

Hypoglycaemia, although not a true side-effect but rather an exaggeration of the expected therapeutic action, may be the result of dosage in excess of the patient's immediate requirements, as is the case with any hypoglycaemic agent. Since the development of hypoglycaemia is a function of many factors including diet, this side-effect is at times seen in patients on the usual recommended dosage. It is readily controlled by administration of glucose. Its occurrence is an obvious indication for immediate re-evaluation and adjustment of the insulin or Diabinese dosage.

Because of the prolonged hypoglycaemic action of Diabinese patients who become hypoglycaemic during therapy with this drug require close supervision for a minimum period of three to five days, during which time frequent feedings or glucose administration are essential. The anorectic patient or the profoundly hypoglycaemic patient should be hospitalised.

Rare cases of phototoxic reactions have been reported.

Oedema associated with hyponatraemia has been infrequently reported with Diabinese therapy. This is thought to occur by potentiation of available ADH with subsequent water retention. The condition is usually readily reversible upon discontinuation of medication.

Overdosage: The treatment of hypoglycaemia is gastric lavage, intravenous glucose and haemodialysis.

Hypoglycaemia may be prolonged and treatment may have to be continued.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Diabinese 100 mg and 250 mg tablets are packed into blister strips of ten tablets each. These are available in packs of 100. Special packs of 500 tablets are also available for hospitals.

Further information Nil.

Product licence numbers

100 mg Tablets 0057/5015

250 mg Tablets 0057/5016

EQUIVERT*

Presentation Equivert brand of buclizine hydrochloride and nicotinic acid is available as a pale yellow tablet marked EVT on the one side and 'Pfizer' on the other side each containing 25 mg buclizine hydrochloride and 25 mg nicotinic acid.

Uses *Actions:* Nicotinic acid is a vasodilator agent. It

has been found effective in the treatment of vertigo due to Menière's syndrome, and to cerebral arteriosclerosis.

Buclizine hydrochloride is an antihistamine. It has been found effective in the treatment of migraine, Menière's syndrome, and vertigo.

Equivert is a combination of these two therapeutic agents. It is of value in the treatment of vertigo due to various causes, because the actions of these two therapeutically effective drugs are combined in one preparation.

Indications: Vertigo due to Menière's syndrome, cerebral arteriosclerosis, senility, labyrinthitis and streptomycin therapy. Recurrent headaches including migraine.

Dosage and administration One tablet to be taken three times daily before meals. Specific requirements for individual patients should be determined by the physician.

Contra-indications, warnings, etc *Precautions:* Since some drowsiness may occur with Equivert therapy, consideration should be given to occupational risks of the patient, such as driving or working at heights.

Equivert is indicated for use in adults only.

Use in pregnancy: As with other drugs, Equivert should be used in pregnancy only when, in the judgement of the physician, it is necessary for the welfare of the patient.

Side-effects: Short-lived flushing and tingling sensations may occur with Equivert therapy due to the vasodilator action of nicotinic acid. Patients should be made aware that such cutaneous reactions, together with increased gastro-intestinal motility and sebaceous gland activity, indicate that nicotinic acid therapy is taking effect and can be considered as desirable indications of therapeutic activity.

Drowsiness, headache or dryness of the mouth have been reported in a few patients.

Overdosage: Sedation with paraldehyde or sodium phenobarbitone intramuscular should be given if marked CNS irritation is present.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Pack of 100 tablets.

Further information Nil.

Product licence number 0057/5021.

FASIGYN* ▼

Presentation Fasigyn (tinidazole) is available as tablets or as an intravenous formulation. Tablets are white film coated tablets containing 500 mg of tinidazole. The intravenous formulation is presented in bottles of 400 ml and 800 ml containing 800 mg or 1600 mg of tinidazole (2 mg tinidazole per ml). Tinidazole is a cream to pale yellow crystalline solid with the chemical name: 1-[2-(ethylsulphonyl)ethyl]-2-methyl-5-nitroimidazole.

Uses Fasigyn is an agent for the treatment of infections due to susceptible obligate anaerobic bacteria. These infections are:

1. The treatment of infections in which anaerobic bacteria have been identified or are suspected as pathogens. The most important organisms are *Bacteroides fragilis*, other species of *Bacteroides* and *Fusobacterium*. Other organisms for which tinidazole is also

bactericidal belong to Species such as Peptococci, Peptostreptococci, Clostridia, Eubacteria and Veillonella.

Fasigyn has been successfully used in the treatment of the following infections from which one or more of the above organisms have been isolated: septicaemia, sinusitis, pneumonia, empyema and lung abscess, osteomyelitis, septic abortion, peritonitis and postoperative intra-abdominal sepsis, cellulitis and postoperative wound infection.

2. The prevention of postoperative infections caused by anaerobic bacteria, especially those after colonic, gastro-intestinal and gynaecological surgery.

3. The treatment of acute ulcerative gingivitis.

Intravenous Fasigyn is indicated in severe anaerobic infections or in those situations where oral treatment is impractical or impossible.

Dosage and administration

Oral Fasigyn: It is recommended that oral Fasigyn should be taken during or after a meal.

1. **Treatment of anaerobic infections:** An initial oral dose of 2 g followed by 1 g daily given as a single dose or as 500 mg twice daily.

Treatment for 5–6 days will generally be adequate but clinical judgement must determine the duration of therapy particularly when eradication of infection from certain sites may be difficult.

2. **Prevention of postoperative infections:** A single oral dose of 2 g with the last oral intake before operation.

3. **Acute ulcerative gingivitis:** A single oral dose of 2 g.

Intravenous Fasigyn

1. **Treatment of anaerobic infections:** An initial dose of 800 mg intravenously followed by 800 mg daily, until oral therapy is feasible. Oral therapy should be at a level of 1 g daily given as a single dose, or as 500 mg twice daily.

Treatment for 5–6 days will generally be adequate but clinical judgement must determine the duration of therapy particularly when eradication of infection from certain sites may be difficult.

Regular clinical and laboratory observation is advised if it is considered necessary to continue therapy for more than 7 days.

2. **Prevention of postoperative infections:** A total dose of 1600 mg tinidazole is recommended given either as a single pre-operative infusion or as two doses of 800 mg – the first dose 2–4 hours and not less than one hour prior to operation and a second dose of 800 mg approximately 12 hours later.

Administration of intravenous formulation: This should be given as an infusion of 800 mg (400 ml) in not less than 30 minutes or 1600 mg (800 ml) in not less than one hour.

Infusion with other intravenous solutions: intravenous tinidazole may be co-administered with the following frequently used intravenous solutions: 5% glucose, 20% glucose, isotonic saline, potassium chloride (20 mmol and 40 mmol).

No other medication should be added to Fasigyn Infusion, as chemical incompatibility may result. Fasigyn is, however, pharmacologically compatible with other antimicrobial agents.

Contra-indications, warnings, etc As with drugs of similar chemical structure, Fasigyn is contra-indicated in patients having, or with a history of, blood dyscrasia although no persistent haematological abnormalities

have been noted in clinical or animal studies. Fasigyn should not be administered to patients with a known hypersensitivity to the drug.

Fasigyn should be avoided in patients with organic neurological disorders.

Pregnancy: Fasigyn crosses the placental barrier and is present in the breast milk when administered to nursing mothers. Since the effects of compounds of this class on foetal developments or the new born are not definitely known, Fasigyn is contra-indicated during the first trimester of pregnancy and in nursing mothers during the neonatal period. While there is no evidence that Fasigyn is harmful during the later stages of pregnancy, its use during the last two trimesters of pregnancy requires that the potential benefits be weighed against possible hazards to mother and foetus.

Precautions: Although believed not to occur with Fasigyn, related compounds when taken together with alcoholic beverages have caused abdominal cramps, flushing and vomiting.

Drugs of similar chemical structure have also produced various neurological disturbances such as dizziness, vertigo, incoordination and ataxia. If, during therapy with Fasigyn, abnormal neurological signs develop, therapy should be discontinued.

Side effects: Mild side effects related to the gastrointestinal tract have been reported; these are rarely disturbing. Nausea and vomiting occur infrequently. As with related compounds, Fasigyn may produce transient leucopenia. Biochemical changes indicative of drug allergy have been reported. Mild thrombophlebitis has occasionally been observed at the infusion site.

Use in children: Fasigyn is not recommended for the treatment of children under the age of 12 years, as safe conditions for use of either the oral or intravenous formulation in this age group have not been established.

Overdosage: There is no specific treatment for gross overdosage of Fasigyn, but early gastric lavage is recommended following overdosage by mouth.

Pharmaceutical precautions

Tablets: store below 25°C in a dry place, away from light. **Intravenous formulation:** store below 25°C, away from light. 800 ml bottle – discard any unused solution.

Legal category POM.

Package quantities 20 x 500 mg tablets

Bottles of 400 ml or 800 ml intravenous infusion (2 mg/ml).

Further information Each 100 ml Fasigyn intravenous infusion includes 5.5 g dextrose monohydrate Ph.Eur.

Product licence numbers

500 mg tablet 0057/0150
Intravenous formulation 0057/0189

FELDENE* ▼

Presentation Feldene is available as a maroon and blue capsule, coded 'Pfizer' FEL 10 each containing 10 mg piroxicam.

Uses Feldene is a non-steroidal anti-inflammatory agent indicated for a variety of conditions requiring anti-inflammatory and/or analgesic activity, such as rheumatoid arthritis, osteoarthritis (arthrosis, degenerative

joint disease), ankylosing spondylitis, acute musculo-skeletal disorders and acute gout.

Dosage and administration *Rheumatoid arthritis, osteoarthritis, ankylosing spondylitis*: In these three indications, the recommended starting dose is 20 mg given as a single daily dose. The majority of patients will be maintained on 20 mg daily. A relatively small group of patients may be maintained on as little as 10 mg daily. Some patients may require up to 30 mg daily given in single or divided doses. Long term administration of doses 30 mg or higher carries an increased risk of gastrointestinal side-effects.

Acute Gout: Therapy should be initiated by a single dose of 40 mg followed on the next 4–6 days with 40 mg daily, given in single or divided doses. Feldene is not indicated for the long-term management of gout.

Acute musculoskeletal disorders: Therapy should be initiated with 40 mg daily for the first 2 days, given in single or divided doses. For the remainder of the 7 to 14 day treatment period, the dose should be reduced to 20 mg daily.

Contra-indications, warnings, etc

Contra-indications: Feldene should not be used in those patients with active peptic ulceration or a history of recurrent ulceration.

Feldene should not be used in those patients who have previously shown a hypersensitivity to the drug. The potential exists for cross sensitivity to aspirin and other non-steroidal anti-inflammatory drugs. Feldene should not be given to patients in whom aspirin and other non-steroidal anti-inflammatory drugs induce the symptoms of asthma, rhinitis or urticaria.

Warnings: *Use in pregnancy*: Although no teratogenic effects were seen in animal testing, the safety of Feldene used during pregnancy or during lactation has not yet been established. Feldene inhibits prostaglandin synthesis and release by an effect on prostaglandin biosynthetase. This effect, as with other non-steroidal anti-inflammatory agents, has been associated with an increased incidence of dystocia and delayed parturition in pregnant animals when drug administration was continued into late pregnancy.

Use in children: Dosage recommendations and indications for use in children have not been established.

Side-effects: Feldene is generally well tolerated. Gastro-intestinal symptoms are the most commonly encountered side-effects. Objective evaluations of gastric mucosal appearance and intestinal blood loss show that 20 mg/day Feldene administered either in single or divided daily doses is significantly less irritating to the gastrointestinal tract than aspirin.

Peptic ulceration and gastrointestinal bleeding have been reported.

Feldene should be withdrawn if peptic ulceration or gastrointestinal bleeding occurs.

As with other non-steroidal anti-inflammatory agents, blood urea nitrogen elevation has been observed in some patients. The rises in blood urea nitrogen are not progressive over the course of treatment with Feldene, a plateau being reached which returns to or towards the baseline levels if treatment is stopped. The rise in blood urea nitrogen is not associated with rises in serum creatinine.

Feldene, like other non-steroidal anti-inflammatory agents, decreases platelet aggregation and prolongs

bleeding time. This effect should be kept in mind when bleeding times are determined.

Long-term administration of doses of 30 mg or higher carries an increased risk of gastrointestinal side effects.

Skin rashes including dermal hypersensitivity have been reported. As with other non-steroidal anti-inflammatory drugs, Stevens-Johnson syndrome may develop in rare cases.

As with other non-steroidal anti-inflammatory agents, oedema, mainly ankle oedema, has been reported in a small percentage of patients.

As with other non-steroidal anti-inflammatory agents the possibility of precipitating congestive cardiac failure in elderly patients or those with compromised cardiac function should therefore be borne in mind.

Routine ophthalmoscopy and slit-lamp examination have revealed no evidence of ocular change.

Decreases in haemoglobin and haematocrit, unassociated with obvious gastrointestinal bleeding, have occurred. Changes in different liver function parameters have been observed. As with most other non-steroidal anti-inflammatory agents, some patients may develop increased serum transaminase levels during treatment with Feldene.

Overdosage: In the event of overdosage with Feldene, supportive and symptomatic therapy is indicated.

Pharmaceutical precautions Store in a cool, dry place.

Legal category POM.

Package quantities Capsules 10 mg – pack of 60.

Further information Feldene is highly protein bound, and therefore might be expected to displace other protein bound drugs. However, *in vitro* studies have shown this not to occur with dicoumarol. Nevertheless, the physician should closely monitor patients for change in dosage requirements when administering Feldene to patients on highly protein bound drugs.

Product licence number 0057/0145.

GLIBENESE*

Presentation Glibenese brand of glipizide is available as white oblong tablets marked GBS/5 on the scored side and 'Pfizer' on the other. Each tablet contains 5 mg glipizide.

Glipizide is 1-cyclohexyl-3-[[p(2-(5-methylpyrazine-2-carboxyamido) -ethyl)-phenyl]sulphonyl]-urea.

Uses **Actions**: Following oral administration, Glibenese is rapidly and almost completely absorbed. A peak plasma level is reached in one to two hours. Some 98% is protein bound. The plasma half-life is two and a half to four hours.

Glibenese is rapidly excreted, some 64–87% appearing in the urine within 24 hours; faecal excretion accounting for the remainder. Glibenese is excreted chiefly in the form of metabolites, the principal metabolites being 3-cis hydroxy and 4-trans hydroxy derivatives.

Following a single oral dose, a hypoglycaemic effect is seen in 30 minutes with a maximum response in two hours. Thereafter, the hypoglycaemic effect persists for over six hours on a diminishing scale.

Indications: Maturity-onset, non-ketotic, diabetes mellitus, not controlled by dietary measures alone.

Glibenese is not an oral insulin. As with other sulphonylureas, the blood glucose lowering capacity of

Glibenese is primarily attributable to a direct action on the beta cells of the pancreas.

Clinical studies have shown Glibenese to be a potent oral hypoglycaemic agent capable of producing satisfactory control in 80–90% of maturity-onset diabetic patients.

Dosage and administration Progress of the patient should be monitored with blood and urine glucose determinations. In order to achieve optimal control of the diabetic state, the dosage of Glibenese should be determined by, and adjusted to, the individual patient's requirement.

Newly diagnosed diabetics: Stabilisation may be carried out on an outpatient basis, starting normally with a daily dose of 5 mg of Glibenese given with breakfast or, if this meal is omitted, with the mid-day meal. Mild diabetic and geriatric patients should be started on 2.5 mg of Glibenese daily as these patients appear to be more sensitive to the sulphonylurea drugs.

Dosage must be adjusted according to the patient's response. If necessary, the daily dosage may be increased by 2.5 mg or 5 mg every three to five days until optimal control is achieved.

If the daily dosage requirement exceeds 10 mg the total daily dose should be subdivided and given in two parts with the two main meals of the day. Care should be taken to avoid hypoglycaemia.

Patients requiring daily doses in excess of 20 mg daily may require that their dosage be given in three parts with breakfast, the mid-day meal and the evening meal.

Maintenance therapy: Patients can usually be stabilised on a dosage varying from 2.5–30 mg daily.

Transfer from other oral agents: Patients poorly controlled on, or experiencing secondary failure with other antidiabetic agents may respond well to Glibenese. If, for these reasons, or previous adverse side effects a change is being made to Glibenese, it is recommended that a starting daily dose of 5 mg of Glibenese be instituted with adjustment upwards by increments of 2.5 or 5 mg daily so as to reach optimal control.

Patients receiving insulin: Maturity-onset diabetics with no ketoacidosis or history of metabolic decompensation and whose insulin requirements are less than 40 units per day may be considered for Glibenese therapy.

It is recommended that patients undergoing conversion from insulin to Glibenese be hospitalised under close physician observation.

Such patients should be carefully observed until optimal control is re-established, especially if the insulin is abruptly discontinued, or the dosage sharply decreased.

Concurrent Glibenese and biguanide therapy: As with other sulphonylureas, a proportion of patients who do not achieve optimal control with Glibenese alone, or who experience secondary failure, may be expected to have their control improved or restored by the addition of a biguanide.

For such patients, it is suggested that the dosage of Glibenese should be maintained and the biguanide chosen should be added using low doses initially and increasing the dosage of the biguanide progressively until adequate control is achieved or restored. Should gastro-intestinal side effects appear, an attempt should be made to reduce the dosage of the biguanide.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to Glibenese.

Diabetes complicated by ketoacidosis.

Juvenile, growth onset or brittle diabetes mellitus.

Severe renal or hepatic insufficiency.

Severe metabolic decompensation.

Use in pregnancy: Safe conditions for the use of Glibenese in pregnancy have not been established. Glibenese is not indicated for the management of diabetes mellitus during pregnancy.

Precautions: In patients subjected to stress, such as fever, trauma, infection or surgical procedures, it may be necessary temporarily to administer insulin instead of, or in addition to, Glibenese.

Patients with mild impairment of hepatic and/or renal function and debilitated or malnourished patients, require careful observation and adjustment of Glibenese dosage to avoid the occurrence of hypoglycaemia.

Care is also required when Glibenese is administered concurrently with certain other drugs which may potentiate its hypoglycaemic action. These include phenylbutazone, oxyphenbutazone, probenecid, salicylates, sulphonamides, chloramphenicol, coumarins, monoamine oxidase inhibitors and beta-adrenergic blocking agents.

Thiazide diuretics may aggravate the diabetic state and alter the Glibenese dosage required. Because of the potent hypoglycaemic activity of Glibenese, close dietary supervision is required during initial stabilisation to avoid the occurrence of hypoglycaemia. To date, hypoglycaemic episodes during Glibenese therapy have occurred only rarely.

Glibenese should be administered with or after meals. If hypoglycaemia occurs, conventional measures should be taken. Clinical experience to date indicates a prompt response may be expected.

Side-effects: Side-effects are uncommon with Glibenese. The side-effects reported consist mainly of gastro-intestinal disturbances (nausea, epigastric fullness, heartburn) – and headache. An antabuse effect has not been reported.

Overdosage: Hypoglycaemia may occur in those patients who do not eat regularly or who exercise without caloric supplementation, or in those who take Glibenese in the fasting state. Hypoglycaemia is treated in the usual manner, by supplying carbohydrate in various forms dependent on the patient's clinical status.

Pharmaceutical precautions Store in a cool dry place.

Legal category POM.

Package quantities Glibenese tablets 5 mg are packed into blister strips of ten tablets each. Available in cartons of 60 tablets.

Further information Nil.

Product licence number 0057/0113.

HYPOVASE®

Presentation Hypovase brand of prazosin hydrochloride is available in tablets as follows:

0.5 mg white tablets, unscored: marked 'Pfizer' on one side.

1 mg scored orange tablets: marked HYP/1 on one side.

2 mg scored white tablets: marked HYP/2 on one side and 'Pfizer' on the other.

5 mg scored white tablets: marked HYP/5 on one side and 'Pfizer' on the other.

Prazosin is 1-(4-amino-6, 7-dimethoxyquinazolin-2-yl)-4 (2-furoyl) piperazine.

Uses Actions: Hypovase causes a decrease in total peripheral resistance, but the exact mechanism of action is unknown. Animal studies suggest that the vasodilator effect of Hypovase is related to blockade of postsynaptic alpha-adrenoceptors. The results of dog forelimb experiments demonstrate that the peripheral vasodilator effect is confined mainly to the level of the resistance vessels (arterioles). Unlike conventional alpha-blockers the antihypertensive action of Hypovase is usually not accompanied by reflex tachycardia.

Haemodynamic studies have been carried out in hypertensive patients following acute single dose administration and during the course of long-term maintenance therapy. The results confirm that the usual therapeutic effect is a fall in blood pressure unaccompanied by a clinically significant change in cardiac output, heart rate, renal blood flow and glomerular filtration rate. In clinical studies where measurements were made, Hypovase has not increased plasma renin activity.

Clinically, the antihypertensive effect is believed to be a direct result of peripheral vasodilation. In man, blood pressure is lowered in both the supine and standing positions. This effect is more pronounced on the diastolic blood pressure. Tolerance does not appear to develop in long-term clinical use. Rebound elevation of blood pressure does not occur following abrupt cessation of Hypovase therapy.

Haemodynamic studies carried out in patients with congestive cardiac failure following acute oral dosing and during the course of longer term maintenance therapy both at rest and on exercise indicate that the therapeutic effect in these patients is due to a reduction in left ventricular filling pressure, reduction in cardiac impedance and an augmentation of cardiac output. These effects, as indicated in forearm plethysmographic studies in humans, are associated with a balanced vasodilator effect on both resistance vessels (arterioles) and capacitance vessels (veins). The use of Hypovase in congestive heart failure does not provoke a reflex tachycardia.

Following oral administration in normal volunteers and hypertensive patients plasma concentrations reach a peak in one to two hours with a plasma half-life of two to three hours. Pharmacokinetic data in a limited number of patients with congestive cardiac failure, most of whom showed evidence of hepatic congestion, indicates that peak plasma concentrations are reached in $2\frac{1}{2}$ hours and plasma half-life is approximately seven hours. The drug is highly bound to plasma protein. Animal studies indicate that Hypovase is extensively metabolized, primarily by demethylation and conjugation and excreted mainly via bile and faeces. Less extensive human studies suggest similar metabolism and excretion in man.

Hypovase has been administered without any adverse drug interaction in clinical experience to date with the following:

- cardiac glycosides – digitalis and digoxin;
- hypoglycaemic agents – insulin, chlorpropamide, phenformin, tolazamide, and tolbutamide;
- tranquilizers and sedatives – chlorthalidopoxide, diazepam, and phenobarbital;
- agents for the treatment of gout – allopurinol, colchicine, and probenecid;

- antiarrhythmic agents – procainamide and quinidine; and

- analgesic, antipyretic; and anti-inflammatory agents – propoxyphene, aspirin, indomethacin, and phenylbutazone.

Indications:

Hypertension: Hypovase is indicated in the treatment of hypertension of varied aetiology and all grades of severity. It can be used as the initial agent or it may be employed in a general treatment programme in conjunction with a diuretic and/or other antihypertensive drugs as needed for proper patient response.

Renal blood flow and glomerular filtration rate are not impaired by long-term oral administration and thus Hypovase can be used with safety in hypertensive patients with impaired renal function.

Congestive Cardiac Failure: Hypovase is indicated in the treatment of moderate to severe congestive cardiac failure. Hypovase may be added to the therapeutic regime in those patients who have not shown a satisfactory response or who have become refractory to conventional therapy with cardiac glycosides and diuretics.

Dosage and administration Hypertension: The dosage range is from 0.5–20 mg daily and treatment is best initiated at a low starting dose. It is recommended that the starting dose of 0.5 mg be given with food preferably with the evening meal, at least two or three hours before retiring.

The b.d. 'Starter Pack' is available for the convenience of prescribers to initiate treatment up to 2 mg b.d.

As is normal practice when potent antihypertensive agents are prescribed, patients should be advised how to recognise and how to avoid symptoms resulting from orthostatic hypotension and what measures to take should they develop. Patients should be cautioned to avoid situations where injury could result (e.g. driving or operating machinery) should dizziness or fainting occur during the initiation of Hypovase therapy.

Specific Recommendations: The following are given as guides to administration.

Patients receiving no antihypertensive therapy: It is recommended that therapy be initiated at 0.5 mg b.d. or t.i.d. for 3–7 days, with the starting dose administered in the evening. Unless poor acceptance suggests the patient is unusually sensitive, this dose should be increased to 1 mg b.d. or t.i.d. for the next 3–7 days.

Thereafter, if necessary, the daily dose should be increased gradually as determined by the patient's response to the blood pressure lowering effect. A significant number (of the order 60–70%) of patients are likely to be maintained on a dosage regimen of Hypovase alone of up to 15 mg daily in divided doses. Maximum recommended daily dosage: 20 mg in divided doses.

An increase in therapeutic effect may be achieved by adding a thiazide (e.g. polythiazide). When adding a thiazide, the dosage of Hypovase being administered should be reduced (e.g. halved) and subsequently adjusted as necessary.

Patients receiving thiazide diuretic therapy with inadequate control of blood pressure: The diuretic should be reduced to a low-dose level for the particular agent and Hypovase initiated at 0.5 mg b.d. or t.i.d. for 3–7 days with the starting dose administered in the evening. Unless poor acceptance suggests the patient is unusually sensitive, the dose should be increased to 1 mg b.d. or t.i.d. for the next 3–7 days.

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In patients with congestive cardiac failure: Hypovase is
not recommended in the treatment of congestive cardiac
failure due to mechanical obstruction such as aortic
valve stenosis, mitral valve stenosis, pulmonary embolism
and restrictive pericardial disease. Adequate data is not
yet available to establish efficacy in patients with
congestive cardiac failure due to a recent myocardial
infarction.

Precautions: In patients with hypertension: A small
percentage of patients may react more rapidly and to a
greater extent than the majority. In some cases this has
led to sudden loss of consciousness generally lasting a
few minutes but which has been up to one hour. In
almost all such cases such a reaction occurs within 30 to
90 minutes of receiving the initial dose, but in a very few
instances may occur after a period of uneventful
treatment. Even when such a response occurs subse-
quent treatment may be satisfactory.

In patients with congestive cardiac failure: In patients
with acute or chronic left ventricular failure who have
undergone vigorous diuretic or vasodilator treatment,
the resultant decrease in left ventricular filling may be
associated with a significant fall in cardiac output and
systemic blood pressure when prazosin is administered.
In such patients, a low initial dose of prazosin and
gradual titration with close observation is recommended.
(See dosage and administration.)

In occasional patients the clinical efficacy of Hypovase
has been reported to diminish after several months of
treatment. In these patients there is usually evidence of
weight gain or peripheral oedema indicating fluid
retention. Since spontaneous deterioration may occur in
such severely ill patients a causal relationship to prazosin
therapy has not been established. Thus, as with all
patients with congestive cardiac failure, careful adjust-
ment of diuretic dosage according to the patient's clinical
condition is required to prevent excessive fluid retention
and consequent relief of symptoms. In those patients
without evidence of fluid retention, when clinical im-
provement has diminished, an increase in the dosage of
Hypovase will usually restore clinical efficacy.

Side-effects: In patients with hypertension: Side-effects
associated with the use of Hypovase have generally
been mild and usually not an indication for the discon-
tinuance of therapy. The most common side-effects
reported with the use of Hypovase consist of the
following: postural dizziness, drowsiness, headache, lack
of energy, weakness, palpitations, nausea, dry mouth,
blurred vision, urinary frequency, oedema, nasal conges-
tion, nervousness, depression, vertigo, constipation,
dyspnoea, vomiting, diarrhoea, syncope, rash, pruritus,
sweating, abdominal discomfort and/or pain, tachycar-
dia, paraesthesia, impotence, reddened sclera, epistaxis,
and tinnitus. The majority of patients who receive
Hypovase at the recommended dose will not experience
troublesome orthostatic effects.

Some of these reactions have occurred rarely and in
many instances the exact causal relationship has not
been established.

In patients with congestive cardiac failure: The following
have been observed in patients being managed for
moderate to severe congestive cardiac failure with
Hypovase when used in conjunction with cardiac
glycosides and diuretics. Drowsiness, dizziness, ortho-
static hypotension, blurred vision, oedema, dry mouth,
palpitations, nausea, headache, impotence, diarrhoea
and nasal congestion. In most instances these occur-
rences have been mild to moderate in severity and have

resolved with continued therapy or have been tolerated with no decrease in drug dose.

Overdosage: Should overdosage lead to hypotension, support of the cardiovascular system is of first importance. Restoration of blood pressure and normalisation of heart rate may be accomplished by keeping the patient in the supine position. If this measure is inadequate, shock should first be treated with volume expanders. If necessary vasopressors should then be used. Renal function should be monitored and supported as needed. Laboratory data indicate Hypovase is not dialysable because it is protein bound.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities *b.d. Starter Pack:* containing 8 × 0.5 mg Hypovase tablets and 32 × 1 mg Hypovase tablets (See 'Further Information').

Hypovase 0.5 mg: white tablets, unscored in packs of 100.

Hypovase 1 mg: scored orange tablets in packs of 100.

Hypovase 2 mg: scored white tablets in packs of 100.

Hypovase 5 mg: scored white tablets in packs of 100.

Further information The two week *b.d.* Starter Pack has the following instructions to the patient:

Step 1. (0.5 mg tablets) – 4 days, first dose in the evening.

Step 2. (1 mg tablets) – 4 days, first dose in the evening.

Step 3. (2 × 1 mg tablets) – 6 days, first dose in the evening.

Your doctor will wish you to follow further dosage instructions beyond step 3 and you should follow those instructions or see your doctor before the end of Step 3.

The tablets (0.5 and 1 mg) are carefully packed in sequence, in blister strips to ensure correct usage.

Product licence numbers

0.5 mg tablet	0057/0149
1 mg tablet	0057/0106
2 mg tablet	0057/0107
5 mg tablet	0057/0108

NEPHRIL®

Presentation Nephрил is available as white scored tablets ($\frac{3}{8}$ " diameter) coded NEP/1 on one side and 'Pfizer' on the other, each containing 1 mg polythiazide.

Uses *Actions:* The mechanism of action results in an interference with the renal tubular mechanism of electrolyte reabsorption. At maximal therapeutic dosage, all thiazides are approximately equal in their diuretic potency. The mechanism whereby thiazides function in the control of hypertension is unknown.

Indications: Nephрил brand of polythiazide is an orally effective, non-mercurial diuretic, saluretic and antihypertensive agent. Nephрил is indicated as adjunctive therapy in oedema associated with congestive heart failure, hepatic cirrhosis and corticosteroid and oestrogen therapy.

Nephрил has also been found useful in oedema due to various forms of renal dysfunction, such as nephrotic syndrome, acute glomerulonephritis and chronic renal failure.

Nephрил is indicated in the management of hypertension either as the sole therapeutic agent or to enhance the

effectiveness of other antihypertensive drugs in the more severe forms of hypertension.

Dosage and administration The usual dosage of Nephрил for diuretic therapy is 1 to 4 mg daily. For antihypertensive therapy the usual maintenance dose is between 1 and 4 mg daily although some patients may be optimally controlled on doses of 0.5 mg daily. However, few patients will require doses as high as 4 mg daily and at such a dose level serum electrolytes should be monitored frequently. Dosage should be individualised according to response and should be titrated to gain the maximum therapeutic effect with the minimum dose required to maintain that therapeutic response.

Contra-indications, warnings, etc

Contra-indications: Anuria. Hypersensitivity to polythiazide or other sulphonamide derived drugs.

Warnings: Thiazides should be used with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotaemia. Cumulative effects of the drug may develop in patients with impaired renal function. If progressive renal impairment becomes evident, as indicated by a rising nonprotein nitrogen or blood urea nitrogen, a careful reappraisal of therapy is necessary with consideration given to withholding or discontinuing diuretic therapy. Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma.

Thiazides may add to or potentiate the action of other antihypertensive drugs. Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs.

Sensitivity reactions may occur in patients with a history of allergy or bronchial asthma. The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

Use in pregnancy: The routine use of diuretics in healthy pregnant women is inappropriate and may expose mother and foetus to unnecessary hazard. Diuretics do not prevent development of toxæmia of pregnancy and there is no satisfactory evidence that they are useful in the treatment of established toxæmia.

Oedema during pregnancy may arise from pathological causes or from physiological and mechanical consequences of pregnancy. Physiological hypervolaemia during pregnancy may be associated with generalised oedema including dependent oedema. This oedema is properly treated by recumbency and support hose. Thiazides may be indicated in pregnancy when oedema is due to pathological causes other than toxæmia. Rarely short courses of thiazides are indicated where physiological oedema is unrelieved by rest and where the oedema causes extreme discomfort.

Thiazides cross the placental barrier and appear in cord blood. The use of thiazides in pregnant women requires that the anticipated benefit be weighed against possible hazards to the foetus. These hazards include foetal or neonatal jaundice, thrombocytopenia and possibly other adverse reactions which have occurred in the adult.

Nursing mothers: Thiazides appear in breast milk. If use of Nephрил is deemed essential, nursing should be discontinued.

Precautions: All patients receiving thiazide therapy should have periodic determinations of serum electrolytes to detect possible electrolyte imbalance. Such patients should also be observed for clinical signs of fluid or electrolyte imbalance; namely hyponatraemia,

hypochlorhaemic alkalosis and hypokalaemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting or receiving parenteral fluids. Warning signs of possible electrolyte imbalance, irrespective of cause, are: dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia and gastro-intestinal disturbances such as nausea and vomiting.

Hypokalaemia may develop with thiazides as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH.

Interference with adequate oral electrolyte intake will also contribute to hypokalaemia. Hypokalaemia may exaggerate metabolic effects of digitalis therapy especially with reference to myocardial activity.

Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatraemia may occur in oedematous patients in hot weather; appropriate therapy is water restriction, rather than administration of salt except in rare instances, when the hyponatraemia is life threatening. In actual salt depletion, appropriate replacement is the therapy of choice. Hyperuricaemia may occur or frank gout may be precipitated in certain patients receiving thiazide therapy.

Insulin requirements in diabetic patients may be increased, decreased or unchanged. Latent diabetes mellitus may become manifest during thiazide administration.

Thiazide drugs may increase the responsiveness to tubocurarine.

The antihypertensive effects of thiazides may be enhanced in the post-sympathectomy patient. Thiazides may decrease arterial responsiveness to noradrenaline. This diminution is not sufficient to preclude effectiveness of the pressor agent for therapeutic use.

Thiazides may decrease serum protein-bound iodine levels without signs of thyroid disturbance.

Use in children: Nephril is not recommended for use in children.

Adverse Reactions:

Gastro-intestinal – anorexia, gastric irritation, nausea, vomiting, cramping, diarrhoea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis.

Central nervous system – dizziness, vertigo, paraesthesia, headache, xanthopsia.

Haematological – leucopenia, agranulocytosis, thrombocytopenia, aplastic anaemia.

Dermatological – purpura, photosensitivity, rash, urticaria, necrotising angitis.

Cardiovascular – orthostatic hypotension may occur and be aggravated by alcohol, barbiturates or narcotics.

Other – hypoglycaemia, glycosuria, hyperuricaemia, muscle spasm, weakness, restlessness.

Whenever adverse reactions are moderate or severe, thiazide dosage should be reduced or therapy withdrawn.

Overdosage: Gastric lavage and supportive therapy. Treatment of acute renal failure if present. Potassium supplements.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Tablets 1 mg packs of 100 and 500.

Further information Nil.

Product licence number 0057/5024.

RONDOMYCIN*

Presentation Rondomycin brand of methacycline hydrochloride is available as:

150 mg capsules coded 'Pfizer' on the red head of the capsule and coded RON 150 on the white body of the capsule.

Rondomycin is a potent broad-spectrum antibiotic, synthetically derived from oxytetracycline.

Uses **Actions:** Rondomycin is well absorbed following oral administration in man. Therapeutic blood levels are rapidly achieved after oral administration of a single 150 mg dose, with a maximum level attained between two and three hours and maintained for over 12 hours. Appreciable amounts of the antibiotic remain in the blood for 24 hours or more after a single administration.

In a double-blind study, Rondomycin produced stable therapeutic blood levels when given continuously for three days at a total daily dose of 600 mg administered in either two or four equally divided doses. Twenty-four hours after completion of the three day period of administration of Rondomycin, blood levels were still within therapeutic range. Rondomycin is excreted in the urine and bile and is partially eliminated unchanged in the faeces.

Rondomycin has a wide spectrum of microbiological activity. *In vitro* tests indicate its activity against both Gram-positive and Gram-negative organisms. *In vivo*, independent animal protection studies have shown Rondomycin to be active against experimental infections produced by *Staphylococcus aureus*, *Streptococcus pyogenes*, *Diplococcus pneumoniae*. In experimental infections with *Salmonella typhosa*, *Escherichia coli* and *Aerobacter aerogenes*, Rondomycin again has shown its effectiveness in protecting the animals.

Acute toxicity studies in mice and rats have shown a high therapeutic index and a wide margin of safety for Rondomycin. Chronic toxicity studies in rats and dogs for periods of three to six months have shown no significant alteration in tissue function.

Indications: Rondomycin is a potent, broadly active, antibiotic effective in the treatment of infections caused by sensitive organisms. Specific conditions which may be expected to respond successfully to Rondomycin therapy include the following:

Respiratory infections: Acute bronchitis and acute exacerbations of chronic bronchitis, bronchiectasis, bronchopneumonia, pneumonia, lung abscess and upper respiratory infections such as pharyngitis, tonsillitis, sinusitis and otitis. Rondomycin may be used as an antibacterial cover in virus infections of the respiratory tract, including influenza and primary atypical pneumonia.

Surgical infections: Abscess, cellulitis, etc. May be used as an antibacterial cover before and after surgery in susceptible infections.

Skin and soft tissue infections: Folliculitis, erysipelas, impetigo, furunculosis, pyoderma, carbuncle, paronychia, acne, etc.

Gastro-intestinal infections: Bacillary dysentery, salmonellosis, typhoid fever, etc. Biliary tract infections.

Genito-urinary infections: Cystitis, pyelitis, pyelonephritis, gonococcal urethritis, etc.

Generalised infections: Septicaemia, bacteraemia. May be used as an antibacterial cover during bacteraemic states in susceptible individuals.

Obstetric and gynaecological infections:

Oral and dental infections:

Dosage and administration Rondomycin is available as 150 mg capsules. Rondomycin has the property of maintaining therapeutic blood levels for at least 24 hours following interruption of several days continuous administration.

Adults: For infections of average severity, the recommended total daily dosage is 600 mg of Rondomycin administered in either two or four equally divided doses. In severe infections, this dosage may be doubled.

Contra-indications, warnings, etc

Contra-indications: Rondomycin is contra-indicated in individuals who have hypersensitivity to tetracyclines.

Rondomycin is contra-indicated in patients with renal failure.

Warnings: As with other antibiotics, side effects have been reported such as nausea, vomiting, increase in frequency of defaecation, diarrhoea, proctitis and stomatitis. Serious gastro-intestinal side-effects have rarely been noted. Reactions of an allergic nature may result, but have not yet been reported for Rondomycin.

As with all other broad spectrum antibiotics, the administration of Rondomycin may result in the overgrowth of nonsusceptible organisms. Constant observation of the patient is essential. Should superimposed infection occur during therapy, the antibiotic should be discontinued and suitable measures should be taken as indicated by susceptibility testing.

Tetracyclines may form a stable calcium complex in any bone forming tissue with no serious harmful effects reported thus far in humans. However, the use of tetracyclines during tooth development (last half of pregnancy, neonatal period and early childhood) may cause discoloration of the teeth (yellow-grey-brownish). This effect occurs mostly during long-term use of the drug but it has also been observed with the usual short treatment courses.

Overdosage: Acute overdosage with antibiotics is rare.

Toxic effects are usually due to hypersensitivity reactions and should be treated as such.

Pharmaceutical precautions Store in a cool place. Protect from light.

Legal category POM.

Package quantities Capsules 150 mg: Packs of 16, 100 and 500.

Further information Nil.

Product licence number

Capsules 150 mg 0057/5071.

SAFAPRYN®

Presentation Safapryn brand of enteric-coated aspirin with paracetamol is available as:

Pink sugar-coated tablets each containing 300 mg aspirin as an enteric coated core, surrounded by an outer layer of 250 mg paracetamol.

Uses Actions: Gastric blood loss following the ingestion of aspirin occurs in over half the patients taking it in the standard form. The average daily loss in such patients has been estimated as 5 ml. Evidence suggests that the effect is a direct one on the gastric mucosa, and that enteric coating of the aspirin, ensuring release in the small intestine, reduces the incidence of blood loss. A trial (Brit. J. Clin. Pract., 1971, **25**, 169) using radioactive chromium labelled red blood cells has shown that the average daily blood loss following the ingestion of Safapryn is less than 1 ml.

Release of the aspirin in the small intestine, rather than in the stomach, results in some delay in the onset of analgesic effect and it is for this reason that the outer coat of the tablet contains paracetamol, which is absorbed rapidly, and which provides initial analgesic effect.

Safapryn is adequately absorbed and gives plasma salicylate levels comparable to those achieved with standard aspirin tablets.

Indications: Safapryn is an analgesic preparation designed to minimise the gastric irritation and blood loss associated with aspirin.

Safapryn is indicated in all conditions where a mild analgesic/anti-inflammatory would be prescribed such as headache, musculoskeletal pain, dysmenorrhoea, also for the long-term treatment of chronic painful conditions such as osteoarthritis and rheumatoid arthritis.

Dosage and administration *Chronic painful conditions:* 1 to 3 tablets (300 to 900 mg aspirin + 250 to 750 mg paracetamol) three or four times a day. Do not exceed 10 tablets in 24 hours.

Each tablet should be swallowed whole, not crushed or broken in any way.

Safapryn is indicated for use in adults only.

Contra-indications, warnings, etc

Contra-indications: Active peptic ulceration, haemophilia, hypersensitivity to either aspirin or paracetamol, hypoprothrombinaemia.

Warnings: An overdose of Safapryn can cause hepatic necrosis.

Precautions: Safapryn may enhance the effect of anti-coagulants. It may inhibit the action of uricosurics. Safapryn may precipitate bronchospasm. It may induce attacks of asthma in susceptible subjects.

Side-effects: Aspirin may cause tinnitus, rashes and anaphylactic phenomena. Skin eruptions and blood dyscrasias have been reported on rare occasions following prolonged administration of paracetamol.

Use in Pregnancy: Aspirin may prolong labour and contribute to maternal and neonatal bleeding and is best avoided at term.

Overdosage: Overdosage with Safapryn is rare but has been reported. High plasma paracetamol levels have occurred early whilst salicylate levels continued to rise for up to 70 hours after ingestion.

Early treatment of paracetamol overdosage with N-acetylcysteine or methionine is important to prevent liver damage. Treatment for salicylate overdosage such as forced diuresis and gastric lavage, can be determined by clinical features, plasma salicylate levels and biochemical parameters.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities Pack of 250.

Further information Nil.

Product licence number 0057/5029.

SAFAPRYN* - CO

Presentation Safapryn-Co brand of enteric-coated aspirin with paracetamol and codeine phosphate is available as lime-green sugar-coated tablets each containing 300 mg aspirin as an enteric-coated core, 250 mg paracetamol and 8 mg codeine phosphate.

Uses Actions: Gastric blood loss following the ingestion of aspirin occurs in over half the patients taking it in the standard form. The average daily blood loss in such patients has been estimated as 5 ml. Evidence suggests that the effect is a direct one on the gastric mucosa and that enteric coating of the aspirin, ensuring release in the small intestine, reduces the incidence of blood loss.

Release of the aspirin in the small intestine, rather than in the stomach, results in some delay in the onset of analgesic effect and it is for this reason that the outer coat of the tablet contains paracetamol and codeine, which are absorbed rapidly and which provide initial analgesic effect.

Safapryn-Co is adequately absorbed and gives plasma salicylate levels comparable to those achieved with standard aspirin tablets.

Indications: Safapryn-Co is an analgesic preparation designed to minimise the gastric irritation and blood loss associated with aspirin.

Safapryn-Co is indicated in all acutely painful conditions where an analgesic would be prescribed: lumbago, fibrositis, sciatica, low back pain, prolapsed intervertebral disc, dysmenorrhoea, toothache and headache.

Dosage and administration 1 to 3 tablets (300 to 900 mg aspirin + 250 to 750 mg paracetamol + 8 to 24 mg codeine) three or four times a day. Do not exceed 10 tablets in 24 hours.

Each tablet should be swallowed whole, not crushed or broken in any way.

Safapryn-Co is indicated for use in adults only.

Contra-indications, warnings, etc

Contra-indications: Active peptic ulceration, haemophilia, hypersensitivity to either aspirin, paracetamol or codeine, hypoprothrombinaemia.

Warnings: An overdose of Safapryn-Co can cause hepatic necrosis.

Precautions: Safapryn-Co may enhance the effect of anticoagulants. It may inhibit the action of uricosurics. Safapryn-Co may precipitate bronchospasm. It may induce attacks of asthma in susceptible subjects. Codeine is a narcotic analgesic.

Side-effects: Aspirin may cause tinnitus, rashes and anaphylactic phenomena. Skin eruptions and blood dyscrasias have been reported on rare occasions following prolonged administration of paracetamol. Codeine may cause constipation.

Use in pregnancy: Aspirin may prolong labour and contribute to maternal and neonatal bleeding and is best avoided at term.

Overdose: To the present no reports of effects of overdose of Safapryn-Co have been received but it is anticipated that high levels of paracetamol will occur

early and salicylate levels may continue to rise for up to 70 hours after ingestion.

Early treatment of paracetamol overdose with N-acetylcysteine or methionine is important to prevent liver damage. Treatment for salicylate overdose such as forced diuresis and gastric lavage, can be determined by clinical features, plasma salicylate levels and biochemical parameters.

Reports of overdose with other codeine containing products suggest that this component is not usually the prime hazard.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities Pack of 100.

Further information Nil.

Product licence number 0057/0064.

SINEQUAN*

Presentation Sinequan brand of doxepin is available in capsules of four strengths. All capsules bear the name 'Pfizer'.

The four sizes of capsules are distinguished by their colour and coding as follows:

Sinequan 10 mg capsule coded 'SQN 10' (opaque orange).

Sinequan 25 mg capsule coded 'SQN 25' (opaque blue cap/opaque orange body).

Sinequan 50 mg capsule coded 'SQN 50' (opaque blue).

Sinequan 75 mg capsule coded 'SQN 75' (opaque blue cap/opaque rich yellow body).

Sinequan contains a dibenzoxepin derivative which consists of a mixture of the *cis* and *trans* isomers in a constant ratio (82–85% *trans*: 15–18% *cis*). Chemically, it is 11-dimethyl-amino-propylidene-6H-dibenz(b,e)-oxepin hydrochloride.

Uses Actions: The mechanism of action of Sinequan is not definitely known. It is not a central nervous system stimulant nor a monoamine oxidase inhibitor. The current hypothesis is that the clinical effects are due, at least in part, to influences on the adrenergic activity at the synapses so that deactivation of norepinephrine by reuptake into the nerve terminals is prevented. Animal studies suggest that Sinequan does not appreciably antagonise the antihypertensive action of guanethidine. In animal studies anticholinergic, antiserotonin and antihistamine effects on smooth muscle have been demonstrated. At higher than usual clinical doses, norepinephrine response was potentiated in animals. This effect was not demonstrated in humans.

At clinical dosages up to 150 mg per day, Sinequan can be given to man concomitantly with guanethidine and related compounds without blocking the antihypertensive effect. At dosages above 150 mg per day blocking of the antihypertensive effect of these compounds has been reported.

There have been no reports of physical dependency or withdrawal symptoms associated with Sinequan therapy. This is consistent with the virtual absence of euphoria as a side-effect and at this dose there was no evidence of toxicity in rats and dogs over a 12 month period.

Indications: Sinequan is a safe and effective psychotherapeutic agent for the treatment of patients with a

wide range of psychoneurotic disorders where anxiety and/or depression are prominent symptoms.

Thus, where these prime symptoms are present, the compound has been shown to be of value in patients with anxiety neuroses, with or without somatic symptoms, reactive depression, mixed anxiety depression and patients with alcoholism with anxiety and/or depression.

In addition, Sinequan is similarly effective in the treatment of patients suffering from psychotic depression, including endogenous depression, involutional melancholia, senile depression, postpartum depression and manic-depressive reaction-depressed phase.

Target symptoms that respond to treatment include: anxiety, depression, tension, apprehension, agitation, functional somatic complaints, insomnia, loss of interest, guilt, psychomotor retardation and hypochondriasis.

Sinequan may be used with benefit where symptoms are of short or long duration prior to treatment and in patients with a wide range of intensity of illness.

As with other psychotherapeutic agents, the degree of response varies with each patient. In patients exhibiting a beneficial response, this may be seen within a few days of commencing therapy, while others may not respond for two weeks or longer.

Due to its excellent toleration, Sinequan is particularly useful in ambulatory patients seen in general practice as well as in the treatment of hospitalised patients.

Clinical studies have also demonstrated Sinequan to be effective in alleviating the temporary anxiety and tension associated with difficult diagnostic procedures such as endoscopies (gastroscopy, oesophagoscopy, bronchoscopy, cystoscopy, laparoscopy, etc.) performed under local anaesthesia.

Dosage and administration The optimum oral dose depends on the severity of the condition and the individual patient's response. The dose varies from 30–300 mg daily, and is usually administered in three divided doses daily.

As an alternative regimen, the total daily dosage, up to 100 mg may be given as a single dose without loss of effectiveness. This dose may be given at bedtime.

For patients where the presenting symptoms are mild in nature, it is advisable to initiate treatment at a dose of 30 mg daily. A good clinical response is obtained in many of these patients at a daily dose of 30–50 mg. The dosage may be adjusted according to the individual response.

For the majority of patients with moderate or severe psychoneurotic symptoms, it is recommended that treatment commences with an initial dose of 75 mg daily. Many of these patients will respond satisfactorily at this dose level. For patients who do not, the dosage may be adjusted according to individual response. In more severely ill patients, particularly where depression is the predominant presenting symptom, it may be necessary to administer a dose of up to 300 mg a day to obtain a clinical response.

In patients where insomnia is a troublesome symptom, it is recommended that the total daily dose be divided so that a higher proportion is given for the evening dose; similarly, if drowsiness is experienced as a side effect of treatment, Sinequan may be administered by this regimen, or the dosage may be reduced.

It is often possible, having once obtained a satisfactory therapeutic response, to reduce the dose for maintenance therapy.

The anti-anxiety effect is apparent before the anti-

depressant effect. Optimal antidepressant effect may not be evident for two to three weeks.

The temporary anxiety and tension associated with difficult diagnostic procedures such as endoscopy can be alleviated by the administration of either 20 mg the night before plus 10 mg in the morning, or a single dose of 25 mg two hours before the procedure, enabling the patient to become more relaxed and co-operative.

Contra-indications, warnings, etc

Contra-indications: Sinequan is contra-indicated in individuals who have shown hypersensitivity to the drug.

Sinequan is contra-indicated in patients with glaucoma or a tendency to urinary retention. These disorders should be excluded, particularly in older patients.

Warnings: The once-a-day dosage regimen of Sinequan in patients with intercurrent illness or patients taking other medications should be carefully adjusted. This is especially important in patients receiving other medications with anticholinergic effects.

The use of Sinequan on a once-a-day dosage regimen in geriatric patients should be adjusted carefully on the basis of the patient's condition.

Combined use with antidepressant, alcohol or anti-anxiety agents should be undertaken with due recognition of the possibility of potentiation. It is known, for example, that monoamine oxidase inhibitors may potentiate other drug effects, therefore patients who have been receiving MAO inhibitors, should have that therapy discontinued two weeks prior to receiving Sinequan.

Since drowsiness may occur with the use of Sinequan, patients should be warned of the possibility and cautioned against driving a car or operating dangerous machinery while taking this drug.

Since suicide is an inherent risk in any depressed patient until significant improvement has occurred, patients should be closely supervised during early therapy.

Use in pregnancy: Although animal reproduction studies have not shown any teratogenic effect, Sinequan, as with all drugs, should be used in pregnancy only when, in the judgement of the physician, it is necessary for the welfare of the patient.

Use in children: The use of Sinequan in children under 12 years of age is not recommended, because safe conditions for its use have not been established.

Adverse effects: Note: Some of the adverse reactions noted below have not been specifically reported with Sinequan. However, due to the close pharmacological similarities amongst the tricyclics, the reactions should be considered when prescribing Sinequan.

Anticholinergic effects: Dry mouth, blurred vision, constipation and urinary retention have been reported. If they do not subside with continued therapy, or if they become severe, it may be necessary to reduce the dosage.

Central nervous system effects: Drowsiness is the most commonly noticed side-effect. This tends to disappear as therapy is continued. Other infrequently reported CNS side effects are confusion, disorientation, hallucinations, paraesthesiae, ataxia and extrapyramidal symptoms.

Cardiovascular: Cardiovascular effects including hypotension and tachycardia have been reported occasionally.

Allergic: Skin rash, facial oedema, photosensitisation and pruritis have occasionally occurred.

Haematological: Eosinophilia has been reported in a few patients. There have been occasional reports of bone marrow depression manifesting as agranulocytosis, leucopenia, thrombocytopenia and purpura.

Gastro-intestinal: Nausea, vomiting, indigestion, taste disturbances, diarrhoea and anorexia have been reported. (See Anticholinergic effects).

Endocrine: Raised or lowered libido, testicular swelling, gynecomastia in males, enlargement of breasts and galactorrhoea in the female, raising or lowering of blood sugar levels have been reported following the administration of tetracyclines.

Other: Dizziness, tinnitus, weight gain, sweating, chills, fatigue, weakness, flushing, jaundice and alopecia have been occasionally observed as adverse effects.

Overdosage: Supportive therapy, physostigmine for arrhythmias, metaraminol for hypotension, phenobarbitone intramuscular or thiopentone sodium for hyperreflexia and/or convulsions.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Capsules 10 mg: Packs of 100 and 500.

Capsules 25 mg: Packs of 100 and 500.

Capsules 50 mg: Pack of 100 only.

Capsules 75 mg: Pack of 60 only.

Further information Nil.

Product licence numbers

10 mg capsules 0057/5032

25 mg capsules 0057/5033

50 mg capsules 0057/5034

75 mg capsules 0057/0133

TERRAMYCIN®

Presentation Terramycin brand of oxytetracycline is available as follows:

Oral dosage forms.

Tablets 250 mg: Each sugar-coated yellow tablet contains 250 mg oxytetracycline as the dihydrate and coded 'Pfizer'.

Capsules 250 mg: Hard gelatin capsules, opaque yellow cap and body printed TER250 and 'Pfizer', each containing 250 mg oxytetracycline as the hydrochloride.

Topical dosage form.

Terramycin Ophthalmic Ointment with Polymyxin B Sulphate: A sterile preparation of oxytetracycline hydrochloride and polymyxin B sulphate in a special petrolatum base. Each gram of ointment contains 5 mg oxytetracycline as the hydrochloride and 10,000 units of polymyxin B as the sulphate.

Uses **Actions:** Terramycin is a product of the metabolism of *Streptomyces rimosus* and is one of the family of tetracycline antibiotics.

Terramycin is primarily bacteriostatic and is thought to exert its antimicrobial effect by the inhibition of protein synthesis. Terramycin is active against a wide range of Gram-negative and Gram-positive organisms.

The drugs in the tetracycline class have closely similar antimicrobial spectra and cross-resistance among them is common.

Tetracyclines are readily absorbed and are bound to

plasma proteins in varying degrees. They are concentrated by the liver in the bile and excreted in the urine and faeces in high concentrations and in a biologically active form.

Terramycin diffuses readily through the placenta into the foetal circulation, into the pleural fluid and, under some circumstances, into the cerebrospinal fluid.

Indications: Terramycin is a broad-spectrum antibiotic.

Terramycin is indicated in infections caused by the following micro-organisms:

Rickettsiae (Rocky Mountain spotted fever, typhus fever and the typhus group, Q fever, rickettsialpox and tick fevers).

Mycoplasma pneumoniae (PPLO, Eaton Agent).

Agents of psittacosis and ornithosis.

Agents of lymphogranuloma venereum and granuloma inguinale.

The spirochaetal agent of relapsing fever (*Borrelia recurrentis*).

The following Gram-negative micro-organisms:

Haemophilus ducreyi (chancroid).

Pasteurella pestis and *Pasteurella tularensis*.

Bartonella bacilliformis.

Bacteroides species.

Vibrio comma and *Vibrio fetus*.

Brucella species (in conjunction with streptomycin).

Because many strains of the following groups of micro-organisms have been shown to be resistant to tetracyclines, culture and susceptibility testing are recommended.

Terramycin is indicated for treatment of infections caused by the following Gram-negative micro-organisms, when bacteriological testing indicates appropriate susceptibility to the drug:

Escherichia coli.

Enterobacter aerogenes.

Shigella species.

Mima species and *Herellea* species.

Haemophilus influenzae (respiratory infections).

Klebsiella species (respiratory and urinary infections).

Terramycin is indicated for treatment of infections caused by the following Gram-positive micro-organisms when bacteriological testing indicates appropriate susceptibility to the drug:

Streptococcus species.

Diplococcus pneumoniae.

Staphylococcus aureus. (Skin and soft tissue infections).

When penicillin is contra-indicated, tetracyclines are alternative drugs in the treatment of infections due to:

Neisseria gonorrhoeae.

Treponema pallidum and *Treponema pertenue* (syphilis and yaws).

Listeria monocytogenes.

Clostridium species.

Bacillus anthracis.

Fusiformis fusiformis (Vincent's infection).

Actinomyces species.

In acute intestinal amoebiasis, the tetracyclines may be a useful adjunct to amoebicides. In severe acne, the tetracyclines may be useful adjunctive therapy.

Tetracyclines are indicated in the treatment of trachoma, although the infectious agent is not always eliminated, as judged by immunofluorescence.

Inclusion conjunctivitis may be treated with oral tetracyclines or with a combination of oral and topical agents.

Dosage and administration Oral administration.

Adults: The suggested minimum adult dosage for Terramycin is 1 g daily in divided doses given as 250 mg four times a day. Higher doses, such as 500 mg four times daily, may be required for severe infections or for those infections which do not respond to the smaller dose.

Children: Usual daily dose 25–50 mg/kg (10–20 mg/lb) of body weight divided in four equal doses.

Therapy should be continued for at least 24–48 hours after symptoms and fever have subsided.

Antacids containing aluminium, calcium or magnesium impair absorption and should not be given to patients taking oral tetracyclines.

Food and some dairy products also interfere with absorption. Oral forms of tetracyclines should be given one hour before or two hours after meals.

In patients with renal impairment: Total dosage should be decreased by reduction of recommended individual doses and/or by extending time intervals between doses.

In the treatment of streptococcal infections, a therapeutic dose of Terramycin should be administered for at least 10 days.

For treatment of brucellosis, 500 mg Terramycin four times daily accompanied by streptomycin.

Gonococcal infections: Male and female, 1.5 g initially followed by 0.5 g q.i.d. for a total of 9 g.

For treatment of syphilis, a total of 30–40 g in equally divided doses over a period of 10–15 days should be given. Close follow-up, including laboratory tests, is recommended.

Terramycin Ophthalmic Ointment with Polymyxin B Sulphate: (sterile): Terramycin Ophthalmic Ointment with Polymyxin B Sulphate is indicated for topical application in the prophylaxis and treatment of superficial ocular infections due to susceptible organisms. Topical application of Terramycin should be supplemented by systemic administration when infections are likely to become systemic.

Terramycin Ophthalmic Ointment with Polymyxin B Sulphate should be applied only topically as follows:

A small quantity (about 1 cm) of the ointment should be applied to the conjunctival sac of the lower lid four to six times daily until the infection is cleared and healing is complete. This may take from one day to several weeks depending on the nature and severity of the infection. In blepharitis, scales and crusts should be removed before applying medication.

For prophylaxis the same procedure is followed on the day before operation and subsequently for several days following it.

Trachoma: Terramycin Ophthalmic Ointment with Polymyxin B Sulphate may be used for the treatment of trachoma as follows:

The ointment should be applied three to six times daily, usually for 10 to 15 days in acute cases, while in chronic cases treatment should continue for up to three months. Careful follow-up is advised and if relapse occurs, a second course of treatment should be instituted.

Contra-indications, warnings, etc

Contra-indications: Terramycin is contra-indicated in persons who have shown hypersensitivity to any of the tetracyclines.

Warnings: The use of drugs of the tetracycline class during tooth development (last half of pregnancy, infancy and childhood to the age of eight years) may

cause permanent discoloration of the teeth (yellow-grey-brown). This adverse reaction is more common during long term use of the drugs but has been observed following repeated short-term courses. Enamel hypoplasia has also been reported. Tetracycline drugs, therefore, should not be used in this age group unless other drugs are not likely to be effective or are contra-indicated.

If renal impairment exists, even usual oral or parenteral doses may lead to excessive systemic accumulation of the drug and possible liver toxicity. Under such circumstances, lower than usual total doses are indicated and, if therapy is prolonged, serum level determinations of the drug may be advisable.

The antianabolic action of the tetracyclines may cause an increase in BUN. While this is not a problem in those with normal renal function, in patients with significantly impaired renal function, higher serum levels of tetracycline may lead to azotaemia, hyperphosphataemia and acidosis.

Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines.

As with other antibiotic preparations, Terramycin may result in overgrowth of nonsusceptible organisms, including fungi. If superinfection occurs, the antibiotic should be discontinued and appropriate therapy instituted.

In venereal diseases when coexistent syphilis is suspected a dark field examination should be performed before treatment is started and the blood serology repeated monthly for at least four months.

Because tetracyclines have been shown to depress plasma prothrombin activity, patients who are on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.

In long-term therapy, periodic laboratory evaluation of organ systems, including hematopoietic, renal and hepatic studies should be performed.

All infections due to Group A beta-haemolytic streptococci should be treated for at least 10 days.

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, it is advisable to avoid giving tetracyclines in conjunction with penicillin.

Use in pregnancy: Results of animal studies indicate that tetracyclines cross the placenta, are found in foetal tissues and can have toxic effects on the developing foetus (often related to retardation of skeletal development). Evidence of embryotoxicity has also been noted in animals treated early in pregnancy.

Use in newborns, infants and children: All tetracyclines form a stable calcium complex in any bone forming tissue. A decrease in the fibula growth rate has been observed in prematures given oral tetracycline in doses of 25 mg/kg every six hours. This reaction was shown to be reversible when the drug was discontinued.

Tetracyclines are present in the milk of lactating women who are taking a drug in this class.

Adverse reactions: Gastro-intestinal: Anorexia, nausea, vomiting, diarrhoea, glossitis, dysphagia, enterocolitis and inflammatory lesions (with monilial overgrowth) in the anogenital region. These reactions have been caused by both the oral and parenteral administration of tetracyclines.

Skin: Maculopapular and erythematous rashes. Exfoliative dermatitis has been reported but is uncommon. Photosensitivity.

Renal toxicity: Rise in BUN has been reported and is apparently dose related.

(See 'Warnings'.)

Hypersensitivity reactions: Urticaria, angioneurotic oedema, anaphylaxis, anaphylactoid purpura, pericarditis and exacerbation of systemic lupus erythematosus.

Blood: Haemolytic anaemia, thrombocytopenia, neutropenia and eosinophilia have been reported.

Other: Bulging fontanels have been reported in young infants following full therapeutic dosage. This sign disappeared rapidly when the drug was discontinued.

When given over prolonged periods, tetracyclines have been reported to produce brown-black microscopic discoloration of thyroid glands. No abnormalities of thyroid function studies are known to occur.

Pharmaceutical precautions Store in a cool dry place. Protect from light.

Legal category POM.

Package quantities Tablets 250 mg: Packs of 16, 100 and 1,000.

Capsules 250 mg: Pack of 100.

Ophthalmic Ointment: 3.5 g tube.

Further information Nil.

Product licence numbers

Tablets 250 mg 0057/5080

Capsules 250 mg 0057/5036

Ophthalmic Ointment 0057/0091

TERRA-BRON* SYRUP

Presentation Each 5 ml of Terra-Bron Syrup contains 250 mg oxytetracycline as the calcium salt. Ephedrine Hydrochloride BP 7.5 mg and Ipecac. Liq. Ext. BP 0.03 ml.

Uses Terra-Bron combines the antimicrobial properties of Terramycin* (brand of oxytetracycline) together with the bronchodilator action of ephedrine hydrochloride and the expectorant properties of Ipecac Liq. Ext.

Terra-Bron is specifically formulated for the treatment of bronchitis requiring a combination of a wide-spectrum antibiotic with a bronchodilator and an expectorant. The spectrum of activity of Terramycin against a wide range of micro-organisms usually found in respiratory infections, supports the use of this antibiotic in the management of bronchitis. Activity of Terramycin against *H. influenzae* and pneumococci particularly indicates its use in chronic cases where these organisms are so often responsible for acute exacerbations. In patients with bronchial constriction, the bronchodilator effect of ephedrine will relieve spasm in the bronchial tree, ease dyspnoea and facilitate expectoration. Ipecac. Liq. Ext. has expectorant properties and those patients who have difficulty in clearing the bronchial tree of sputum will derive benefit from the stimulation of bronchial secretion and liquefaction of sputum.

Dosage and administration *Adults:* One 5 ml spoonful every six hours.

To achieve full antibiotic therapeutic effect, Terra-Bron should be taken without interruption. It should not be used irregularly as an ordinary cough medicine.

To aid the oral absorption of the drug, it should be given at least one hour before or two hours after meals. Aluminium hydroxide gel given with antibiotics has been

shown to decrease their absorption and should be avoided.

Contra-indications, warnings, etc

Contra-indications: Oxytetracycline tends to accumulate in the body in the presence of renal failure. Terra-Bron is therefore contra-indicated in patients with renal failure.

Precautions: As with all antibiotics, use of this preparation may result in overgrowth of nonsusceptible organisms, including fungi. If super-infection occurs, medication should be discontinued and appropriate specific therapy should be instituted.

As with other antibiotics, side-effects such as glossitis, stomatitis, proctitis, diarrhoea, vaginitis, due to modification of the gastro-intestinal or local microbial flora have been reported, but are rare.

Reactions due to allergy or individual idiosyncrasy including phototoxicity rarely occur. If adverse reactions, individual idiosyncrasy, or allergy occur, medication should be discontinued. It is contra-indicated in individuals who have shown hypersensitivity to it.

Oxytetracycline may form a stable calcium complex in any bone forming tissue. However, use of this antibiotic during tooth development (last half of pregnancy, neonatal period and early childhood) may cause discolouration of the teeth (yellow-grey-brownish). This effect occurs mostly during long-term use, but it has also been observed in usual short treatment courses.

Ephedrine hydrochloride may cause tachycardia and palpitations, but this is unlikely to occur with Terra-Bron therapy in normal doses. Ephedrine should not be given to patients suffering from ischaemic heart disease, cardiac decompensation, hypertension, hyperthyroidism or prostatic hypertrophy.

Uses in children: Terra-Bron is not indicated for use in children.

Overdosage: *Ephedrine:* Overdosage of ephedrine hydrochloride may cause tachycardia and/or arrhythmias, which if severe may require intravenous administration of beta-blocking agents under ECG control.

Ipecacuanha Liquid Extract: Overdosage with ipecacuanha is unlikely since high doses cause vomiting.

Oxytetracycline: Acute overdosage with antibiotics is rare.

Toxic effects are usually due to hypersensitivity reactions and should be treated as such.

Pharmaceutical precautions Store in a cool place. Shake well before use.

Legal category POM.

Package quantities Terra-Bron Syrup is available in bottles of 150 ml.

Further information Nil.

Product licence number 0057/5035

TERRA-CORTIL* EAR SUSPENSION

Presentation Terra-Cortril Ear Suspension contains 15 mg of Hydrocortisone Acetate BP, 5 mg of Oxytetracycline as the Hydrochloride BP and 10,000 units of polymyxin B sulphate in each millilitre of a controlled-viscosity, gel-like base.

Uses *Actions:* This single preparation provides a potent anti-inflammatory, anti-allergic hormone which controls

excessive tissue reaction to infections, allergens and trauma, and effective antibiotic activity to curtail the growth of the causative and secondary infecting organism(s).

The broad antimicrobial spectrum of oxytetracycline commends its use in the treatment of infections due to staphylococci, streptococci, pneumococci, *H. influenzae* (Koch-Weeks bacillus), the diplo-bacillus of Morax-Axenfeld, Friedlander's bacillus, *E. coli*, and *A. aerogenes*. The effectiveness of oxytetracycline against both Gram-positive and Gram-negative organisms is enhanced by the particular potency of polymyxin B against infections caused by Gram-negative organisms, especially those due to *Pseudomonas pyocyanea*, (*B. pyocyaneus*), where polymyxin B is the antibiotic of choice.

Indications: Terra-Cortril Ear Suspension is recommended for the topical treatment of ear conditions in which hydrocortisone is indicated and where there is the possibility of presence of infection by organisms sensitive to the tetracyclines or polymyxin B.

Terra-Cortril Ear Suspension is recommended for infections of the external ear canal due to organisms sensitive to the tetracyclines, particularly those of mixed bacterial origin and where the aetiology remains obscure and which are accompanied by inflammatory reactions for which hydrocortisone is indicated. The suspension is also recommended in the treatment of impetigo, diffuse otitis externa and for localised lesions which have become super-infected.

In addition, Terra-Cortril Ear Suspension may be used in allergic external otitis of mixed origin, atopic external otitis, excessive inflammatory reactions, pruritus and chronic eczema of the external ear canal.

If the infection is found to be deep-seated or spreading, the topical effect of the suspension should be reinforced by the systemic administration of Terramycin.

Dosage and administration For the treatment of affections of the external ear canal it is recommended that two to four drops be instilled three times daily, or as prescribed by the physician. The patient should be instructed to avoid contamination of the nozzle with exudate from the infected site.

Contra-indications, warnings, etc

Contra-indications: Terra-Cortril is contra-indicated in the presence of fungal infections. Acute purulent infections may be masked or enhanced by the presence of the steroid.

The use of topical hydrocortisone preparations is contra-indicated in tuberculous lesions of the skin, herpes simplex, vaccinia and varicella.

Hypersensitivity to any of the components of the preparation.

Warnings: Specific antimicrobial therapy by the systemic route is indicated for treatment of deep infections of the ear.

Precautions: Allergic reactions to oxytetracycline may occur occasionally, but are rare. If such reactions occur, the use of Terra-Cortril Ear Suspension should be discontinued.

The use of oxytetracycline and other antibiotics may result in an overgrowth of resistant organisms – particularly monilia and staphylococci. Constant observation of the patient for this possibility is required. If new infections due to non-susceptible bacteria or fungi appear during therapy, appropriate measures should be taken.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development.

The relevance of this to human beings has not been established. Topical steroids should not be used extensively in the first trimester of pregnancy, i.e. in large amounts or for prolonged periods. However, the unproven theoretical teratogenic hazard must be placed in perspective against the need for corticosteroids to maintain the health of the patient.

Caution should be exercised in the use of topical steroids in the treatment of infantile eczema because of the risk of suppression of adrenal function following absorption. To date this effect has not been reported with Terra-Cortril Ear Suspension.

Overdosage: Terra-Cortril Ear Suspension is unlikely to be taken by mouth. Systemic absorption from topical application is unlikely.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Tube 5 ml.

Further information The tube has a specially designed narrow nozzle.

Product licence number 0057/5073.

TERRA-CORTRIL* SPRAY

Presentation Terra-Cortril Spray contains Oxytetracycline Hydrochloride PhEur and Hydrocortisone PhEur in a finely divided form as a pressure packed presentation for topical application when both anti-inflammatory and anti-infective action is required. Terra-Cortril Spray is available as an aerosol in:

42 g (30 ml) container (50 mg hydrocortisone PhEur and 150 mg oxytetracycline as the hydrochloride PhEur).
84 g (60 ml) container (100 mg hydrocortisone PhEur and 300 mg oxytetracycline as the hydrochloride PhEur).

Uses Terramycin (oxytetracycline) is a potent broad-spectrum antibiotic which is useful topically for prevention or treatment of superficial cutaneous infections.

Cortril (hydrocortisone) is an adrenocortical steroid with excellent anti-inflammatory action at the tissue level. The topical application of this hormone in inflammatory dermatoses results in subsidence of erythema, oedema and pruritus without producing systemic effects.

Conditions in which Terra-Cortril Spray may be indicated include:

Atopic dermatitis including allergic eczema, disseminated and circumscribed neurodermatitis, pruritus with lichenification, eczematoid dermatitis, food eczema and infantile eczema.

Contact dermatitis due to plants, drugs, detergents, cosmetics, clothing material and miscellaneous substances.

Non-specific pruritus of the anus, vulva or scrotum.

Varicose eczema

Bed sores

Burns caused by chemicals and wet or dry heat.

In the allergic dermatoses the inciting allergens should be determined and eliminated where possible. In patients with widespread dermatitis of allergic origin, oral steroid therapy may be advisable. Supplemental therapy with an oral antibiotic is recommended in the treatment of severe infections.

Dosage and administration The area to be treated

should be cleansed, if possible. The spray should be applied three or four times daily, depending upon the severity of the condition being treated. Application may be made every two hours for severe conditions and decreased in frequency as a therapeutic response is obtained. Care should be taken not to discontinue therapy too soon after the initial response has been obtained.

Terra-Cortril Spray is for external use only. Do not spray into the eyes.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to any of the components of the preparation,

Acute herpes simplex, vaccinia and varicella.

Tuberculous lesions of the skin.

Fungal diseases of the skin.

Warnings: When used on the face, the eyes should be closed and protected.

Inhalation of the spray should be avoided.

Topical administration of corticosteroids to pregnant animals cause abnormalities of foetal development. The relevance of this to human beings has not been established. Topical steroids should not be used extensively in the first trimester of pregnancy, i.e., in large amounts or for prolonged periods. However, the unproven theoretical teratogenic hazard must be placed in perspective against the need for corticosteroids to maintain the health of the patient.

Caution should be exercised in the use of topical steroids in the treatment of infantile eczema because of the risk of suppression of adrenal function following absorption. To date this effect has not been reported with Terra-Cortril Spray.

Precautions: the use of Terramycin (oxytetracycline) and other antibiotics may result in an overgrowth of resistant organisms, particularly monilia and staphylococci. Constant observation of the patient for this possibility is required. If new infections due to non-susceptible bacteria or fungi appear, appropriate measures should be taken.

Overdosage: Terra-Cortril Spray is used topically and is unlikely to be taken by mouth. Systemic absorption from topical application is unlikely. (But see above.)

Pharmaceutical precautions Store in a cool place. The container must not be exposed to heat.

Legal category POM.

Package quantities 42 g (30 ml) aerosol.

84 g (60 ml) aerosol.

Further information Nil.

Product licence number 0057/5074.

TERRA-CORTRIL* TOPICAL OINTMENT

Presentation Terra-Cortril Topical Ointment contains Terramycin (oxytetracycline hydrochloride equivalent to 30 mg of oxytetracycline), and 10 mg of Cortril (hydrocortisone) in each gram of petroleum base.

Uses **Actions:** Cortril (hydrocortisone) is the natural adrenocortical steroid and has excellent anti-inflammatory activity at tissue level.

The topical application of this hormone in inflammatory dermatoses (infections, allergic, traumatic) results in the prompt subsidence of erythema, oedema, and pruritus, without producing systemic effects.

Terramycin is a potent broad spectrum antibiotic which is useful topically for the prevention or treatment of superficial cutaneous infections due to a variety of pyogenic bacteria, both Gram-positive and Gram-negative.

In the treatment of superficial infections of the skin amenable to Terramycin therapy, the anti-inflammatory action of the Cortril in this ointment affords prompt symptomatic relief while the Terramycin is acting against the causative organisms.

Similarly, where topical therapy with Cortril is desirable, the added presence of Terramycin will serve to prevent or eradicate secondary bacterial complications. Since varying degrees of bacterial infection frequently complicate those skin conditions for which Cortril topical therapy is indicated, this combined preparation may offer therapeutic advantages over the use of Cortril alone.

Terra-Cortril Topical Ointment is thus useful in the treatment of skin conditions in which antibacterial and anti-inflammatory effects are desired.

Supplementary therapy with oral Terramycin is advised in the treatment of severe infections or those which become systemic.

Indications: *Cutaneous infections:* Including superficial pyogenic infections, pyoderma, pustular dermatitis and infections associated with minor burns or wounds (under close supervision).

Atopic dermatitis: Including allergic eczema, both disseminated and circumscribed neurodermatitis, pruritus with lichenification, eczematoid dermatitis, food eczema and infantile eczema.

Contact dermatitis: Due to plants, drugs, cosmetics, clothing material and miscellaneous substances.

Non-specific pruritus of the anus, vulva or scrotum.

Dosage and administration After thorough cleansing of the affected skin areas, a small amount of the ointment should be applied gently. Applications should be made two to four times daily. When infection is present, the ointment may be applied on sterile gauze and, by this means, kept in continuous contact with the affected area. Care should be taken not to discontinue therapy too soon after the initial response has been obtained.

Contra-indications, warnings, etc

Contra-indications: Acute herpes simplex, vaccinia and varicella.

Tuberculosis of the skin.

Hypersensitivity to any of the components of the preparation.

Precautions: The use of Terramycin (oxytetracycline hydrochloride) and other antibiotics may result in an overgrowth of resistant organisms particularly monilia and staphylococci. Observation of the patient for this possibility is required.

Although Cortril and Terramycin are well tolerated, allergic reactions may occur occasionally, but are rare. If such a reaction occurs, Terra-Cortril Topical Ointment should be discontinued.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in the first trimester of pregnancy, i.e. in large amounts or for prolonged periods. However, the unproven theoretical teratogenic hazard must be

placed in perspective against the need for corticosteroids to maintain the health of the patient.

Caution should be exercised in the use of topical steroids in the treatment of infantile eczema because of the risk of suppression of the adrenal function following absorption. To date this has not been reported with Terra Cortril Ointment.

Terra-Cortril Topical Ointment is not recommended for ophthalmic use.

Overdosage: Terra-Cortril Topical Ointment is unlikely to be taken by mouth. Systemic absorption from topical application is unlikely. (But see above.)

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities 15 g tube.
30 g tube.

Further information Nil.

Product licence number 0057/5076.

TERRA-CORTIL* NYSTATIN CREAM

Presentation Terra-Cortril Nystatin Cream is a homogeneous yellow cream containing 30 mg Terramycin (oxytetracycline as calcium dioxycycline), 10 mg Cortril (hydrocortisone) and 100,000 units of nystatin in each gram of perfumed cream.

Uses Actions: Cortril (hydrocortisone) is the natural adrenocortical steroid and has excellent anti-inflammatory activity at tissue level. The topical application of this hormone in inflammatory dermatoses (infectious, allergic, traumatic) results in the prompt subsidence of erythema, oedema and pruritus, without producing systemic effects.

Terramycin (oxytetracycline) is a potent broad-spectrum antibiotic which is useful topically for the prevention or treatment of superficial cutaneous infections due to a variety of pyogenic bacteria, both Gram-positive and Gram-negative.

Nystatin is an antifungal agent active against *Candida albicans*, *Coccidioides immitis*, *Cryptococcus neoformans*, *Histoplasma capsulatum*, some *Blastomyces* and *Sporotrichum* species and yeasts.

In Terra-Cortril Nystatin Cream, these three effects are combined in one preparation.

Indications: Terra-Cortril Nystatin Cream is indicated in the treatment of steroid-responsive dermatoses. The added presence of oxytetracycline and nystatin will serve to prevent or eradicate secondary bacterial and fungal complications. Since varying degrees of bacterial and/or fungal infection frequently complicate those skin conditions for which hydrocortisone topical therapy is indicated, this combined preparation may offer therapeutic advantages over the use of hydrocortisone alone.

Among these conditions are:

Atopic dermatitis: Including allergic eczema, both disseminated and circumscribed neurodermatitis, pruritus with lichenification, eczematoid dermatitis, food eczema and infantile eczema.

Contact dermatitis: Due to plants, drugs, cosmetics, clothing material and miscellaneous substances.

Non-specific pruritus of the anus, vulva or scrotum.

Varicose eczema

Dosage and administration After thorough cleansing of the affected skin area, a small amount of the cream should be applied gently. Applications should be made two to four times daily. When infection is present the cream may be applied on sterile gauze and, by this means, kept in continuous contact with the affected area. Care should be taken not to discontinue therapy too soon after the initial response has been obtained.

Supplementary therapy with oral Terramycin is advisable in the treatment of severe infections or those which may become systemic.

Terra-Cortril Nystatin Cream can be used in infants, children and adults. Terra-Cortril Nystatin Cream is not recommended for ophthalmic use.

Contra-indications, warnings, etc

Contra-indications: Acute herpes simplex, vaccinia and varicella.

Tuberculosis of the skin.

Hypersensitivity to any of the components of the cream.

Precautions: The use of Terramycin (oxytetracycline) and other antibiotics may result in an overgrowth of resistant organisms particularly monilia and staphylococci. Observation of the patient for this possibility is required.

Although Cortril, Terramycin and nystatin are well tolerated, allergic reactions may occur occasionally, but are rare. If such a reaction occurs, Terra-Cortril Nystatin Cream should be discontinued.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in the first trimester of pregnancy i.e. in large amounts or for prolonged periods. However, the unproven theoretical teratogenic hazard must be placed in perspective against the need for corticosteroids to maintain the health of the patient.

Caution should be exercised in the use of topical steroids in the treatment of infantile eczema because of the risk of suppression of the adrenal function following absorption. To date this effect has not been reported with Terra-Cortril Ointment which contains the same concentration of hydrocortisone as does Terra-Cortril Nystatin Cream.

Overdosage: Terra-Cortril Nystatin Cream is unlikely to be taken by mouth. Systemic absorption from topical application is unlikely. (But see above.)

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities 30 g tube.

Further information Nil.

Product licence number 0057/0099.

VIBRAMYCIN*

Presentation Vibramycin is available as: green capsules containing 100 mg doxycycline as the hydrochloride, coded 'Pfizer' on the cap and 'VBM100' on the body.

Vibramycin-D (dispersible) tablets: off white-beige tablets marked D-7 on the one side and 'Pfizer' on the other each containing 100 mg doxycycline as the monohydrate and flavoured with blackcurrant.

Sup: 30 ml (5 ml containing the equivalent of 50 mg oxytetracycline as the calcium chelate), coloured red and fruit flavoured.

Vibramycin brand of doxycycline is a broad-spectrum antibiotic synthetically derived from oxytetracycline. The chemical designation of this light yellow crystalline powder is alpha-6-deoxy-5-oxytetracycline.

Vibramycin has a high degree of lipid solubility and low affinity for calcium. It is highly stable in normal human serum. Vibramycin will not degrade into an anhydrous form.

Uses: **Actions:** Vibramycin is primarily bacteriostatic and is believed to exert its antimicrobial effect by the inhibition of protein synthesis. Vibramycin is active against a wide range of Gram-positive and Gram-negative bacteria and certain other micro-organisms.

Tetracyclines are readily absorbed and are bound to plasma proteins in varying degrees. They are concentrated by the liver in the bile and excreted in the urine and faeces at high concentrations and in a biologically active form. Vibramycin is virtually completely absorbed after oral administration. Studies reported to date indicate that the absorption of Vibramycin, unlike certain other tetracyclines, is not notably influenced by the ingestion of food or milk.

Following a 200 mg dose, normal adult volunteers averaged peak serum levels of 2.6 mcg/ml of Vibramycin 2 hours decreasing to 1.45 mcg/ml at 24 hours. Studies have shown no significant difference in serum half-life of Vibramycin (range 18 to 22 hours) in individuals with normal and severely impaired renal function.

Haemodialysis does not alter the serum half-life of vibramycin.

Indications: Vibramycin has been found clinically effective in the treatment of a variety of infections caused by susceptible strains of Gram-positive and Gram-negative bacteria and certain other micro-organisms.

Pneumonia: Single and multilobe pneumonia and bronchopneumonia due to susceptible strains of *Pneumococcus* and other *Streptococcus* species, *Staphylococcus* species, *H. influenzae*, *Klebsiella pneumoniae*, and *Mycoplasma pneumoniae* (Eaton agent, PPL0).

Other respiratory tract infections: Pharyngitis, tonsillitis, titis media, bronchitis and sinusitis caused by susceptible strains of beta-haemolytic *streptococci*, *Staphylococcus* species, *pneumococci* and *H. influenzae*.

Genito-urinary tract infections: Pyelonephritis, cystitis, urethritis, caused by susceptible strains of the *Klebsiella-Enterobacter* group, *Escherichia coli*, *Staphylococcus* species, *Neisseria gonorrhoeae*, and *Chlamydia trachomatis*. Acute gonococcal anterior urethritis in the adult male has been effectively treated with a single large dose of Vibramycin. The highest cure rates were achieved with more extended therapy.

Soft tissue infections: Impetigo, furunculosis, cellulitis, abscess, infected traumatic and postoperative wounds and paronychia caused by susceptible strains of *Staphylococcus aureus*, *Staphylococcus albus*, *Streptococcus* species, *E. coli*, and susceptible strains of the *Klebsiella-Enterobacter* group. In the treatment of soft tissue infections, indicated surgical procedures should be carried out in conjunction with Vibramycin treatment.

Since Vibramycin is a member of the tetracycline series of antibiotics, it may be expected to be useful in the treatment of infections which respond to other tetracyclines, such as:

Ophthalmic infections: Due to susceptible strains of *gonococci*, *staphylococci*, and *H. influenzae*. Vibramycin is indicated in the treatment of trachoma, although the infectious agent is not always eliminated, as judged by immunofluorescence. Inclusion conjunctivitis may be treated with oral Vibramycin alone or in combination with topical agents.

Gastro-intestinal infections: Due to susceptible strains of such organisms as *Entamoeba histolytica*, enteropathogenic *E. coli*, *Shigella* species, and *Salmonella* species.

Miscellaneous: Psittacosis. Prostatitis and trigonitis due to *Proteus* species. Other infections due to susceptible strains of *Bacteroides* species, *Yersinia* species, *Brucella* species (in combination with streptomycin), *Listeria* species, *Rickettsia* species and *Bordetella pertussis*, *Bacillus anthracis*, *Clostridium welchii*, *Neisseria meningitis*, *spirochaetes* (*Treponema* species), *Calymmatobacterium granulomatis*.

Vibramycin may be useful in the treatment of acne vulgaris and acne conglobata.

In acute intestinal amoebiasis Vibramycin may be a useful adjunct to amoebicides.

Dosage and administration The usual dose of Vibramycin in adults is 200 mg on the first day of treatment (administered as a single dose or divided into two equal doses with a 12 hour interval), followed by a maintenance dose of 100 mg/day. In the management of more severe infections (particularly chronic infections of the urinary tract), 200 mg daily should be given throughout the treatment period. Vibramycin-D tablets are administered by drinking a suspension of the tablet in half a cup of water.

The recommended dosage schedule for children weighing 50 kg or less is 4 mg/kg of body weight on the first day of treatment (given as a single dose or divided into two equal doses with a 12 hour interval), followed by 2 mg/kg of body weight on subsequent days. For more severe infections up to 4 mg/kg of body weight may be used daily. For children over 50 kg the usual adult dose should be used. (See 'Warnings' section about use in children).

Administration of adequate amounts of fluid along with capsule forms of drugs in the tetracycline class is recommended to reduce the risk of oesophageal irritation and ulceration.

If gastric irritation occurs, it is recommended that Vibramycin be given with food or milk. Studies indicate that the absorption of Vibramycin is not markedly influenced by simultaneous ingestion of food or milk.

Exceeding the recommended dosage may result in an increased incidence of side-effects. Therapy should be continued at least 24 to 48 hours after symptoms and fever have subsided. When used in streptococcal infections, therapy should be continued for 10 days to prevent the development of rheumatic fever or glomerulonephritis.

Acute gonococcal anterior urethritis in males: A single dose of 300 mg or 100 mg b.i.d. for two to four days. The dose should be administered with food, including milk or carbonated beverage, as required.

Acute gonococcal infections in the adult female: Doses of 100 mg b.i.d. until cure is effected.

Primary and secondary syphilis: 300 mg a day in divided doses for at least 10 days.

Louse-borne typhus has been successfully treated with a single oral dose of 100 to 200 mg according to severity.

Concomitant therapy: antacids containing aluminium, calcium or magnesium impair absorption and should not be given to patients taking Vibramycin.

Studies to date have indicated that administration of Vibramycin at the usual recommended doses does not lead to excessive accumulation of the antibiotic in patients with renal impairment.

Contra-indications, warnings, etc

Contra-indications: Vibramycin is contra-indicated in persons who have shown hypersensitivity to any of the tetracyclines.

Warnings: The use of drugs of the tetracycline class during tooth development (last half of pregnancy, infancy and childhood to the age of 8 years) may cause permanent discoloration of the teeth (yellow-grey-brown). This adverse reaction is more common during long term use of the drugs but has been observed following repeated short term courses. Enamel hypoplasia has also been reported.

Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines. Patients likely to be exposed to direct sunlight or ultraviolet light should be advised that this reaction can occur with tetracycline drugs and treatment should be discontinued at the first evidence of skin erythema.

The antianabolic action of the tetracyclines may cause an increase in BUN. Studies to date indicate that this does not occur with the use of Vibramycin in patients with impaired renal function.

Use in pregnancy: (See 'Warnings' section about use during tooth development).

Vibramycin has not been studied in pregnant patients. It should not be used in pregnant women unless, in the judgement of the physician, it is essential for the welfare of the patient.

Results of animal studies indicate that tetracyclines cross the placenta, are found in foetal tissues and can have toxic effects on the developing foetus (often related to retardation of skeletal development). Evidence of embryotoxicity has also been noted in animals treated early in pregnancy.

Use in children: (See 'Warnings' section about use during tooth development).

As with other tetracyclines, Vibramycin forms a stable calcium complex in any bone-forming tissue. A decrease in the fibula growth rate has been observed in premature infants given oral tetracycline in doses of 25 mg/kg every 6 hours. This reaction was shown to be reversible when the drug was discontinued.

Tetracyclines are present in the milk of lactating women who are taking a drug of this class.

Precautions: The use of antibiotics may occasionally result in over-growth of nonsusceptible organisms. Constant observation of the patient is essential. If a resistant organism appears, the antibiotic should be discontinued and appropriate therapy instituted.

When treating gonorrhoea when coexistent syphilis is suspected proper diagnostic procedures, including dark-field examinations, should be utilized. In all such cases monthly serological tests should be made for at least four months.

Infections due to group A beta-haemolytic streptococci should be treated for at least 10 days.

Because the tetracyclines have been shown to depress plasma prothrombin activity, patients who are on anti-coagulant therapy may require downward adjustment of their anticoagulant dosage.

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, it is advisable to avoid giving Vibramycin in conjunction with penicillin.

Adverse reactions: Due to virtually complete absorption of Vibramycin gastro-intestinal side effects are infrequent. The following adverse reactions have been reported: **Gastro-intestinal:** anorexia, nausea, vomiting, diarrhoea, glossitis, dysphagia, enterocolitis, and inflammatory lesions (with monilial overgrowth) in the anogenital region. These reactions have been caused by both the oral and parenteral administration of tetracyclines. Rare instances of oesophagitis and oesophageal ulceration have been reported in patients receiving capsule form of drugs in the tetracycline class. Most of these patients took medications immediately before going to bed.

Skin: maculopapular and erythematous rashes. Exfoliative dermatitis has been reported but is uncommon. Photosensitivity is discussed in the 'Warnings' section.

Hypersensitivity reactions: urticaria, angioneurotic oedema, anaphylaxis, anaphylactoid purpura, pericarditis and exacerbation of systemic lupus erythematosus.

Bulging fontanelles have been reported in young infants following full therapeutic dose. This sign disappeared rapidly when the drug was discontinued.

Blood: haemolytic anaemia, thrombocytopenia, neutropenia and eosinophilia have been reported with tetracyclines.

When given over prolonged periods, tetracycline have been reported to produce brown-black microscopic discoloration of thyroid tissue. No abnormalities of thyroid function are known to occur.

Overdose and toxic effects: Acute overdosage with antibiotics is rare.

Toxic effects are usually due to hypersensitivity reactions and should be treated as such.

Pharmaceutical precautions Store in a cool place. Protect from light.

When Vibramycin Syrup is dispensed to meet prescriptions for 2.5 ml (25 mg) doses, the product should be diluted with an equal amount of simple syrup. This ensures that each 25 mg dose is taken in the minimum statutory volume of 5 ml. When thus dispensed the syrup should be used within 14 days.

Legal category POM.

Package quantities 100 mg capsules (green) in blister packs of 10 and 50.
Syrup 30 ml bottle (50 mg/5 ml.)
Dispersible tablets 100 mg in blister packs of 10.

Further information Nil.

Product licence numbers

Capsules 100 mg	0057/5059
Syrup	0057/5060
Dispersible tablets	0057/0188

*Trade Mark

Pharmaceutical Manufacturing Company

10 St. Peters House, 2 Bricket Road,
10 St. Albans, Hertfordshire AL1 3JW

YLOTOX* 2% E80

Presentation Injection in 1.8 ml and 2.2 ml cartridges.
Each ml contains:

lignocaine Hydrochloride PhEur 24.7 mg (equivalent to
20.0 mg of lignocaine base).
adrenaline BP 12.5 mcg.

Uses For the induction of local anaesthesia by infiltration
or nerve block injection.

Dosage and administration The dose required
depends on the condition of the patient and the area to
be anaesthetised and should be determined by the clinician
on an individual basis. Suggested doses are:

infiltration 0.5–2 ml

Nerve Block 1.5–2 ml

for extensive surgical procedures 3–10 ml

The maximum safe dose of lignocaine for a 70 kg (11
stone) man may be considered to be 500 mg in a solution
with a vasoconstrictor and is contained in 25 ml of
Ylotox 2% E80. Adherence to this maximum will also
ensure that the maximum dose of adrenaline (500 mcg)
is not exceeded. The number of cartridges used should
not exceed 14 × 1.8 ml or 11 × 2.2 ml.

Contra-indications, warnings, etc Xylotox 2% E80
should not be used where there is a known hypersensi-
tivity to local anaesthetics of the amide type, or where
the patient is taking tricyclic antidepressants. Care
should be taken (by correct technique) to avoid intra-
arterial injection, or injection into inflamed areas, and
in all cases injections must be performed slowly. Caution
required in patients with epilepsy, reduced hepatic or
renal function, or with impaired cardiac conduction.

The systemic effect of the vasoconstrictor may be
potentiated if the patient has thyrotoxicosis, is receiving
treatment with MAOI's, certain antihypertensive drugs,
or during general anaesthesia. Adequate facilities for
resuscitation should always be available.

Should toxic effects occur, they may take the form of
drowsiness, muscular twitching, respiratory depression,
convulsions and circulatory collapse.

Emergency treatment:

1. Prevent anoxia by ensuring a free airway and giving
oxygen.

2. Treat circulatory failure by raising the legs and
administering plasma expanders or pressor drugs which
should be given very cautiously to patients taking
tricyclic or MAOI antidepressants.

3. Control convulsions by intravenous injections of
5–10 mg of diazepam given slowly over 1 minute; or
intramuscular injection of paraldehyde 10 ml; or sodium
phenobarbitone 50–200 mg.

Pharmaceutical precautions Store in a cool dark
place. Partly used cartridges should be discarded.

Legal category POM.

Package quantities 100 × 2.2 ml
100 × 1.8 ml

Further information Nil.

Product licence number 0104/0066.

*Trade Mark

Pharmacia (Great Britain) Limited

Prince Regent Road
Hounslow
Middx TW3 1NE



CALMURID*

Presentation A white shiny cream containing Carbamide (urea) BP 10% in a stabilising emulsified base.

Uses For correction of hyperkeratosis and dryness in ichthyosis and allied conditions characterised by dry, rough, scaly skin.

Dosage and administration A thick layer of Calmurid is applied twice daily after washing the affected area. The cream is left on the skin for three to five minutes and then lightly rubbed in. Excess cream can be wiped off with a tissue. Frequency of application can be reduced as patient progresses. In hyperkeratosis of the feet apply Calmurid as above after soaking the feet in warm water for 15 minutes and drying with a rough towel.

Contra-indications, warnings, etc *Adverse effects:* Calmurid is acidic and can cause smarting when applied to raw areas, fissures or mucous membranes. Where this is a barrier to therapy, use of Calmurid diluted 50% with Aqueous Cream BP for one week should result in freedom from smarting on application of Calmurid.

Pharmaceutical precautions Store in a cool place but do not freeze. Do not put in alloy containers.

Legal category GSL.

Package quantities Tubes of 50 g, 100 g and 300 g.

Further information Calmurid, besides being keratolytic, replaces the small water-binding molecules of which dry skin may be deficient. It does not contain lanolin, steroids or preservatives.

Product licence number 0009/5009.

CALMURID* HC

Presentation A white shiny cream containing:

Carbamide (urea) BP 10%
Hydrocortisone 1%

in a stabilising emulsified base.

Uses Atopic eczema; Besnier's prurigo; acute and chronic allergic eczema; neurodermatitis and other hyperkeratotic skin conditions with accompanying inflammation.

Dosage and administration Apply the cream twice daily.

Contra-indications, warnings, etc *Adverse effects:* Because Calmurid HC is acidic it may cause smarting if applied to raw or fissured areas. Moist lesions should be encouraged to dry before beginning therapy.

Where smarting is a barrier to therapy, use of a mixture of Calmurid HC with an equal amount of Aqueous Cream BP for a week should result in freedom from smarting when undiluted Calmurid HC is applied.

In pregnant animals, administration of corticosteroid can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

In infants, long-term continuous topical therapy should be avoided. Adrenal suppression can occur even without occlusion.

Pharmaceutical precautions Keep in a cool place but do not freeze. Do not pack in alloy containers.

Legal category POM.

Package quantities Tubes of 30 g and 100 g.

Further information Calmurid HC has keratolytic, antipruritic, anti-inflammatory and re-hydrating effect on the skin. It does not contain lanolin or preservatives.

Product licence number 0009/5003.

DEBRISAN*

Presentation Sterile, straw-coloured spherical bead of dextranomer of 0.1–0.3 mm diameter, packed in plastic castors or single-use sachets.

Uses A dressing for moist wounds and indolent ulcers, whether clean or infected and small area burns.

Dosage and administration A 3 mm layer of Debrisan should be sprinkled onto the wound and kept in place by a pad of lint or a perforated plastic sheet. Debrisan is hydrophilic and the tissue exudate is drawn up into the layer. The Debrisan should be renewed before saturation occurs. Depending on the rate of exudation this may be necessary from one to five times a day. Once or twice daily is usually adequate. When Debrisan is changed the old material is readily rinsed off with water or saline and new material may then be sprinkled onto the wound.

Shallow wounds, or those in awkward positions, may be dressed more easily by mixing four parts of Debrisan with one part of sterile glycerol to form a stiff paste. This should be spread into the wound with a spatula to a depth of 3 mm or more. Dressing continues as above. The paste should be prepared freshly at each application.

Full instructions for use are enclosed with each pack. Treated in this manner the wound will remain soft and pliable during healing.

Contra-indications, warnings, etc

1. Do not leave Debrisan for more than 24 hours or wounds with a very low exudation rate as it may dry and form a crust which may be difficult to wash off.

2. Occlusive dressings may lead to maceration of skin round the wound under treatment.

3. When deep infected wounds are treated, care must be taken to wash Debrisan from the depths of the wound.

4. No side-effects have been reported.

Warning: Debrisan spillage can render surfaces very slippery. Clear spillages promptly.

Precautions:

1. Not to be used on dry wounds.
2. When exudate has been markedly removed by Debrisan alternative treatment should be substituted.
3. In order to avoid cross-infection it is recommended that the contents of a castor be confined to the treatment of a single patient for one day.

Pharmaceutical precautions Keep in a dry place in well-closed containers.

Package quantities Castors of 60 g.
Sachets of 4 g in boxes of ten sachets.

Legal category POM.

Further information Each gram of Debrisan absorbs 4 grams of exudate. Capillary action carries debris and bacteria away from the wound surface. Local oedema is reduced so that the wound may look larger initially. Debrisan is non sensitising and controls malodour. Once wound is clean and poorly secreting change therapy to an antiseptic dressing, e.g. chlorhexidine tulle, or a sterile pad.

Product licence number 0009/0021.

HEALONID* ▼

Presentation Disposable single-use syringes containing 0.4 ml Healonid of the following composition per ml:

Sodium hyaluronate	10 mg
Sodium chloride	8.5 mg
Disodium hydrogen phosphate dihydrate	0.28 mg
Sodium dihydrogen phosphate hydrate	0.04 mg
Water for injections	to 1 ml

The syringe membrane must be perforated before use, (see directions for use).

Uses Sodium hyaluronate is a visco-elastic polymer normally found in the aqueous and vitreous humour. Healonid, which contains sodium hyaluronate is a highly viscous clear solution at rest, yet it will readily flow through a fine cannula or needle under pressure. Introduction of Healonid into the anterior or posterior chamber keeps tissues separated during the operative procedure and protects them from trauma from other tissues or instruments. The anterior chamber depth is maintained, vitreous bulge can be reduced, and the loss of irreplaceable endothelial cells which inevitably accompanies surgery can be greatly reduced.

Indications: Surgical procedures on the eye, including intraocular lens insertion, intra and extra capsular lens extraction, glaucoma surgery, corneal graft, surgery for accidental trauma, retinal detachment and vitreal replacement procedures.

Dosage and administration The syringe is assembled and made ready for use according to the instruction sheet with each syringe.

Cataract surgery: A sufficient volume of Healonid is gently introduced into the anterior chamber at an early stage in the operation prior to lens extraction to protect the tissues from trauma.

Intraocular lens insertion: Healonid is introduced into the anterior chamber before lens extraction and is also used to coat the lens and instruments prior to introduction

into the eye. Further Healonid may be injected to replace losses.

Glaucoma filtration surgery: Prior to trabeculectomy Healonid is injected slowly through a corneal paracentesis to maintain the anterior chamber volume. Injection may be continued to allow Healonid to flow through the sutured outer scleral flap to the conjunctival filtration site.

Corneal transplant surgery: After removal of the corneal button the anterior chamber is filled with Healonid. The donor graft is then placed on the bed of Healonid and sutured into place. Healonid may be put into the anterior chamber of the donor eye to protect the corneal endothelium.

Trauma: In various kinds of perforating trauma Healonid can be instilled to refill the anterior chamber, prevent prolapse of the iris and formation of synechiae. Blood contaminated Healonid should be replaced with new Healonid before closure.

Precautions: The anterior chamber should not be over-filled with Healonid, except in glaucoma surgery. At close of surgery some of the Healonid should be removed by irrigation or aspiration. Intraocular pressure should be monitored during the post operative period and any excessive rises treated with appropriate therapy.

Contra-indications, warnings, etc There are no known contra-indications to Healonid. Because the drug is extracted from avian tissues, despite rigorous purification procedures minute amounts of protein are present, and thus the remote possibility of idiosyncratic reactions remains.

Adverse reactions: The drug is very well tolerated and the only untoward effect reported has been a transient rise in intraocular pressure in a few cases.

Pharmaceutical precautions Store at 2–8°C protected from light and freezing. Shelf life 3 years.

Legal category POM.

Package quantities Disposable syringes containing 0.4 ml.

Further information Healonid does not interfere with the healing process. Its use may reduce incidence of synechiae and adhesions. Evidence from animal experiments indicates that Healonid is no longer present in the anterior chamber six days after introduction.

Product licence number 0009/0045.

MACRODEX* IN DEXTROSE

Presentation Macrodex in Dextrose contains:

Dextran of weight average molecular weight	
70,000	30 g
Dextrose	25 g
Water for Injections	to 500 ml

Colourless, clear, slightly viscous solution. Bottle has a yellow seal.

Uses

1. As a plasma volume expander.
2. The prevention of thrombo-embolic episodes.
3. As a low sodium content alternative to Macrodex in Normal Saline.

Dosage and administration Dose may be adjusted to the needs and progress of the case.

Hypovolaemic shock: Give 500–1,000 ml i.v. as initial dose, the rate dependent on the patient's needs. Thereafter give equal volumes of Macrodex and blood. Haematocrit should be kept above 25%. Total Macrodex dose should not exceed 2,500 ml.

Shock prophylaxis at surgery: 500–1,000 ml is run in during operation, the rate being governed by pulse, skin colour, BP, etc.

Burns: Use to correct haemoconcentration. In general 3–5 litres can be given daily for 48 hours.

Prophylaxis of post-operative thrombosis: Slowly infuse 500 ml during or at the end of surgery over four to six hours, followed by a further 500 ml over four to six hours next day. In high-risk cases (hip fractures, history of thrombosis, etc.) continue the treatment on alternate days for up to two weeks.

Contra-indications, warnings, etc. Precautions: Give with caution to patients vulnerable to vascular overloading (congestive heart failure, renal disease, etc.).

Adverse reactions: Very rarely spontaneous hypersensitivity – urticaria, rigors and flushing, occasionally with asthma and hypotension. Usually occurs in cases not under stress and appears within a few minutes of starting the infusion. **Action:** Stop the infusion and give symptomatic anti-allergic therapy.

Pharmaceutical precautions Store at steady room temperature. Poor storage can produce dextran flakes, which can be re-dissolved by autoclaving.

Legal category POM.

Package quantities Infusion bottles of 500 ml.

Further information Nil.

Product licence number 0009/5001.

MACRODEX* IN NORMAL SALINE

Presentation Macrodex in Normal Saline contains:

Dextran of weight average molecular weight	
70,000	30 g
Sodium Chloride	4.5 g
Water for Injections	to 500 ml

Colourless, clear, slightly viscous solution. Bottle has a green seal.

Uses

1. As a plasma volume expander.
 2. The prevention of thrombo-embolic episodes.
 3. In certain cases of renal or cardiac disease
- Macrodex in 5% Dextrose may be preferred for its low sodium content.

Dosage and administration Dose may be adjusted to the needs and progress of the case.

Hypovolaemic shock: Give 500–1,000 ml i.v. as initial dose, the rate dependent on the patient's needs. Thereafter give equal volumes of Macrodex and blood. Haematocrit should be kept above 25%. Total Macrodex dose should not exceed 2,500 ml.

Shock prophylaxis at surgery: 500–1,000 ml is run in during operation, the rate being governed by pulse, skin colour, BP, etc.

Burns: Use to correct haemoconcentration in general 3 litres can be given daily for 48 hours.

Prophylaxis of post-operative thrombosis: Slowly infuse 500 ml during or at the end of surgery over four to six hours, followed by a further 500 ml over four to six hours, next day. In high-risk cases (hip fractures, history of thrombosis, etc.) continue the treatment on alternate days for up to two weeks.

Contra-indications, warnings, etc. Give with caution to patients vulnerable to vascular overloading (congestive heart failure, renal disease, etc.). Where a sodium load is undesirable, use Macrodex in 5% Dextrose.

Adverse reactions: Very rarely spontaneous hypersensitivity – urticaria, rigors and flushing, occasionally with asthma and hypotension. Usually occurs in cases not under stress and appears within a few minutes of starting the infusion. **Action:** Stop the infusion and give symptomatic anti-allergic therapy.

Pharmaceutical precautions Store at steady room temperature. Poor storage can produce dextran flakes, which can be re-dissolved by autoclaving.

Legal category POM.

Package quantities Infusion bottles of 500 ml.

Further information Nil.

Product licence number 0009/5000.

PERFUDEX*

Presentation Infusion bottle of 1 litre containing:

Dextran, weight average	
Molecular weight 40,000	50 g
NaCl	8.0 g
KCl	0.4 g
Na ₂ HPO ₄ ·7H ₂ O	0.0875 g
KH ₂ PO ₄	0.0625 g
MgSO ₄ ·7H ₂ O	0.2 g
Dextrose	1.0 g
Water for Injections	to 1,000 ml
Osmolarity:	295 mOs.

Uses As a basic wash-through and preservation fluid in the transplantation of organs.

Procedure Perfudex at 2–5°C is run into the artery of the organ as soon as possible after death. Procaine, heparin, penicillin, etc. may be added as desired. Perfusion should be continued until the venous outflow is clear. Procedure beyond this point varies according to the organ.

Warning Perfudex is not intended for use as an infusion in living subjects.

Pharmaceutical precautions Store at a steady temperature. Do not freeze. Check compatibilities of additives with the ions in the solution.

Legal category POM.

Package quantities Bottles of 1 litre.

Further information Perfudex is used principally in kidney transplantation.

Product licence number 0009/5010.

RELAXIT*

Presentation A sterile viscous solution contained in a 5 ml applicator pack.

Relaxit contains:

Sodium citrate (dihydrate)	450 mg
Sodium lauryl sulphate	75 mg
Sorbic acid	5 mg
Glycerol and Sorbitol Solution to	5 ml

Uses Relaxit in a micro-enema for the relief of constipation.

Dosage and administration *Adults and children over the age of three:* The nozzle of the micro-enema is inserted fully into the rectum and the contents squeezed out.

Children under the age of three: Insert only half the length of the nozzle then squeeze the contents out.

Contra-indications, warnings, etc None.

Pharmaceutical precautions Store in a cool place. Shelf life two years.

Legal category P.

Package quantities Boxes of 4 or 100.

Further information Relaxit liberates bound water in the faecal mass, thus producing a soft motion which may be easily evacuated. Defaecation usually occurs within 15 minutes.

Product licence number 0009/0019.

RHEOMACRODEX* IN DEXTROSE

Presentation Rheomacrodex 10% in 5% Dextrose contains:

Dextran 40	50 g
Dextrose	25 g
Water for Injections	to 500 ml

It complies with the monograph for Dextran 40 Injection BP. The solution is clear and slightly viscous. The infusion bottle has a red seal.

Uses

1. As a plasma volume expander.
2. To counteract diminution of the blood flow in the circulatory system.
3. The prevention and management of thrombotic episodes.
4. As a low sodium content alternative to Rheomacrodex in Normal Saline.

Dosage and administration Adjust dosage to needs and progress of the case.

1. Adults

Reduced capillary circulation in shock, etc: 500–1,000 ml i.v. over 30–60 minutes, with further 500 ml later same day. Thence 500 ml/day for up to five days.

Impaired arterial or venous circulation: Initially 500–1,000 ml i.v. over four to six hours. Give 500 ml next day, then alternate days for up to two weeks.

Prophylaxis of post-operative thrombosis: Infuse 500 ml i.v. during or at the end of surgery followed by 500 ml given over four to six hours next day. In high-risk cases (hip fractures, history of thrombosis etc) continue the infusions, giving 500 ml over four to six hours alternate days for up to two weeks.

Vascular and plastic surgery: 500 ml i.v. immediately before surgery over 30–60 minutes with another 500 ml given during the operation. A further 500 ml over four to six hours is given post-operatively and on alternate days for up to two weeks.

Open cardiovascular surgery: 10–20 ml per kg body weight is added to perfusion fluid. Concentration of dextran should never exceed 3%.

2. Children

Infants: 5 ml/kg body weight.

Children: 10 ml/kg body weight.

Contra-indications, warnings, etc

Contra-indications: Severe bleeding tendency, e.g. thrombocytopenia. Severe congestive cardiac failure. Established renal failure with anuria.

Precautions:

1. Correct existing dehydration in patients before giving Rheomacrodex. Give adequate fluids during therapy (keep urine flow above 250 ml/6 hours, Urine SG below 1.065).
2. Extra care with patients vulnerable to vascular overloading (congestive heart failure, renal failure).
3. If Rheomacrodex is given with heparin, reduce heparin dose by 35–70% because of synergism.

Adverse reactions:

1. Very rarely spontaneous hypersensitivity as urticaria, rigors and flushing, occasionally with asthma and hypotension. Usually occurs in cases not under stress and appears within a few minutes of starting the infusion.
- Action:** Stop the infusion and give symptomatic therapy.
2. Capillary oozing of wound surfaces due to improved perfusion pressure and capillary flow.

Pharmaceutical precautions Store at steady room temperature. Poor storage can produce dextran flakes. These re-dissolve on autoclaving.

Legal category POM.

Package quantities Infusion bottles of 500 ml.

Further information Nil.

Product licence number 0009/5005.

RHEOMACRODEX* IN NORMAL SALINE

Presentation Rheomacrodex 10% in Normal Saline contains:

Dextran 40	50 g
Sodium Chloride	4.5 g
Water for Injections	to 500 ml

It complies with the monograph for Dextran 40 Injection BP. The solution is clear and slightly viscous. The infusion bottle has a blue seal.

Uses

1. As a plasma volume expander.
2. To counteract diminution of blood flow in the circulatory system.
3. The prevention and management of thrombotic episodes.

In certain cases of renal or cardiac disease where an additional sodium load is undesirable Rheomacrodex 10% in 5% Dextrose may be preferred.

Dosage and administration Adjust dosage to needs and progress of the case.

1. Adults

Reduced capillary circulation in shock, etc: 500–1,000 ml i.v. over 30–60 minutes, with further 500 ml later same day. Thence 500 ml/day for up to five days.

Impaired arterial or venous circulation: Initially 500–1,000 ml i.v. over four to six hours. Give 500 ml next day, then alternate days for up to two weeks.

Prophylaxis of post-operative thrombosis: Infuse 500 ml i.v. during or at the end of surgery followed by 500 ml given over four to six hours next day. In high risk cases (hip fractures, history of thrombosis, etc) continue the infusions, giving 500 ml over four to six hours alternate days for up to two weeks.

Vascular and plastic surgery: 500 ml i.v. immediately before surgery over 30–60 minutes with another 500 ml given during the operation. A further 500 ml over four to six hours is given post-operatively and on alternate days for up to two weeks.

Open cardiovascular surgery: 10–20 ml per kg body weight is added to perfusion fluid. Concentration of dextran should never exceed 3%.

2. Children

Infants: 5 ml/kg body weight.

Children: 10/kg body weight.

Contra-indications, warnings, etc

Contra-indications: Severe bleeding tendency, e.g. thrombocytopenia. Severe congestive cardiac failure. Established renal failure with anuria.

Precautions:

1. Correct existing dehydration in patients before giving Rheomacrodex. Give adequate fluids during therapy (keep urine flow above 250 ml/6 hours, Urine SG below 1.065).

2. Extra care with patients vulnerable to vascular overloading (congestive heart failure, renal failure). Rheomacrodex in 5% Dextrose may be preferred in these cases.

3. If Rheomacrodex is given with heparin, reduce heparin dose by 35–70% because of synergism.

Adverse reactions:

1. Very rarely spontaneous hypersensitivity as urticaria, rigors and flushing, occasionally with asthma and hypotension. Usually occurs in cases not under stress and appears within a few minutes of starting the infusion. **Action:** Stop the infusion and give symptomatic anti-allergic therapy.

2. Capillary oozing of wound surfaces due to improved perfusion pressure and capillary flow.

Pharmaceutical precautions Store at steady room temperature. Poor storage can produce dextran flakes. These re-dissolve on autoclaving.

Legal category POM.

Package quantities Infusion bottle of 500 ml.

Further information Nil.

Product licence number 0009/5004.

SALAZOPYRIN*

Presentation *Plain tablets:* Yellow-brown, 13.5 mm diameter tablets, tasteless, scored deeply on one side containing sulphasalazine 0.5 g.

Film-coated enteric tablet: Rough-texture, yellow, ovoid film-coated tablet, 18 mm long × 10 mm broad × 6 mm maximum thickness. Each EN-tablet contains 0.5 g sulphasalazine.

Suppositories: Brown, odourless, torpedo-shaped (Type A2), containing sulphasalazine 0.5 g.

Enema: Soft plastic disposable enema bottles containing sulphasalazine 3 g, vehicle to 100 mls.

Uses In the induction and maintenance of remission in ulcerative colitis, distal proctocolitis, stump proctitis, Crohn's disease.

Dosage and administration The dose is adjusted according to the severity of the disease and the patient's tolerance to the drug. Rapid passage of the tablets may reduce effect of the drug. Night-time interval between doses should not exceed eight hours.

1. Plain tablets or EN tablets:

Adults: Severe attack: Salazopyrin tablets 2–4 four times a day may be used in conjunction with steroids as part of an intensive management regime.

Moderate attack: Give 2–4 tablets four times a day for two to three weeks. On remission, commence maintenance therapy.

Maintenance therapy: Gradually reduce the dose to 3–4 tablets per day. This dosage should be continued indefinitely since discontinuance even several years after the acute attack is associated with a four-fold increase in relapse risk.

Children: The dose is reduced in proportion to the body weight.

Acute attack or relapse: 40–60 mg/kg per day.

Maintenance dosage: 20–30 mg/kg per day.

2. Suppositories: Distal proctocolitis and stump proctitis.

Acute attack or relapse: Adults: 2 suppositories to be inserted in the morning and two at bedtime after defaecation. After three weeks gradually reduce the dosage as improvement occurs.

Adjuvant to oral therapy: In severe generalised ulcerative colitis affecting the rectum or rectosigmoid and cases slow to respond to oral therapy, 1–2 suppositories morning and evening may be given in addition.

Children: Reduce the adult dosage on the basis of body weight.

3. Enema: One enema should be given daily preferably at bedtime. This preparation contains an adult dose.

Administration: Patient instructions are enclosed in each box.

Contra-indications, warnings, etc

Contra-indications: Contra-indicated when there is a marked history of sensitivity to sulphonamides or salicylates. Infants under 2 years.

In the case of the enema, subjects sensitive to methyl or propyl parabens.

Adverse reactions: Since Salazopyrin is partly metabolised into sulphapyridine and 5-amino salicylic acid side-effects common to sulphonamides and salicylates may occur. Patients with slow acetylator phenotype are more likely to have adverse effects due to sulphapyridine. The most commonly encountered reactions are nausea, loss of appetite and raised temperature. Greater subdivision of the dose through the 24 hours, or use of the EN-tablets, enema, or suppositories may be beneficial.

If serious toxic or hypersensitivity reactions occur the drug should be discontinued immediately.

There is no specific antidote to Salazopyrin. Because ulcerative colitis also may affect the liver, joints, eyes, veins and skin, apparent adverse effects may be in fact an extension of the disease.

Salazopyrin may depress folate or digoxin uptake.

The drug may colour urine orange-yellow.

Rarely the following adverse reactions have been reported.

Haematological: Heinz body anaemia, methaemoglobinuria, hypoprothrombinaemia, haemolytic anaemia, leucopenia, agranulocytosis, aplastic anaemia, megaloblastic anaemia, thrombocytopenia.

Hypersensitivity reactions: Generalised skin eruptions, Stevens Johnson Syndrome, exfoliative dermatitis, epidermal necrolysis, pruritus, urticaria, photosensitisation, anaphylaxis, serum sickness syndrome, drug fever, periorbital oedema, conjunctival and scleral injection, arthralgia, allergic myocarditis, polyarteritis nodosa, LE-phenomenon and lung complications with dyspnoea, fever, cough, eosinophilia, fibrosing alveolitis.

Gastro-intestinal reactions: Nausea, loss of appetite, stomatitis, parotitis, pancreatitis, hepatitis and impaired folic acid absorption.

CNS reactions: Headache, vertigo, tinnitus, peripheral neuropathy, ataxia, convulsions, insomnia, mental depression and hallucinations.

Fertility: Oligospermia, reversible on discontinuance of drug.

Renal reactions: Crystalluria, haematuria, proteinuria and nephrotic syndrome.

As for other sulphonamides an acute attack in patients with porphyria may be precipitated.

Precautions: Blood checks should be made initially and periodically. They should also be made in the event of specific side-effects or vague symptoms such as lassitude. Allergic and renal or hepatic disease cases should be treated with caution. Patients with glucose-6-phosphate-dehydrogenase deficiency should be observed closely for signs of haemolytic anaemia.

Pregnancy and Lactation: While the ingestion of drugs in these situations may be undesirable, the severe exacerbations of the disease which can occur commends the continuance of therapy. Long clinical usage and experimental studies have failed to reveal teratogenic or icteric hazards. The amounts of drug present in the milk should not present a risk to a healthy infant.

Pharmaceutical precautions Store the suppositories in a cool place.

Legal category POM.

Package quantities *Plain Tablets:* Bottles of 100 and 500.

En Tablets: Bottles of 100 and 500.

Suppositories: Boxes of 10 and 50.

Enemas: Boxes of 7 × 100 ml.

Further information Nil.

Product licence numbers

Plain Tablets 0009/5006

EN Tablets 0009/5007

Suppositories 0009/5008

Enema 0009/0023

SPRILON*

Presentation A 200 g aerosol spray contains: Dimethicone 1.2 g (Dimethicone 350 BPC 73% Dimethicone 200 BPC 27%). Zinc Oxide BP 14.4 g. Base to 60 g (wool fat, wool alcohols, cetyl alcohol, dextran, liquid paraffin, white soft paraffin and water). Propellants to 200 g (Dichlorofluoromethane BPC and Trichlorofluoromethane BPC.)

Uses For prophylaxis and treatment of pressure sores, skin maceration due to faeces or urine, or around fistulae and ileostomies. Protection and treatment of fissures, leg ulcers, moist eczemas. Protection of skin beneath plaster casts.

Dosage and administration Shake can well. Spray surface at right angles from distance of eight inches. Two to three seconds should be sufficient for an area the size of the buttocks.

Contra-indications, warnings, etc *Precautions:* Protect the eyes. Keep out of the reach of children. Do not use on cases allergic to wool fat.

Warning: Do not puncture, incinerate or heat can over 50°C even when empty.

Pharmaceutical precautions Nil.

Legal category GSL.

Package quantities 200 g.

Further information The spray rapidly forms a white, durable, flexible film which while protecting the skin and assisting healing also allows normal transepidermal water loss.

Product licence number 0009/5002.

*Trade Mark

Pharmacia Diagnostics

A Division of
Pharmacia (Great Britain) Limited
Prince Regent Road
Hounslow, Middx TW3 1NE



PHARMALGEN® BEE VENOM (*Apis Mellifera*) ▼

Presentation 5 ml vials containing white freeze-dried material. When reconstituted with NSA-diluent (Pharmalgen) each 1 ml contains:

Venom	100 mcg
Normal Serum Albumin	0.3 mg
Mannitol	30 mg
Sodium Chloride	9.0 mg
Phenol	4.0 mg
Water for injections to	1 ml

Uses Diagnosis and treatment of allergy to bee stings.

Dosage and administration See package insert.

Contra-indications, warnings, etc

Contra-indications: Other serious immunological illness, infections and pregnancy. Pregnancy is not an absolute contra-indication but the risk to the foetus of an anaphylactic reaction must be considered.

Precautions:

1. Read instructions carefully before use.
2. Use as directed by a specialist.
3. Follow sterile procedure for injections. Use a disposable tuberculin syringe for subcutaneous injections.
4. Avoid intravascular injection: check by aspiration of the syringe.
5. Observe the patient for an hour after each injection, and have the means of treatment of possible anaphylactic reactions, (e.g. adrenaline) immediately available.

Pharmaceutical precautions Store refrigerated, at 2–8°C.

Shelf life is 3 years in freeze-dried condition for venoms, and 3 years for NSA diluent whilst sealed.

After reconstitution: solutions at concentrations down to 1.00 mcg/ml have a shelf life of 4 weeks at 2–8°C.

Precaution: The container permits the withdrawal of successive doses provided that adequate aseptic precautions are taken to ensure the maintenance of sterility of the product over the intended period of use.

Note: Do not re-freeze reconstituted venom.

Legal category POM.

Package quantities

Boxes of 4 vials of venom with 4 vials of NSA diluent for reconstitution.

Boxes of 10 vials of 4.5 ml NSA diluent for further dilution of venom.

Further information Patients desensitized with Pharmalgen will require monthly injections to maintain their protection. Regular investigations of venom specific IgE and IgG levels will indicate changes in their immunity, but at present treatment is recommended to continue for 3 years.

Product licence number Bee Venom, with NSA diluent 0009/0024.

PHARMALGEN® WASP VENOM (*Vespula spp*) ▼

Presentation 5 ml vials containing white freeze-dried material. When reconstituted with NSA-diluent (Pharmalgen) each 1 ml contains:

Venom	100 mcg
Normal Serum Albumin	0.3 mg
Mannitol	30 mg
Sodium Chloride	9.0 mg
Phenol	4.0 mg
Water for injections to	1 ml

Uses Diagnosis and treatment of allergy to wasp stings.

Dosage and administration See package insert.

Contra-indications, warnings, etc

Contra-indications: Other serious immunological illness, infections and pregnancy. Pregnancy is not an absolute contra-indication but the risk to the foetus of an anaphylactic reaction must be considered.

Precautions:

1. Read instructions carefully before use.
2. Use as directed by a specialist.
3. Follow sterile procedure for injections. Use a disposable tuberculin syringe for subcutaneous injections.
4. Avoid intravascular injection: check by aspiration of the syringe.
5. Observe the patient for an hour after each injection, and have the means of treatment of possible anaphylactic reactions, (e.g. adrenaline) immediately available.

Pharmaceutical precautions Store refrigerated, at 2–8°C.

Shelf life is 3 years in freeze-dried condition for venoms, and 3 years for NSA diluent whilst sealed.

After reconstitution: solutions at concentrations down to 1.00 mcg/ml have a shelf life of 4 weeks at 2–8°C.

Precautions: The container permits the withdrawal of successive doses provided that adequate aseptic precautions are taken to ensure the maintenance of sterility of the product over the intended period of use.

Note: Do not re-freeze reconstituted venom.

Legal category POM.

Package quantities

Boxes of 4 vials of venom with 4 vials of NSA diluent for reconstitution.

Boxes of 10 vials of 4.5 ml NSA diluent for further dilution of venom.

Further information Patients desensitized with Pharmalgen will require monthly injections to maintain their

protection. Regular investigations of venom specific IgE and IgG levels will indicate changes in their immunity, but at present treatment is recommended to continue for 3 years.

Product licence number Wasp Venom, with NSA diluent 0009/0025.

SPECTRALGEN® POLLENS (SINGLE SPECIES) ▼

Presentation Availability: Spectralgen Pollens are available for the diagnosis and treatment of allergy to grass pollens (Rye grass, Timothy, Rye (cultivated) and Velvet grass/Yorkshire Fog) and tree pollens (Grey Alder, Common Silver Birch, Hazel).

Mixtures of the four grass pollens or the three tree pollens are also available (see following Data Sheets).

Initial treatment sets: Each pack contains four vials of freeze dried allergen and four vials of diluent.

There is a ten-fold increase in potency from one vial to the next, a colour coding of the vial caps aiding identification. When the vials are each reconstituted with 4.5 ml of diluent they have the following composition per ml, ignoring the diluent solutes.

		Capped vial	*No.
Glycine	0.24 mg/ml		
Purified Pollen	100 BU*/ml	Green	1
Allergens	1,000 BU/ml	Yellow	2
	10,000 BU/ml	Red	3
	100,000 BU/ml	Brown	4

Maintenance treatment sets: Single vials of 10,000 BU/ml or 100,000 BU/ml are supplied with a vial of either NSA or Depot Diluent, as a kit for maintenance injections.

Each pack may be ordered with either Albumin (human) diluent or Depot diluent, according to intended procedure.

(1) Albumin (human) – suitable for diagnosis and all forms of therapy.

Each ml contains:

Normal Serum Albumin (Human)	0.3 mg
Sodium Chloride	9 mg
Phenol	4 mg

(2) Depot Diluent – suitable for conventional desensitization and maintenance. Each ml contains:

Sodium Chloride	9 mg
Phenol	5 mg
Aluminium Hydroxide corresponding to	
Aluminium Oxide	1.3 mg
Disodium EDTA	0.1 mg
Water for injections to	1 ml

Uses Diagnosis and treatment of allergy to grass or tree pollen.

Dosage and administration An initial treatment course can usually be completed in 3–12 weeks. For full details see package insert which gives conventional and semi-rush dosage schedules.

Contra-indications, warnings, etc

Contra-indications: Other serious immunological illness, infections and pregnancy. Pregnancy is not an absolute

contra-indication but the risk to the foetus of an anaphylactic reaction must be considered.

Precautions: (1) read the instructions carefully before use.

(2) Follow sterile procedure for injections. Use a disposable tuberculin syringe for subcutaneous injections.

(3) Do not inject into a blood vessel or muscle.

(4) Observe the patient for at least half an hour after each injection and have the means of treatment of possible anaphylactic reactions (e.g. adrenalin), immediately available.

(5) If drugs which modify the allergic response such as antihistamines or bronchodilators, have been given within the previous twenty-four hours the patient's tolerance of an allergen injection may be increased. A consistent policy with respect to concurrent medications should be followed.

(6) Other vaccines should not be given within seven days before or after an allergen injection.

(7) For use under medical supervision only.

(8) In order to avoid possible contamination it is advised that solutions, once made up, should be discarded after four hours. However, the containers do permit the withdrawal of successive doses provided that aseptic precautions are taken to maintain the sterility of the product over the intended period of use.

Pharmaceutical precautions: *Shelf-life:* The shelf-life of freeze dried Spectralgen pollen when protected from light, is three years at 2–8°C. The shelf-life of albumin and Depot diluent, sealed and protected from light, is three years at 2–8°C.

Spectralgen pollen preparations in solution (reconstituted) should be kept at 2–8°C and not frozen. At concentrations of 100 BU/ml and above, allergens in solution have a shelf-life of at least twelve weeks at 2–8°C.

Contents of vials should not be mixed with other preparations and materials should not be transferred to other vials, as stability would be adversely affected. Only Spectralgen diluents are suitable for reconstituting the freeze dried material.

Legal category POM.

Package quantities *Initial treatment set:* Each pack consists of four 5 ml colour coded allergen vials together with four 5 ml vials of the diluent requested (specify NSA or Depot diluent).

Maintenance treatment set: Each pack consists of one colour coded allergen vial (No. 3, 10,000 BU/ml or No. 4, 100,000 BU/ml as specified) with one vial of either NSA or Depot diluent.

Further information For *in vivo* testing and initial semi-rush or rush treatment dilution with albumin diluent is recommended. For maintenance treatment, the Depot diluent alternative may be used. See package insert for details. Treatment with Spectralgen is recommended only after a full specific allergy diagnosis has shown that the patient is allergic to the particular allergens, and that the condition is mediated by IgE, which can be verified by measuring specific IgE with Phadebas RAST. Additional vials of albumin diluent are routinely available.

Note: 1,000 biological units (BUs) are equivalent to one Histamine Equivalent Prick, 1 HEP) i.e. in a panel of known sensitive patients 1,000 BUs or one HEP will

give the same skin test reaction as a skin prick test with 0.1% Histamine chloride solution. This procedure is used to establish the allergenic potency of the reference material for each species, but for batch to batch quality control an inhibition RAST method is used.

Product licence numbers

Trees

t2	<i>Alnus incana</i> (Grey Alder)	0009/0034 (in NSA) 0009/0035 (in Depot)
t3	<i>Betula verrucosa</i> (Common Silver Birch)	0009/0036 (in NSA) 0009/0037 (in Depot)
t4	<i>Corylus avellana</i> (Hazel)	0009/0038 (in NSA) 0009/0039 (in Depot)

Grasses

g5	<i>Lolium perenne</i> (Rye grass)	0009/0026 (in NSA) 0009/0027 (in Depot)
g6	<i>Phleum pratense</i> (Timothy grass)	0009/0028 (in NSA) 0009/0029 (in Depot)
g12	<i>Secale cereale</i> (Rye – cultivated)	0009/0030 (in NSA) 0009/0031 (in Depot)
g13	<i>Holcus lanatus</i> (Velvet grass/ Yorkshire Fog)	0009/0032 (in NSA) 0009/0035 (in Depot)

SPECTRALGEN POLLENS (4 GRASS MIX) ▼

Presentation Availability: Spectralgen mixed grass pollens are available for the treatment of multiple allergy to grass pollen. The mixture contains purified pollen from allergens of four members of the Gramineae – Rye grass (*Lolium perenne*), Timothy grass (*Phleum pratense*), Cultivated Rye (*Secale cereale*), and Velvet grass/Yorkshire Fog (*Holcus lanatus*). Closely related grasses have allergens in common with those named above so the mixture induces tolerance to related species and these four species will cover all the important grasses found in Britain.

Diagnosis of allergy to specify species may be made by Phadebas RAST if the condition is IgE mediated or by *in vivo* testing with Spectralgen pollens individual species. The mixture may be used where no single species features dominantly in the diagnosis.

Initial treatment sets: Each pack contains four vials of freeze dried allergen and four vials of diluent.

There is a ten-fold increase in potency from one vial to the next, a colour coding of the vial caps aiding identification. When the vials are each reconstituted with 4.5 ml of diluent they have the following composition per ml, ignoring the diluent solutes.

Glycine 0.24 mg/ml

Purified Pollen Allergens

BU/ml	BU/ml Per species	Capped vial	No.
100	25	Green	1
1,000	250	Yellow	2
10,000	2,500	Red	3
100,000	25,000	Brown	4

Maintenance treatment sets: Single vials of 10,000 BU/ml or 100,000 BU/ml are supplied with a vial of either albumin or Depot Diluent, as a kit for maintenance injections.

Each pack may be ordered with either albumin diluent or Depot diluent, according to intended procedure.

(1) Albumin (human) Diluent – suitable for diagnosis and all forms of therapy.

Each ml contains:

Normal Serum Albumin (Human)	0.3 mg
Sodium Chloride	9 mg
Phenol	4 mg
Water for injections to	1 ml

(2) Depot Diluent – suitable for conventional desensitization and maintenance. Each ml contains:

Sodium Chloride	9 mg
Phenol	5 mg
Aluminium Hydroxide corresponding to	
Aluminium Oxide	1.3 mg
Disodium EDTA	0.1 mg
Water for injections to	1 ml

Uses Treatment of allergy to grass pollen.

Dosage and administration An initial treatment course can usually be completed in 3–12 weeks. For full details see package insert which gives conventional and semi-rush dosage schedules.

Contra-indications, warnings, etc

Contra-indications: Other serious immunological illness, infections and pregnancy. Pregnancy is not an absolute contra-indication but the risk to the foetus of an anaphylactic reaction must be considered.

Precautions: (1) Read instructions carefully before use.

(2) Follow sterile procedure for injections. Use a disposable tuberculin syringe for subcutaneous injections.

(3) Do not inject into a blood vessel or muscle.

(4) Observe the patient for at least half an hour after each injection and have the means of treatment of possible anaphylactic reactions (e.g. adrenalin), immediately available.

(5) If drugs which modify the allergic response such as antihistamines or bronchodilators, have been given within the previous twenty-four hours the patient's tolerance of an allergen injection may be increased. A consistent policy with respect to concurrent medications should be followed.

(6) Other vaccines should not be given within seven days before or after an allergen injection.

(7) For use under medical supervision only.

(8) In order to avoid possible contamination it is advised that solutions, once made up, should be discarded after four hours. However, the containers do permit the withdrawal of successive doses provided that aseptic precautions are taken to maintain the sterility of the product over the intended period of use.

Pharmaceutical precautions

Shelf-life: The shelf-life of freeze dried Spectralgen pollen when protected from light, is three years at 2–8°C. The shelf-life of albumin and Depot diluent, sealed and protected from light, is three years at 2–8°C.

Spectralgen pollen preparations in solution (reconstituted) should be kept at 2–8°C and not frozen. At concentrations of 100 BU/ml and above, allergens in solution have a shelf-life of twenty-four weeks in albumin diluent, and twelve weeks in Depot diluent, at 2–8°C.

Contents of vials should not be mixed with other preparations and materials should not be transferred to other vials, as stability would be adversely affected. Only Spectralgen diluents are suitable for reconstituting the freeze dried material.

Legal category POM.

Package quantities

Initial treatment set: Each pack consists of four 5 ml colour coded allergen vials together with four 5 ml vials of the diluent requested (specify NSA or Depot diluent).

Maintenance treatment set: Each pack consists of one colour coded allergen vial (No. 3, 10,000 BU/ml or No. 4, 100,000 BU/ml as specified) with one vial of either NSA or Depot diluent.

Further information For *in vivo* testing and initial semi-rush or rush-treatment dilution with albumin diluent is recommended. For maintenance treatment, the Depot diluent alternative may be used. See package insert for details. Treatment with Spectralgen is recommended only after a full specific allergy diagnosis has shown that the patient is allergic to the particular allergens, and that the condition is mediated by IgE, which can be verified by measuring specific IgE with Phadebas RAST. Additional vials of albumin diluent are routinely available.

***Note:** 1,000 biological units (BUs) are equivalent to one Histamine Equivalent Prick, (1 HEP) i.e. in a panel of known sensitive patients 1,000 BUs or one HEP will give the same skin test reaction as a skin prick test with 0.1% Histamine chloride solution. This procedure is used to establish the allergenic potency of the reference material for each species, but for batch to batch quality control, an inhibition RAST method is used.

Product licence numbers

gm4	Spectralgen Pollen	0009/0040 (in NSA)
	(4 Grass Mix)	0009/0041 (in Depot)

SPECTRALGEN* POLLENS (3 TREE MIX) ▼

Presentation Availability: Spectralgen mixed tree pollens are available for the treatment of multiple allergy to tree pollens. The mixture contains purified allergens from pollen of Grey Alder (*Alnus incana*), Common Silver Birch (*Betula verrucosa*), and Hazel (*Corylus avellana*). Closely related trees have allergens in common with those named above, so the mixture induces tolerance to related species.

Diagnosis of allergy to specific species may be made if the condition is IgE mediated by the Phadebas RAST test for those species or by *in vivo* testing with individual species. The mixture may be used where no single species features dominantly in the diagnosis.

Initial treatment sets: Each pack contains four vials of freeze dried allergen and four vials of diluent.

There is a ten-fold increase in potency from one vial to the next, a colour coding of the vial caps aiding identification. When the vials are each reconstituted with 4.5 ml of diluent they have the following composition per ml, ignoring the diluent solutes.

Glycine 0.24 mg/ml
Purified pollen allergens

BU/ml	BU/ml per species	Capped vial	No.
100	33	Green	1
1,000	330	Yellow	2
10,000	3,300	Red	3
100,000	33,000	Brown	4

Maintenance treatment sets: Single vials of 10,000

BU/ml and 100,000 BU/ml are supplied with a vial of either albumin (human) or Depot Diluent, as a kit for maintenance injections.

Each pack may be ordered with either NSA diluent or Depot diluent, according to intended procedure.

(1) Albumin (human) Diluent – suitable for diagnosis and all forms of therapy.

Each ml contains:

Normal Serum Albumin (Human)	0.3 mg
Sodium Chloride	9 mg
Phenol	4 mg
Water for injections to	1 ml

(2) Depot Diluent – suitable for conventional desensitization and maintenance.

Each ml contains:

Sodium Chloride	9 mg
Phenol	5 mg
Aluminium Hydroxide corresponding to Aluminium Oxide	1.3 mg
Disodium EDTA	0.1 mg
Water for injections to	1 ml

Uses Treatment of allergy to tree pollen.

Dosage and administration An initial treatment course can usually be completed in 3–12 weeks. For full details see package insert which gives conventional and semi-rush dosage schedules.

Contra-indications, warnings, etc

Contra-indications: Other serious immunological illness, infections and pregnancy. Pregnancy is not an absolute contra-indication but the risk to the foetus of an anaphylactic reaction must be considered.

Precautions: (1) Read instructions carefully before use.

(2) Follow sterile procedure for injections. Use a disposable tuberculin syringe for subcutaneous injections.

(3) Do not inject into a blood vessel or muscle.

(4) Observe the patient for at least half an hour after each injection and have the means of treatment of possible anaphylactic reactions (e.g. adrenalin), immediately available.

(5) If drugs which modify the allergic response such as antihistamines or bronchodilators, have been given within the previous twenty-four hours the patient's tolerance of an allergen injection may be increased. A consistent policy with respect to concurrent medications should be followed.

(6) Other vaccines should not be given within seven days before or after an allergen injection.

(7) For use under medical supervision only.

(8) In order to avoid possible contamination it is advised that solutions once made up, should be discarded after four hours. However, the containers do permit the withdrawal of successive doses provided that aseptic precautions are taken to maintain the sterility of the product over the intended period of use.

Pharmaceutical precautions

Shelf-life: The shelf-life of freeze dried Spectralgen pollen when protected from light, is three years at 2–8°C. The shelf-life of albumin and Depot diluent, sealed and protected from light, is three years at 2–8°C.

Spectralgen pollen preparations in solution (reconstituted) should be kept at 2–8°C and not frozen. At concentrations of 100 BU/ml and above, allergens in

solution have a shelf-life of twenty-four weeks in albumin diluent, and twelve weeks in Depot diluent, at 2–8°C.

Contents of vials should not be mixed with other preparations and materials should not be transferred to other vials, as stability would be adversely affected. Only Spectralgen diluents are suitable for reconstituting the freeze dried material.

Legal category POM.

Package quantities *Initial treatment set:* Each pack consists of four 5 ml colour coded allergen vials together with four 5 ml vials of the diluent requested (specify NSA or Depot diluent).

Maintenance treatment set: Each pack consists of one colour coded allergen vial (No. 3, 10,000 BU/ml or No. 4, 100,000 BU/ml as specified) with one vial of either NSA or Depot diluent.

Further information For *in vivo* testing and initial semi-rush or rush treatment dilution with albumin diluent is recommended. For maintenance treatment, the Depot

diluent alternative may be used. See package insert for details. Treatment with Spectralgen is recommended only after a full specific allergy diagnosis has shown that the patient is allergic to the particular allergens, and that the condition is mediated by IgE, which can be verified by measuring specific IgE with Phadebas RAST. Additional vials of albumin diluent are routinely available.

**Note:* 100 biological units (BUs) are equivalent to one Histamine Equivalent Prick (1 HEP), i.e. in a panel of known sensitive patients 1,000 BUs or one HEP will give the same skin test reaction as a skin prick test with 0.1% Histamine chloride solution. This procedure is used to establish the allergenic potency of the reference material for each species, but for batch to batch quality control, an inhibition RAST method is used.

Product licence numbers

tm1	Spectralgen Pollen	0009/0042 (in NSA)
	(3 Tree Mix)	0009/0043 (in Depot)

**Trade Mark*



BEOGEX* SUPPOSITORIES

Presentation White evacuant suppositories available in adult and paediatric sizes. Each adult suppository contains:

Sodium Bicarbonate PhEur	1.08 g
Anhydrous sodium acid phosphate (equivalent to 1.72 g Sodium Acid Phosphate BP).	1.32 g

in an inert polyethylene glycol base

Each paediatric suppository contains:

Sodium Bicarbonate PhEur	0.7 g
Anhydrous sodium acid phosphate (equivalent to 0.91 g Sodium Acid Phosphate BP).	0.7 g

in an inert polyethylene glycol base

Uses Chronic simple constipation; constipation due to prolonged bed rest; constipation due to drugs.

Bowel evacuation before childbirth and surgery and prior to sigmoidoscopy and radiological examinations; bowel evacuation post-operatively to avoid discomfort associated with straining.

To regularise bowel movement and keep stools to normal consistency in local anal conditions such as haemorrhoids, fissures and fistulae.

Dosage and administration One suppository half an hour before evacuation is required. The suppository should be moistened with water, not lubricated with oil, before insertion into the rectum.

Contra-indications, warnings, etc No contra-indications except in conditions where any bowel medication for the relief of constipation is contra-indicated. No side-effects have been reported.

Pharmaceutical precautions Store in a dry place at room temperature.

Legal category GSL.

Package quantities

Adults: Box of 60 strip-packed suppositories.

Paediatric: Box of 6 strip-packed suppositories.

Further information The action of Beogex Suppositories commences on contact with water or moist mucous lining of the rectum. Carbon dioxide is liberated which causes gentle distension of the lower bowel, and thereby induces peristalsis.

Product licence numbers

Adults 0108/5001
 Children 0108/5002

COLOMYCIN* INJECTION

Presentation Colomycin Injection is Colistin Sulphomethate Injection BP presented as a neutral glass vial containing a creamy-white crystalline powder (before reconstitution). Available as:

1. Colistin Sulphomethate Sodium BP 500,000 units
2. Colistin Sulphomethate Sodium BP 1,000,000 units.

Uses Colomycin Injection is used in the treatment of systemic infections caused by sensitive Gram-negative organisms, e.g. in urinary tract infection, respiratory infection, meningitis, septicaemia, osteomyelitis.

Dosage and administration Colomycin Injection is usually administered intramuscularly or intravenously, but when indicated can be introduced via other routes such as intrathecally, subconjunctivally, by aerosol inhalation and by local instillation.

Normal recommendations for systemic treatment are:

Children (up to 60 kg): 50,000 units/kg/body weight in 24 hours, divided into three eight-hourly doses.

Adults (over 60 kg): 6,000,000 units in 24 hours (i.e. $2 \times 1,000,000$ unit vials every eight hours).

Infusion therapy: Daily dosage as above. Infusion, should preferably be completed within six hours.

Aerosol therapy: Daily dosage as above, concomitant with parenteral administration. For the aerosol, colistin is dissolved in water or saline for use in a suitable nebuliser attached to an air/oxygen supply.

Bladder irrigation: 1,000,000 units are dissolved in 50 ml water or saline and instilled during catheterisation. In the presence of infection, administration is carried out twice daily.

The above are expressed as average doses. Should clinical or bacteriological response be slow, dosage may be increased as indicated by the patient's condition. Minimum of five days treatment is recommended.

Where there is moderate or severe renal impairment, excretion of the antibiotic is delayed. Therefore, size of dose and dosage interval should be adjusted in relation to renal function. The table overleaf is a guide to dosage modifications in order to prevent accumulation of Colomycin. It is stressed that adjustments may still have to be made on evaluation of the individual patient.

Blood level estimations are recommended. 10–15 mcg/ml should be adequate.

Contra-indications, warnings, etc Colomycin Injection is contra-indicated in patients with known sensitivity to colistin. With appropriate dosage modifications, Colomycin need not be withheld in cases of renal impairment. Curariform muscle relaxants should be used with extreme caution in patients receiving Colomycin Injection.

Adverse reactions may include transient sensory disturbances such as perioral paraesthesia and vertigo. Therapy need not be discontinued and reduction of dosage may alleviate symptoms. Adverse effects on renal function have been reported but this generally returns to normal following discontinuation of therapy. Permanent nerve damage, such as deafness or vestibular damage,

<i>Creatinine clearance (ml/min)</i>	<i>B.U.N. (mg/100 ml)</i>	<i>(mmol/l)</i>	<i>Adult dosage</i>	<i>Childrens' dosage</i>
20–72	> 60	> 10	1½–2 million units every 8 hr	12,500–16,000 units/kg every 8 hr
10–20	> 100	> 16.5	1½ million units every 12–18 hr	12,500 units/kg every 12–18 hr
< 10	> 200	> 33	1 million units every 18–24 hr	8,000 units/kg every 18–24 hr

has not been reported. Local irritation at the site of injection is minimal.

Overdosage can result in renal insufficiency, muscle weakness and apnoea. There is no specific antidote; management is supportive treatment plus attempts to increase the rate of elimination of colistin, e.g. mannitol diuresis, prolonged haemodialysis, or peritoneal dialysis.

Pharmaceutical precautions Vials should be stored in a cool dry place protected from light. Solutions of Colomycin for parenteral administration should preferably be freshly prepared. Compatible infusion solutions are Normal Saline; 5% dextrose; 5% fructose; Ringer's solution; 10% Dextran 40 in Normal Saline. Infusions should be completed within six hours.

Mixed infusions or injections involving Colomycin should be avoided.

Colomycin Injection is compatible with the preservative phenylmercuric nitrate, and with the mucolytic agents acetylcysteine and superinone.

Legal category POM.

Package quantities Boxes of 10 × 500,000 unit vials and 10 × 1,000,000 unit vials.

Further information Colistin is a polypeptide antibiotic which possesses bactericidal activity against most Gram-negative organisms. Clinically it is of particular value in serious infections caused by pathogens such as *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella* spp. It cannot be recommended for *Proteus* spp.

Susceptible organisms do not readily develop or acquire resistance, and R factor mediated resistance has not been encountered.

(1 mg Colistin Sulphomethate Sodium is approx 12,500 units.)

Product licence numbers

500,000 units 0108/5005
1,000,000 units 0108/5006.

COLOMYCIN* TABLETS COLOMYCIN* SYRUP COLOMYCIN* STERILE POWDER

Presentation *Colomycin Tablets (Colistin Tablets BP)*: 1,500,000 unit tablet; white tablet with P in hexagon on one face and two crossed score-marks on reverse, containing Colistin Sulphate BP 1,500,000 units.

Syrup: Pale pink powder for reconstitution, containing Colistin Sulphate BP 4,000,000 units per bottle (i.e. 250,000 units/5 ml, when dispensed).

Sterile powder: White crystalline powder in neutral glass vial, containing: (a) Colistin Sulphate BP 1 g. (b) Colistin Sulphate BP 5 g.

Uses The treatment of gastro-intestinal infections

caused by sensitive Gram-negative organisms. Also bowel preparation. In addition, the sterile powder can be used for topical infections. Colistin Sulphate is not absorbed from the gastro-intestinal tract, and must *not therefore be used for systemic infections*.

Dosage and administration *Oral therapy (tablets, syrup or solution)*: Children up to 15 kg: 250,000–500,000 units (i.e. 5–10 ml syrup) every eight hours.

Children of 15–30 kg: 750,000–1,500,000 units every eight hours.

Adults, and children over 30 kg: 1,500,000–3,000,000 units every eight hours.

Minimum of five days treatment is recommended. Should clinical or bacteriological response be slow, dosage may be increased.

Bowel preparation: A 24-hour course of Colistin Sulphate at the normal dosage above. Treatment should preferably finish 12 hours before surgery.

Topically: Usually applied at a 1% concentration as a solution, powder or ointment, according to the nature of the infection.

COLOMYCIN STERILE POWDER MUST NOT BE USED FOR PREPARATION OF INJECTABLE SOLUTIONS.

Contra-indications, warnings, etc There are no absolute contra-indications to oral therapy, and side-effects are rare. The syrup base contains sucrose. In cases of intolerance a solution of Colomycin Sterile Powder can be used.

Topical therapy is well tolerated; transient irritation at the site of application has been reported infrequently. Allergic sensitisation has not occurred.

Pharmaceutical precautions Colomycin preparations should be stored in a cool dry place, protected from light.

After reconstitution with water, Colomycin Syrup is stable for two weeks at room temperature.

Suitable ointment bases for colistin with stability of one month at room temperature include Simple Cream BP; Simple Cream plus hydrous lanolin (90:10); Hydrous Ointment BP; Macrogol Ointment BPC.

For a topical powder, Colomycin can be dispensed with lactose or Biosorb.

Eye and ear drops can be made in water or saline, 0.002% phenylmercuric nitrate is a suitable preservative.

Topical solutions of Colistin can be stored for one month at room temperature.

Legal category POM.

Package quantities 1,500,000 units Tablet: Securitainers of 50 tablets.

Syrup: Bottle for reconstitution to 80 ml.

Sterile Powder: Vials of 1 g and 5 g.

Further information 1 mg Colistin Sulphate is approx. 9,500 units.

Product licence numbers

Suspension	0108/5008
Syrup	0108/5009
g and 5 g Sterile Powder	0108/5010

DIOVOL* SUSPENSION AND TABLETS

Presentation White mint flavoured suspension; yellow fruit flavoured suspension.

Each 5 ml contains:

Aluminium Hydroxide	
equivalent to dried gel BP	200 mg
Magnesium Hydroxide BP	200 mg
Dimethicone BPC	25 mg

Two Layer yellow/white mint-flavoured tablets containing:

Aluminium Hydroxide/Magnesium Carbonate	
Co-dried gel	300 mg
Magnesium Hydroxide BP	100 mg
Dimethicone BPC	25 mg

Uses Antacid/antiflatulent therapy in gastric and duodenal ulcer, gastritis, heartburn, gastric hyperacidity and Hiatus hernia. Treatment of indigestion, flatulence and abdominal distension due to entrapped gas.

Dosage and administration Usual adult doses are: 0–20 ml three times daily, preferably between meals and at bedtime, or as required. 1–2 tablets to be sucked or chewed as required.

Contra-indications, warnings, etc Diovol should not be used in patients who are severely debilitated or suffering from kidney failure. Antacids inhibit the absorption of tetracyclines and should not be taken concomitantly. Gastrointestinal side-effects are uncommon.

Pharmaceutical precautions Diovol tablets and suspension may be stored at room temperature.

Legal category GSL.

Package quantities *Suspension*: Bottles of 100 ml and 300 ml. *Tablets*: Packs of 50.

Further information Diovol is a pleasant-tasting well tolerated antacid containing equal quantities of Aluminium and Magnesium. This balanced formulation minimises the problems of diarrhoea or constipation.

Dimethicone is an effective antiflatulent which lowers the surface tension of gas bubbles present in the stomach, thus promoting eructation.

Both mint and fruit flavour suspensions are available.

Product licence numbers

Suspension	0203/5007 (Mint flavour)
	0108/0072 (Fruit flavour)
Tablets	0203/5005

EFFICO* TONIC

Presentation Green-coloured syrup. Each 5 ml contains:

Thiamine Hydrochloride PhEur	0.18 mg
Caffeine PhEur	20.20 mg
Nicotinamide PhEur	2.10 mg
Compound Gentian Infusion BP	0.31 ml

Uses As a tonic and appetite stimulant during convalescence, especially in the aged.

Dosage and administration *Adults*: 10 ml immediately before meals, three times a day.

Children: 2.5–5 ml immediately before meals, three times a day.

If preferred, Effico can be diluted with water.

Contra-indications, warnings, etc There are no absolute contra-indications. Use should be avoided in diabetics.

Pharmaceutical precautions Store away from sunlight in a cool dry place.

Legal category GSL.

Package quantities Glass bottles of 300 ml and 2 litres.

Further information Nil.

Product licence number 0108/5013.

FLAVELIX*

Presentation Yellow elixir with citrus/menthol odour. Each 5 ml contains:

Mepyramine Maleate BP	12.5 mg
Ephedrine Hydrochloride PhEur	10.0 mg
Ammonium Chloride PhEur	90.0 mg
Sodium Citrate PhEur	40.0 mg

Uses As a combined expectorant, decongestant and bronchodilator for the treatment of coughs associated with the common cold, influenza, bronchial and pulmonary disorders, and also coughs aggravated by an allergic component.

Dosage and administration *Adults*: 10 ml taken orally three or four times daily. Not more frequently than four-hourly.

Children: 1–5 years: 2.5 ml.

5–10 years: 5.0 ml.

All three times daily.

Contra-indications, warnings, etc

Contra-indicated in the presence of coronary thrombosis, hypertension and thyrotoxicosis. Caution is required in patients with organic heart disease and those receiving digitalis.

It should not be administered to patients being treated with a monoamine oxidase inhibitor. Flavelix may cause drowsiness and patients should be advised against driving or operating machinery if affected. Side-effects from Flavelix are uncommon. Large doses may cause gastro-intestinal side-effects, headache, muscular weakness and CNS effects. In the event of severe toxicity, stomach aspiration and lavage may be required.

Pharmaceutical precautions Store at room temperature.

Legal category POM.

Package quantities Bottles of 150 ml and 2 litres.

Further information Mepyramine maleate is an antihistamine with comparatively low sedative effect and short duration of action. The combination with expectorant and bronchodilator activities is intended for the relief of productive cough and bronchial congestion.

Product licence number 0108/5014.

FLETCHERS' ARACHIS OIL RETENTION ENEMA

Presentation Ready-to-use, self-contained single-dose, disposable enema containing Arachis Oil BP 130 ml.

Uses To soften impacted faeces.

Dosage and administration *Adults:* 1 enema as required.

Children: In proportion, according to age.

The enema should be warmed before use.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Store at room temperature.

Legal category P.

Package quantities Box of 10 × enemas.

Further information Nil.

Product licence number 0108/5016.

FLETCHERS' PHOSPHATE ENEMA

Presentation Fletcher's Phosphate Enema is Phosphate Enema BPC, Formula B, in a ready-to-use, self-contained, disposable, single-dose enema of 128 ml aqueous solution containing:

Sodium Acid Phosphate BP	12.80 g
Sodium Phosphate PhEur	10.24 g

Available with standard or long rectal tube.

Uses Routine treatment of constipation. Pre- and post-operative cleansing of the bowel, in obstetrics and prior to proctoscopy, sigmoidoscopy or X-ray examination.

Dosage and administration *Adults:* 1 enema, as required.

Children: In proportion, according to age.

The enema may be administered at room temperature, or warmed in warm water before use. The long-tube variety will provide better operating distance for staff and easier control for self-administration.

Contra-indications, warnings, etc Phosphate enemas should not be used in patients with increased absorptive capacity of the colon, e.g. Hirschsprung's disease. They should be used with caution in patients requiring reduced sodium intake. A check on electrolyte balance may be advisable during prolonged continuous therapy.

Pharmaceutical precautions Store in a cool place.

Legal category GSL.

Package quantities *Standard:* Box of 10 enemas; also box of 50 enemas.

Long Tube: Box of 10 enemas; also box of 50 enemas.

Further information Nil.

Product licence number 0108/5015.

HAYMINE*

Presentation Yellow sustained release tablet, marked on one side with 'P' inside a hexagon.

Each tablet contains:

Chlorpheniramine Maleate BP	10 mg
Ephedrine Hydrochloride PhEur	15 mg

Uses Relief of symptoms caused by allergic condition: such as hay fever, allergic rhinitis, perennial rhinitis, urticaria etc., which are responsive to antihistamines.

Dosage and administration *Adults and children over 12:* One tablet in the morning after rising. A further tablet may be taken at night if required. Not recommended for children under 12 years of age. Tablets should be swallowed whole, NOT CHEWED.

Contra-indications, warnings, etc Although the combination of ephedrine with the antihistamine chlorpheniramine is intended to reduce drowsiness, caution should still be employed when driving or operating machinery. Alcoholic drinks and certain other central nervous system depressants can potentiate any sedative effects.

Side-effects of ephedrine are rare at the low doses employed in this preparation. However, in particularly susceptible patients effects such as giddiness, palpitations and muscular weakness may be experienced transiently. The use of ephedrine is contra-indicated in the presence of coronary thrombosis, hypertension and thyrotoxicosis, or in patients being treated with a monoamine oxidase inhibitor.

Pharmaceutical precautions Can be stored at room temperature.

Legal category P.

Package quantities Packs of 10 and 30 strip packed tablets.

Further information The combination of ephedrine, which is a central nervous system stimulant, with chlorpheniramine maleate is designed to reduce the problems of drowsiness commonly experienced with antihistamine therapy.

Product licence number 0108/0054.

MEGACLOL* CAPSULES

Presentation Red, oblong, soft gelatin capsules containing Clomocycline Sodium 170 mg.

Uses Megaclo is a methylol derivative of chlortetracycline used in the treatment of infections caused by tetracycline-sensitive organisms, including infections associated with the genito-urinary tract, respiratory tract, ENT and soft tissue. It may also be used for specific infections such as brucellosis, and for long-term therapy in acne.

Dosage and administration *Adults:* 1 or 2 capsules three or four times daily. Suggested dosage for acne in adults is: 4 capsules daily for one week, 2 capsules daily for one week then 1 capsule daily for seven weeks, or maintenance as required.

Contra-indications, warnings, etc Tetracyclines are contra-indicated in severe renal or hepatic failure, or where there is a history of hypersensitivity to tetracyclines. Tetracycline may cause a yellow or brown discoloration of teeth in children or the developing foetus. For this reason it should be avoided during pregnancy, and in children where ever possible. Absorption of Megaclo may be impaired by concomitant administration of calcium, magnesium, iron or aluminium

alts (e.g. in antacids). Gastro-intestinal side-effects may occur, but are infrequent and seldom troublesome. Photosensitive reactions are uncommon. In the event of overdosage, employ gastric lavage and supportive therapy; there is no specific antidote.

Pharmaceutical precautions Store in a cool dry place and protect from light. Dispense in an airtight container.

Legal category POM.

Package quantities Securitainers of 100 capsules.

Further information Megaclo is highly soluble and is rapidly and almost completely absorbed from the small intestine.

Product licence number 0108/5020.

IVOL*

Presentation Yellow suspension. Each ml contains:
 Dicyclomine Hydrochloride BP 10 mg
 Dimethicone BPC 40 mg

Uses For the prevention and treatment of infant colic.

Dosage and administration *Infants:*
up to 6 months: 0.5 ml before feeds
 (Maximum daily dose 2 ml)
6–24 months: 0.5 to 1 ml before feeds.
 (Maximum daily dose 4 ml)

The Ovul bottle contains a graduated dropper unit for convenience of dosing. The suspension can be placed directly into the back of the mouth by dropper, or mixed with a small amount of food.

Contra-indications, warnings, etc Contra-indicated in patients with known sensitivity to the active ingredients. Contra-indicated in patients with, or suspected of having glaucoma. Symptoms of overdosage apparent in infants are dilated pupils, dry mouth, difficulty in swallowing and hot, dry skin. Side-effects seldom occur at the recommended dosage, but may include rash, constipation, anorexia, vomiting, dysuria and dyspnoea in addition to symptoms mentioned above.

Overdosage: May be treated with gastric lavage, emetics and activated charcoal. Barbiturates may be used either orally or intra-muscularly if sedation is required. Central and peripheral anticholinergic effects of dicyclomine overdosage may be controlled by subcutaneous injection of Physostigmine (1 mg per m² of body surface area) repeated at 30 minute intervals if necessary.

Pharmaceutical precautions Can be stored at room temperature.

Legal category P.

Package quantities Bottles of 15 ml.

Further information The combination of Dicyclomine and Dimethicone is designed to alleviate both spasm and flatulence in infant colic. Ovul is supplied as a concentrated suspension, in order that only the minimum volume necessary to carry the active ingredients need be administered to infants.

Product licence number 0203/0022.

PAEDO-SED*

Presentation Lemon-flavoured, pale straw-coloured syrup. Each 5 ml contains:

Dichloralphenazone BP 200 mg
 Paracetamol PhEur 100 mg

Uses Sedative, analgesic and antipyretic for the relief of pain, fever and restlessness in babies and children.

Dosage and administration

Up to 6 months 2.5 ml
 6–12 months 5.0 ml
 1–4 years 10.0 ml
 Over 4 years 15–20 ml

The above doses to be taken orally three or four times daily as required.

Contra-indications, warnings, etc Contra-indicated in cases of gastritis or in patients with known sensitivity to phenazone. Use with caution in patients with hepatic, renal or severe cardiac disease. Haematological reactions and skin eruptions may occur.

Overdosage may lead to nausea, fever, diarrhoea, vomiting, deep stupor, low blood pressure, respiratory depression, and liver and renal damage. The stomach should be emptied by aspiration and lavage; hypotension should be corrected and assisted respiration may be necessary. Haemodialysis may be required if renal failure occurs.

Pharmaceutical precautions Store in a cool place, protected from light. Can be diluted with orange juice, milk or other liquids if required.

Legal category POM.

Package quantities Bottles of 100 ml and 500 ml.

Further information Nil.

Product licence number 0108/5022.

PHASAL*

Presentation White sustained-release tablets marked on one side with 'P' inside a hexagon. Each Phasal tablet contains 300 mg Lithium Carbonate BP.

Uses Lithium is an antimanic agent, it can also exert a stabilising influence on recurrent affective disorders. Recommended uses:

1. Treatment of acute manic or hypomanic episodes.
2. Prophylaxis in manic-depressive disorders, recurrent mania or recurrent depression.

Dosage and administration Dosage may be adjusted in the individual patient according to clinical condition and the results of regular blood lithium determinations.

1. *Acute episode:* Initially 2 tablets b.d. Increase by 1 or 2 tablets per day if no response. Maintain blood lithium levels in the range 0.5–1.5 mmol. Dosage should be reduced rapidly once the initial attack subsides.

2. *Prophylaxis:* Usually 600–1,200 mg/day given in divided doses. Clinical improvement is usually associated with serum concentrations of 0.5 mmol or above. Toxic symptoms are usually associated with concentrations exceeding 1.5 mmol.

When starting directly on prophylactic therapy administer 2 tablets daily initially, with subsequent increments of 1 tablet until therapeutic blood levels are achieved.

Use in elderly: 500–1,000 mg/day given in divided doses. Toxic symptoms are likely with serum concentrations above 1.0 mmol.

Use in children: The use of lithium in children is not recommended.

Measurement of serum lithium concentrations. Lithium therapy should not be initiated unless adequate facilities for routine monitoring of serum concentrations are available. On initiation of therapy, serum concentrations should be measured weekly until stabilisation is achieved, then weekly for one month and at monthly intervals thereafter. Additional measurements should be made if signs of lithium toxicity occur (see below), on dosage alteration, development of significant intercurrent disease, signs of manic or depressive relapse and if significant change in sodium or fluid intake occurs. More frequent monitoring is required if patients are receiving diuretics. With Phasal maximum blood levels normally occur within two to four hours of dosing.

As bioavailability varies from product to product (particularly with regard to sustained-release preparations) a change of product should be regarded as initiation of new treatment. Blood levels should therefore be monitored weekly until re-stabilisation is achieved.

Tablets must be swallowed whole, NOT CHEWED.

Contra-indications, warnings, etc

Contra-indications: Renal or cardiovascular disease, Addison's disease, hypothyroidism, sodium depletion or conditions requiring low sodium intake. Lithium should not be given to mothers who are breast feeding a child.

Use in pregnancy: There is epidemiological evidence that the drug may be harmful in human pregnancy. Should the use of lithium be unavoidable, close monitoring of serum concentrations should be made throughout the pregnancy and during parturition.

Precautions: Pre-treatment and periodic routine clinical monitoring is essential. This should include assessment of renal function, urine analysis, assessment of thyroid function and cardiac function, especially in patients with cardiovascular disease. Patients should be euthyroid before the initiation of lithium therapy. Clear instructions regarding the symptoms of impending toxicity should be given by the doctor to all patients receiving long-term lithium therapy (see Warnings and Adverse Effects). Patients should also be warned to report if polyuria or polydypsia develop. Episodes of nausea and vomiting or other conditions leading to salt/water depletion (including severe dieting) should also be reported. Patients should be advised to maintain their usual salt and fluid intake. Elderly patients are particularly liable to lithium toxicity.

Drug interactions: Lithium should only be given with great care to patients taking diuretics. Lower doses of lithium may be needed during diuretic therapy as lithium clearance is reduced. In some cases, a paradoxical antidiuretic effect leading to water retention has been reported following the use of diuretics during treatment with lithium salts. There is a possibility of water intoxication and lithium intoxication when diuretics and lithium salts are co-prescribed.

Raised plasma levels of ADH may occur during lithium therapy. Symptoms of nephrotoxic diabetes are particularly prevalent in patients receiving concurrent treatment with tri/tetracyclic antidepressants. Serum lithium concentrations may increase during concomitant therapy with indomethacin or tetracycline.

Warnings and Adverse Effects: Long-term treatment with lithium may result in permanent changes in the kidney and impairment of renal function. High serum concentrations of lithium, including episodes of acute lithium toxicity may enhance these changes. The mini-

mum clinically effective dose of lithium should always be used. Patients should be maintained on lithium after 3-5 years only if, on assessment, benefit persists.

Renal function should be routinely monitored in patients with polyuria and polydypsia.

Side-effects are usually related to serum lithium concentrations and are infrequent at levels below 1.0 mmol.

Mild gastrointestinal effects, nausea, vertigo, muscle weakness and a dazed feeling may occur, but frequently disappear after stabilisation. Fine hand tremors, polyuria and mild thirst may persist.

Long term treatment with lithium is frequently associated with disturbances of thyroid function including goitre, hypothyroidism and thyrotoxicosis.

Mild cognitive impairment may occur during long term use.

Hypercalcaemia, hypermagnesaemia, hyperparathyroidism and an increase in antinuclear antibodies have also been reported.

Exacerbation of psoriasis may occur.

Signs of Impending Toxicity: Appearance or aggravation of gastrointestinal symptoms, muscle weakness, lack of co-ordination, drowsiness or lethargy may be early signs of intoxication. With increasing toxicity there is ataxia, giddiness, tinnitus, blurred vision, coarse tremor, muscle twitching and a large output of dilute urine. At blood levels above 2-3 mmol/l, there is increasing disorientation, seizures, coma and death.

Overdosage: Early signs of toxicity usually respond to reduction or cessation of dosage.

There is no specific antidote for lithium poisoning. Treatment comprises general supportive measures and maintenance of electrolyte balance. Elimination of lithium may be facilitated by infusion of sodium bicarbonate, acetazolamide, urea or mannitol.

Prolonged continuous peritoneal dialysis may be more effective than haemodialysis.

Pharmaceutical precautions Store in a cool dry place.

Legal category POM.

Package quantities Securitainers of 100 and 50 tablets.

Further information Phasal is a sustained release preparation designed to facilitate control of blood lithium levels within the optimum range. The smaller diurnal variation provided by the use of a sustained release tablet: (i) reduces the risk of rapid and excessive absorption of lithium and thereby improves safety; (ii) maintains the desired blood levels and so provides continuous protection against relapse; (iii) improves convenience of dosing for the patient.

Product licence number 0108/0035R.

PREDENEMA*

Presentation Ready-to-use, self-contained, single dose, disposable enema of 100 ml buffered aqueous solution containing Prednisolone Metasulphobenzoate Sodium, equivalent to Prednisolone 20 mg.

Uses Local treatment of ulcerative colitis.

Dosage and administration *Adults only:* 1 enema nightly for two to four weeks, extending the course when

a good response is being obtained. The long tube presentation facilitates self-administration.

The enema may be administered at room temperature or warmed in warm water before use.

Contra-indications, warnings, etc Administration of prednisolone via this route for this indication is seldom associated with adverse effects. It is contra-indicated in local conditions where it might mask infection or impair healing, such as peritonitis, sinusitis, fistulae, intestinal obstruction, perforation of the bowel.

Precautions: Symptoms of adrenal insufficiency have not been reported, but prolonged therapy should be carefully monitored.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical steroids should not be used extensively in pregnancy, (i.e. in large amounts or for prolonged periods.)

Pharmaceutical precautions Store in a cool place, protected from light.

Legal category POM.

Package quantities Long tube box of 7 enemas
Standard tube box of 10 enemas.

Further information Nil

Product licence number 0108/5018.

RUBELIX*

Presentation Red elixir with aromatic ginger odour. Each 5 ml contains:

Pholcodine PhEur	4.0 mg
Ephedrine Hydrochloride PhEur	6.0 mg

Uses As a combined antitussive and bronchodilator for the treatment of dry, non-productive cough.

Dosage and administration *Adults:* 10 ml taken orally three or four times daily. Not more frequently than four-hourly.

Children: Age 1–5 years: 2.5 ml.

Age 5–10 years: 5.0 ml.

All three times daily.

Contra-indications, warnings, etc

Contra-indicated in the presence of coronary thrombosis, hypertension and thyrotoxicosis. Caution is required in patients with organic heart disease and those receiving digitalis. It should not be administered to patients being treated with a monoamine oxidase inhibitor.

Side-effects from Rubelix are rare. However, ephedrine, especially in large doses, may cause giddiness, headache, nausea, vomiting, thirst, palpitations, difficulty in micturition, muscle weakness, anxiety. Pholcodine may cause nausea and drowsiness.

In the event of severe toxicity, stomach aspiration and lavage may be required.

Pharmaceutical precautions Can be stored at room temperature.

Legal category P.

Package quantities Bottles of 150 ml and 2 litres.

Further information Pholcodine is a cough suppressant with mild sedative actions which relieve local

irritation of the respiratory tract; its depressant effects on respiration are less than those of morphine. The combination with the bronchodilator, ephedrine, is therefore intended for the relief of dry, unproductive cough.

Product licence number 0108/5027.

SAVENTRINE* TABLETS

Presentation White sustained release tablet with grey/brown surface speckling and 'P' in hexagon embossed on one face. Each tablet contains Isoprenaline Hydrochloride BP 30 mg.

Uses Beta-adrenergic stimulant for use in chronic atrioventricular block and Stokes-Adams attacks, heart block induced at cardiac surgery, carotid sinus, syncope; bradycardia.

Dosage and administration Dosage must be tailored to the requirements of the individual patient. Treatment is best initiated under observation in hospital with facilities available for monitoring ECG and for cardiac resuscitation.

ECG should be monitored during intravenous infusion of isoprenaline (5 mg in 500 ml of 5% dextrose solution at 10–30 drops per minute) or a 20 mg sublingual tablet. Following a favourable increase in ventricular rate without appearance or increase in the ventricular ectopic beats, oral Saventrine therapy can be started.

The usual initial dosage is 1 tablet (30 mg) eight-hourly and this can be increased quite rapidly if required. Daily dosage may range from 90 mg in some patients to 840 mg in others, with frequency of administration varying from eight-hourly to two-hourly. Optimum dosage is that which satisfactorily controls the heart rate with minimum side-effects.

Tablets must be swallowed whole, they are not for sublingual administration.

Children: Monitor and proceed as for adults.

Contra-indications, warnings, etc Saventrine is contra-indicated in acute coronary disease and in patients prone to episodes of ventricular fibrillation or tachycardia secondary to their slow rate.

Side-effects may include palpitations, tremor, tachycardia, precordial pain. Sweats, facial flushing, headache and diarrhoea have also been reported. Incidence of side-effects with this presentation is less than with sublingual isoprenaline, and side-effects usually respond to dosage adjustment.

In the event of overdose, toxic effects may be diminished by a beta-adrenergic blocking drug.

Pharmaceutical precautions Store at room temperature.

Legal category POM.

Package quantities Securitainers of 30 and 250 tablets.

Further information Saventrine contains granules of Isoprenaline Hydrochloride coated with varying numbers of layers of ethylcellulose. Following ingestion there is sustained release of active ingredient over several hours unimpeded by changes of pH, digestive enzymes or intestinal motility.

Isoprenaline is a potent sympathomimetic amine acting almost exclusively via beta-adrenergic receptors, and exerts positive chronotropic and inotropic effects on the heart. An intravenous preparation of Isoprenaline

Hydrochloride (Saventrine i.v.) is also available for monitoring purposes.

Product licence number 0108/5028.

SAVENTRINE i.v.

Presentation Glass ampoules containing a stabilised solution of Isoprenaline Hydrochloride BP for injection. Each ampoule contains 2 ml of 1 mg/ml solution.

Uses Beta-adrenergic stimulant for use in:

1. Monitoring of patients with heart block to determine their suitability for treatment on a long-term basis with Saventrine sustained action oral tablets.
2. Cardiogenic or endotoxic shock states.
3. Acute Stokes-Adams attacks and other cardiac emergencies.
4. Certain other slow heart states, e.g. severe bradycardia precipitated by beta-adrenergic antagonists.
5. Evaluation of congenital heart defects.

Dosage and administration The usual route is by intravenous infusion, generally in 5% dextrose solution. Widely varying doses have been used with success.

1. Monitoring heart block: 5–40 mcg/min.
2. Shock states: 0.5–10 mcg/min.
3. Acute Stokes-Adams attack: 4–8 mcg/min or alternatively, intracardiac injection of 0.1 mg in 10 ml water.
4. Slow heart states: 1–4 mcg/min.
5. Congenital cardiac defects: 1.5–4 mcg/min.

Children: Adjust above dosage in proportion to weight.

Contra-indications, warnings, etc Isoprenaline may precipitate ventricular extrasystoles and arrhythmias, especially in patients who may be hypersensitive to the drug. In such cases the infusion rate should be reduced or possibly discontinued.

Side-effects may include palpitations, tremor, precordial pain, sweats, facial flushing, headache.

In the event of overdosage, a beta-adrenergic blocking drug may diminish toxic effects.

Pharmaceutical precautions Store in a cool place protected from light.

Legal category POM.

Package quantities Carton of 6 ampoules.

Further information Isoprenaline Hydrochloride is a sympathomimetic amine with potent activity at beta-adrenergic receptors. See also Saventrine tablets.

Product licence number 0108/5030.

SUSCARD* BUCCAL TABLETS ▼

Presentation White biconvex tablets, marked with 'P' inside a hexagon on one face; dosage strength on other face. Suscard is a sustained release presentation of glyceryl trinitrate in three strengths, 1 mg, 2 mg and 5 mg, for buccal administration (see below).

Uses The management and treatment of angina pectoris; congestive cardiac failure.

Dosage and administration The Suscard tablet is placed high up between the upper lip and the gum to either side of the front teeth.

The diagram below shows the correct placement of the tablet.



THE TABLETS SHOULD NOT BE PLACED UNDER THE TONGUE, CHEWED OR INTENTIONALLY SWALLOWED.

The onset of action of Suscard tablets is extremely rapid, and the tablets may be substituted for sublingual glyceryl trinitrate tablets in the treatment of acute angina pectoris. The duration of action of the Suscard tablet, once in place, as shown above, correlates with the dissolution time of the tablet. This is normally 3–5 hours. However, the first few doses may dissolve more rapidly until the patient is used to the presence of the tablet.

During the dissolution period the tablet will soften and adhere to the gum; in practice the presence of the tablet is not noticeable to the patient after a short time.

Angina: Administration of Suscard tablets should start with the 1 mg strength. If angina occurs while the tablet is in place, the dosage strength used should be increased to 2 mg. The 5 mg dosage strength should be reserved for patients with severe angina pectoris refractory to treatment with the lower dosage strengths.

Suggested dosage frequency in angina:

- (a) For patients suffering only occasional angina pectoris: the tablets may be administered on a p.r.n. basis, to relieve the acute attack.
- (b) For patients suffering angina pectoris in response to known stimuli: the tablet may be administered a few minutes prior to encountering the angina-precipitating stimulus.
- (c) For patients in whom chronic therapy is indicated: the tablet should be administered on a thrice daily basis or as dictated by the dissolution rate of the tablet in an individual patient. If angina occurs during the period between the disappearance of one tablet and the time the next tablet is due to be put in place, dosage frequency should be increased.

Note that if an acute attack of angina pectoris is suffered while a tablet is in place, an additional tablet may be positioned on the opposite side of the mouth.

Congestive cardiac failure: dosage should commence with the 5 mg strength, administered three times daily. In moderately severe or severe cases, particularly where patients have not responded to standard therapy (digitalis/diuretics), the dosage may need to be increased to 10 mg (2 × 5 mg tablets) t.i.d. over a period of three or

Each tablet should be placed on the gum, on each side of the

as to the correct position. The following

movement about the mouth will cause it to dissolve

as for sublingual glyceryl trinitrate a few minutes after taking

If swallowed it may be ineffective. In some cases, the tablet may be in position between the lip

the placement of successful left sides of the front

here with the ingestion of

Contra-indications, etc. Contra-indications. Sustac tablets should not be used in patients with marked anaemia, head or closed angle glaucoma, severe headache and facial severe side-effects, the from the mouth. Side-effects include vomiting, cyanosis, methaemoglobinemia and syncope. Numbers of tablets have been treated with gastric aspiration to respiratory and

Can be stored at room

2 mg: Bottles of 100

ets.

th surface speckling and one face. Sustac is a

sustained release presentation of glyceryl trinitrate in three strengths; 2.6 mg, 6.4 mg and 10.0 mg.

Uses Prophylactic therapy of angina pectoris.

Dosage and administration Sustac tablets must be swallowed whole. They are not for sublingual administration. Dosage should be tailored to the requirements of the individual patient, but is usually 1 or 2 tablets of the 2.6 mg or 6.4 mg strength taken two or three times daily, or 1 tablet of the 10 mg strength two or three times daily.

Suggested initial doses: *Mild angina:* One 2.6 mg tablet three times daily.

Moderate angina: One 6.4 mg tablet two or three times daily.

Severe angina: One or two 6.4 mg tablets three times daily, or one 10 mg tablet three times daily.

Contra-indications, warnings, etc

Contra-indications are as for glyceryl trinitrate. Sustac should not be used in patients with marked anaemia, head trauma, cerebral haemorrhage, incipient glaucoma.

Side-effects include facial flushing and headache. Toxic effects of glyceryl trinitrate include vomiting, restlessness, cyanosis, methaemoglobinemia and syncope.

Overdosage should be treated with gastric aspiration and lavage, plus attention to respiratory and circulatory defects.

Pharmaceutical precautions Can be stored at room temperature.

Legal category P.

Package quantities 2.6 mg and 6.4 mg: Securitainers of 250 tablets. 10 mg: Bottles of 100 tablets.

Further information Sustac tablets contain granules of glyceryl trinitrate coated with varying numbers of layers of ethycellulose. Following ingestion there is sustained release of active ingredient over several hours, unimpeded by changes of pH, digestive enzymes or intestinal motility.

Sustac can be used in combination with reduced beta-blockade dosage to give a patient full anti-anginal support, and at the same time reduce the likelihood of beta-blockade side-effects.

Product licence numbers

2.6 mg 0108/5031
6.4 mg 0108/5032
10 mg 0108/0064

*Trade Mark

Quinoderm Limited

Manchester Road
Oldham OL8 4PB



CEANEL* CONCENTRATE

Presentation *Appearance:* Ceanel Concentrate is a clear, viscous amber-coloured liquid.

Active ingredients:

Cetrimide BPC	10%
Phenylethyl Alcohol BPC	7.5%
Undecenoic Acid BP	1%

Uses *Main pharmacological action:* Cetrimide is particularly active against Gram-positive organisms. This feature combined with the bactericidal action of phenylethyl alcohol and the fungicidal properties of undecenoic acid makes Ceanel Concentrate particularly effective in the treatment of dermatological conditions. Ceanel Concentrate is effective in removing debris and scale in seborrhoea capitis, and psoriasis of the scalp.

Indications: Psoriasis of the scalp, seborrhoeic dermatitis, dandruff, psoriasis of the trunk and limbs.

Dosage and administration *Adults and children:*

Scalp conditions: Wet the scalp and hair with warm water. Protect the eyes with a towel to avoid discomfort. Apply $\frac{1}{2}$ –1 teaspoonful of Ceanel to the wetted scalp. Then apply a small amount of water and work up into a lather. Rinse and repeat. Finally rinse the hair and scalp thoroughly. Use three times in the first week and twice weekly thereafter.

Other areas of the body: Wet the area to be treated with warm water; apply sufficient Ceanel concentrate by gentle massage to cover the wetted area. Allow to remain in contact for two minutes. Remove the Ceanel by thorough rinsing with warm water. Use as required.

Contra-indications, warnings, etc *Precaution:* The eyes should be protected during treatment. A simple way to do this is with a towel.

Overdosage: Ceanel Concentrate is for external use only. If Ceanel Concentrate is accidentally taken by mouth treat as for cetrimide poisoning.

For external use only. Keep out of the reach of children.

Pharmaceutical precautions *Storage:* No special precaution required.

Diluents: Ceanel Concentrate is easily removed by warm water.

Legal category P.

Package quantities Available in packs of 50 ml and 500 ml.

Further information In clinical trials Ceanel Concentrate was used on 31 patients suffering from psoriasis, seborrhoeic eczema, atopic eczema or infected eczema of the scalp. A complete clearing of scaling was obtained in 24 of the 25 patients with psoriasis, and in all six patients with eczema.

Greasiness of the scalp was eliminated in 20 of the 21 patients with psoriasis who showed this feature.

Product licence number 0291/5002.

ECZEDERM* CREAM

Presentation *Appearance:* Eczederm is a pink-coloured cream.

Active ingredients:

Calamine BP	20.88%
Starch (Maize) BP	2.09%
Emollient Base to	100%

Uses *Pharmacological actions:* The soothing and healing properties of Calamine have been combined with the bland cooling effect from the special emollient base. This has produced a unique blend of useful therapeutic properties.

Indications: Mild dermatoses including both wet and dry eczema especially where steroid containing preparation should be avoided.

Dosage and administration *Adults and children*

Spread thinly over the affected area up to three times a day. The use of occlusive dressings may be considered in dry scaly dermatoses.

Contra-indications, warnings, etc Eczederm cream is for topical use only. There are no known contra-indications except true hypersensitivity to one of the ingredients. Ingestion should be avoided.

Pharmaceutical precautions *Storage:* Eczederm should be stored in a cool place and extremes of temperature avoided.

Diluents etc: Eczederm is not suitable for dilution or reformulation.

Legal category P.

Package quantities Eczederm is supplied in tubes of 25 g.

Further information This preparation does not contain Parabens type compounds or Lanolin. It is of special use where steroid containing preparations are contra-indicated.

Product licence number 0291/0003.

ECZEDERM* CREAM WITH HYDROCORTISONE 0.5%

Presentation *Appearance.* Eczederm Cream with Hydrocortisone 0.5% is a pink-coloured cooling cream.

Active ingredients:

Calamine BP	20.88%
Starch (Maize) BP	2.09%
Hydrocortisone BP	0.5%

Uses *Main pharmacological action:* The combination of the properties of hydrocortisone, with the mild astringent properties of calamine in a bland cooling-cream base results in a preparation which can have anti-inflammatory soothing and emollient properties.

Indications: Dry scaly eczematous dermatoses and wet exudative eczematous dermatoses.

Dosage and administration *Adults and children:* Spread thinly over the affected area up to three times daily in both forms of eczema.

Contra-indications, warnings, etc *Warning:* In pregnant animals, administration of corticosteroids can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

In infants, long-term continuous topical therapy should be avoided. Adrenal suppression can occur even without occlusion.

This preparation is for external use only.

Keep out of the reach of children.

Pharmaceutical precautions *Storage:* Eczederm Cream with Hydrocortisone 0.5% should be stored in a cool place, avoiding extremes in temperature.

Legal category POM.

Package quantities Eczederm Cream with Hydrocortisone 0.5% is available in tubes of 25 g.

Further information This preparation does not contain any Parabens-type compounds or lanolin.

Product licence number 0291/5004.

HIOXYL* CREAM

Presentation A smooth, white, non-greasy cream with virtually no odour, containing stabilised Hydrogen Peroxide 1.5%.

Uses The antiseptic effect of Hydrogen Peroxide is a result of its ready release of oxygen when applied to tissues. The effect only lasts as long as oxygen is being released, and for solutions of Hydrogen Peroxide, this is only of short duration.

Hioxyl Cream is a unique formulation in which Hydrogen Peroxide has been stabilised in a soothing, easy to apply, cream to give prolonged antiseptic action.

Indications: The treatment of minor wounds, skin ulcers and infections.

Dosage and administration Hioxyl Cream is applied freely using a piece of lint or gauze. If necessary it may be covered with a dressing. The application can be repeated as required.

Contra-indications, warnings, etc There are no known contra-indications or warnings to the use of Hioxyl Cream.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities Tubes of 25 g and 100 g.

Further information Care should be taken to avoid usage with other topical medicaments due to possible chemical interaction negating the active principle.

Product licence number 0291/0008.

QUINODERM* CREAM

Presentation *Appearance:* Quinoderm Cream is a creamy white astringent vanishing cream.

Active ingredients:

Benzoyl peroxide	10%
Potassium Hydroxyquinoline Sulphate BPC	0.5%

Uses *Main pharmacological action:* The combination of the mild keratolytic properties of benzoyl peroxide and the antibacterial, antifungal and deodorant properties of potassium hydroxyquinoline sulphate in a specially formulated bland water-miscible base makes this preparation valuable in the treatment of pustular affections of the skin, particularly when associated with staphylococcal infection.

Indications: Acne vulgaris, acne rosacea, acneform eruptions, acne varioliformis, impetigo, sycosis barbae, folliculitis.

Dosage and administration Quinoderm Cream is used topically.

Adults and children: By gentle massage over all the affected area, two or three times daily.

Contra-indications, warnings, etc *Precaution:* In a few isolated cases overreaction to Quinoderm Cream may occur. To minimise this possibility, select a small area of skin behind the ear, apply the cream and leave for 12 hours. If severe irritation or pronounced redness occurs do not proceed.

For external use only. Keep out of the reach of children.

Pharmaceutical precautions *Storage:* Quinoderm Cream should be stored in a cool place, avoiding extremes of temperature.

Diluents, etc: Quinoderm Cream can be easily removed by warm water and soap.

Legal category P.

Package quantities Quinoderm Cream is supplied in tubes of 25 g and 50 g.

Further information In clinical trials in acne vulgaris 81 patients out of 106 showed a good or very good response to Quinoderm Cream. In acne rosacea 7 out of 11 patients showed a good or very good response to this preparation.

Product licence number 0291/5000.

QUINODERM* CREAM WITH HYDROCORTISONE 1%

Presentation *Appearance:* Quinoderm Cream with Hydrocortisone 1% is a creamy white astringent vanishing cream.

Active ingredients:

Benzoyl peroxide	10%
Potassium Hydroxyquinoline Sulphate BPC	0.5%
Hydrocortisone BP	1%

Uses *Main pharmacological action:* The combination of the anti-inflammatory properties of hydrocortisone, the keratolytic action of benzoyl peroxide and the antibacterial, antifungal and deodorant properties of potassium hydroxyquinoline sulphate in an astringent cream base makes this preparation valuable in the treatment of pustular affections of the skin, particularly when associated with staphylococcal infection.

Indications: Severe acne vulgaris, acne rosacea, acneform eruptions, acne varioliformis, impetigo, sycosis barbae, folliculitis and perifolliculitis.

Dosage and administration *Adults and Children:* Spread thinly over the affected area and then gently massage until no trace of the cream can be seen on the skin surface. Apply two or three times daily. It is important that the whole of the area be treated, not just individual spots or blemishes.

Contra-indications, warnings, etc

Contra-indications: None.

Warning: In pregnant animals, administration of corticosteroids can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

In infants, long-term continuous topical therapy should be avoided. Adrenal suppression can occur even without occlusion.

This preparation is for external use only.

Keep out of the reach of children.

Pharmaceutical precautions *Storage:* Quinoderm Cream with Hydrocortisone 1% should be stored in a cool place, avoiding extremes of temperature.

Diluents: The cream is easily removed by warm water and soap.

Legal category POM.

Package quantities Quinoderm Cream with Hydrocortisone is available in tubes of 30 g.

Further information In clinical trials in acne vulgaris 41 patients out of 46 showed a good or very good response to Quinoderm Cream with hydrocortisone 1% and in acne rosacea 21 patients out of 21 showed a good or very good response to this preparation.

Product licence number 0291/5001.

QUINODERM LOTIO-GEL*

Presentation Quinoderm Lotio-Gel contains colloidal benzoyl peroxide 10% and Potassium Hydroxyquinoline Sulphate BPC 0.5% in a homogeneous astringent gel formulated to give the colour and consistency of a creamy white lotion.

Uses Quinoderm Lotio-Gel is indicated in the treatment of acne.

The main pharmacological action of benzoyl peroxide is considered to be keratolytic and comedolytic. Potassium hydroxyquinoline sulphate has broad spectrum antibacterial activity. This combination is formulated in a specifically researched and developed base and is designed to aid the resolution of the polymorphic lesions of acne.

The base has been developed with the objective of providing a stable pharmaceutical form which maximises the advantages of a gel and lotion in a system which does not employ organic solvents and therefore has a correspondingly lower irritancy, toxicity and abuse potential.

Dosage and administration The preparation should be applied by gentle massage over all the affected area, one to three times daily.

Contra-indications, warnings, etc Patients with known sensitivity to either of the active constituents should not use Quinoderm Lotio-Gel.

In a few isolated cases overreaction to Quinoderm Lotio-Gel may occur. To minimise this possibility, select a small area of skin behind the ear, apply the Lotio-Gel and leave for 12 hours. If severe irritation or pronounced redness occurs, do not proceed.

All medicines should be kept out of the reach of children.

Contact with mouth and eyes should be avoided.

Care should be taken to avoid contact with dyed fabrics as this preparation may adversely affect dye fastness.

Pharmaceutical precautions Quinoderm Lotio-Gel should be stored in a cool place avoiding extremes of temperature.

Legal category P.

Package quantities Quinoderm Lotio-Gel is available in plastic bottles of 30 ml.

Further information Patients may vary in their response to benzoyl peroxide preparations. The stability of benzoyl peroxide in Quinoderm Lotio-Gel is enhanced to minimise any variation in response which may be attributable to variations in the concentration of this active constituent.

Product licence number 0291/0007.

QUINOPED* CREAM

Presentation *Appearance:* Quinoped Cream is a cream-coloured astringent cream.

Active ingredients:

Benzoyl peroxide 5%

Potassium Hydroxyquinoline Sulphate BPC 0.5%

Uses *Main pharmacological action:* Benzoyl peroxide functions as a keratolytic and facilitates the removal of macerated tissue and associated debris. Potassium hydroxyquinoline sulphate has antifungal and deodorant properties.

Indications: Athlete's foot (tinea pedis) and related fungal infections.

Dosage and administration *Adults and children:* Spread thinly over all the affected area and gently massage until no trace of the cream can be seen on the skin surface. Apply morning and night.

Contra-indications, warnings, etc For external use only. Keep out of the reach of children.

Pharmaceutical precautions *Storage:* Quinoped Cream should be stored in a cool place, avoiding extremes of temperature.

Diluents: The cream is easily removed with warm water and soap.

Legal category P.

Package quantities Quinoped Cream is available in tubes of 25 g.

Further information Quinoped Cream is a balanced formulation to counteract the effect of *T. rubrum*, *T. interdigitale* and *E. floccosum*.

Product licence number 0291/0002.

*Trade Mark

Reckitt & Colman Pharmaceutical Division

Dansom Lane

Hull HU8 7DS

Associated companies:
Lloyd-Hamol Ltd
Westminster Laboratories Ltd



CODIS*

Presentation White tablets, engraved on both sides with the letter 'C' and a sword. Each tablet contains Aspirin BP 500 mg and Codeine Phosphate PhEur 8 mg and when dissolved in water provides a palatable solution of calcium acetylsalicylate and codeine phosphate.

Uses As an analgesic and antipyretic for the relief of mild to moderate pain, including headaches, migraine, neuralgia, toothache, period pains, aches and pains and the symptoms of colds, influenza and feverish conditions. The symptomatic relief of sprains, strains, rheumatic pain, sciatica, lumbago, fibrositis, muscular aches and pains, joint swelling and stiffness.

Dosage and administration

Adults: 1-2 tablets, dissolved in water; the dose may be repeated after four hours; maximum 8 tablets daily, in divided doses. Codis is not recommended for children under 12 years of age.

Contra-indications, warnings, etc The unwanted effects of Codis are those normally associated with soluble aspirin and codeine. It should not be given to patients known to be allergic to aspirin, or suffering from active peptic ulceration or haemophilia.

There is clinical and epidemiological evidence for the safety of aspirin in human pregnancy, but it may prolong labour and contribute to maternal and neonatal bleeding, and is therefore best avoided at term. Aspirin may precipitate bronchospasm, and induce attacks of asthma in susceptible subjects; it may also induce gastro-intestinal haemorrhage, occasionally major. Aspirin may enhance the effects of anticoagulants and inhibit the effects of uricosurics.

For *overdosage*, water or milk, given immediately, may delay absorption. The usual procedures for aspirin overdosage should be followed, including general supportive measures and gastric lavage if necessary. For respiratory depression caused by the codeine, nalorphine or naloxone should be given by injection. It is advisable for the patient to be sent to hospital for appropriate biochemical assessment and treatment.

Pharmaceutical precautions Keep in a cool, dry place.

Legal category P.

Package quantities Cartons of 8, 20, 48 and 500 tablets in foil.

Further information Because the aspirin and codeine phosphate are taken in solution, effective blood levels and relief of pain may be achieved more rapidly than with ordinary aspirin or codeine tablets. The superiority of soluble aspirin over ordinary aspirin in the rapid achievement of demonstrable blood levels has been confirmed by several clinicians.

Product licence number 0044/5003R.

Product licence held by Reckitt & Colman Pharmaceutical Division.

FLENAC*

Presentation White, biconvex tablets each containing 300 mg fenclofenac, engraved on one side with 'Flenac' and on the other with a sword.

Uses For the treatment of chronic and sub-acute rheumatological conditions, such as rheumatoid arthritis, ankylosing spondylitis and osteoarthritis.

Dosage and administration The dose range is up to 1,200 mg (4 tablets) daily, on a twice-daily (night and morning) regimen, taken with or after food.

A maintenance dose of 900 mg (3 tablets) daily is suitable for most adult patients, with two tablets at night and one in the morning to combat early morning stiffness, as in rheumatoid arthritis, or alternatively one tablet at night and two in the morning for daytime pain and stiffness, as in osteoarthritis.

An initial regimen based on these criteria can be adjusted to between 600 mg and 1,200 mg daily according to the response and needs of the patient.

Flenac is not at present recommended for children.

Contra-indications, warnings, etc Flenac is contra-indicated if the patient is known to be suffering from active peptic ulceration or gastric bleeding.

Warnings: Flenac should not be prescribed for children or for pregnant or lactating women, until paediatric indications and dosage have been established, and its safety in pregnancy demonstrated.

Due to the high plasma protein binding of Flenac, patients simultaneously receiving hydatants, anticoagulants or the sulphonamide hypoglycaemic drugs, should be observed for signs of possible interaction.

Care should be taken when treating patients with known renal or hepatic dysfunction, eczema, asthma or known sensitivity to aspirin or other non-steroidal anti-inflammatory drugs. As with other drugs of this type, small increases in blood urea levels have been observed.

Side-effects: Cases of gastro-intestinal discomfort, including nausea, have been reported, but were infrequent and generally mild, and usually responded to a reduction of dosage; symptoms severe or persistent enough to require withdrawal were rare.

Rashes are the most frequently encountered adverse reaction. They are usually relatively mild and regress when treatment is stopped. Erythema multiforme has been reported and also, though more rarely, the Stevens-Johnson Syndrome and toxic epidermal necrolysis. In some patients with a mild rash, therapy has been reintroduced without any recurrence.

Overdosage: No case of overdosage has been reported. There is no specific antidote to fenclofenac, but in the

event of overdosage standard procedures such as gastric lavage and supportive treatment should be used, and the patient kept under strict observation.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Blister packs of 10 tablets, in boxes of 100 tablets.

Further information The long duration of action of Flenac indicates that twice daily dosage is usually sufficient. Flenac is well tolerated by most patients, even over a long period, and offers effective relief of the pain, inflammation and early-morning stiffness associated with rheumatological conditions.

In patients with rheumatoid arthritis, treatment with Flenac has been associated with highly significant falls in E.S.R. over prolonged periods.

Flenac has also been shown to be an effective prostaglandin synthetase inhibitor, with a potency approximately eight times greater than that of aspirin.

Animal and human studies indicate a lower level of gastro-intestinal toxicity than that of most anti-inflammatory agents. However, caution should clearly be exercised when it is proposed to administer Flenac to patients with a history of ulceration of other gastro-intestinal disturbance.

Total levels of thyroid hormones are reduced below normal in patients on Flenac therapy due to a plasma protein binding interaction and this effect makes interpretation of thyroid function tests difficult. If assessment of thyroid function is required during Flenac therapy, then TSH and/or free T_3 and T_4 levels should be measured since these should be within the normal ranges. Fenclofenac interferes with competitive binding assays for thyroid hormones, which use thyroxine binding globulin as the binding protein, and therefore radio-immunoassay methods are recommended.

Product licence number 0044/0060.

Product licence held by Reckitt & Colman Pharmaceutical Division.

FYBOGEL® FYBOGEL® ORANGE

Presentation *Fybogel*: Flaky granules of a pale buff colour.

Fybogel Orange: Flaky granules of a pale orange colour with an orange flavouring.

One sachet of granules contains Ispaghula Husk BPC 3.5 g.

Uses Fybogel is recommended for the treatment of patients requiring a high-fibre regimen.

Dosage and administration *Adults: children over 12*: One sachet morning and evening.

Children under 12: $\frac{1}{2}$ –1 level 5 ml spoonful depending on age and size morning and evening.

Fybogel should be stirred into water and taken as soon as possible, preferably after meals.

Contra-indications, warnings, etc Fybogel is contra-indicated in cases of intestinal obstruction and colonic atony such as senile megacolon.

In the event of overdosage conservative measures should be taken. The patient may notice abdominal discomfort and flatulence, and attention should be paid

to maintaining an adequate fluid intake particularly if the granules have been taken without water contrary to the administration instructions.

Pharmaceutical precautions Nil.

Legal category GSL.

Package quantities Carton of 10 sachets.

Further information Daily Fybogel therapy provides a high-fibre regimen. Ispaghula husk; is capable of retaining 40 times its weight of water, promoting easy evacuation and avoiding episodes of straining. Fybogel effervescent granules disperse readily to form a palatable drink in water. The unflavoured form of Fybogel may be mixed with fruit squash to vary the flavour. Each sachet of Fybogel contains 6.0 mmol sodium. Each sachet of Fybogel Orange contains 6.1 mmol sodium.

Product licence numbers

Fybogel 0044/0041

Fybogel Orange 0044/0068.

Product licence held by Reckitt & Colman Pharmaceutical Division.

LIQUID GAVISCON®

Presentation A pink suspension with a flavour of fennel (similar to aniseed).

10 ml of Liquid Gaviscon contains Sodium Alginate BPC 500 mg, Sodium Bicarbonate PhEur 267 mg in an inert base including Saccharin BP.

Uses Gaviscon alleviates the painful conditions resulting from the reflux of gastric acid and bile into the oesophagus, by suppressing the reflux itself. It is indicated in heartburn, including heartburn of pregnancy, dyspepsia associated with gastric reflux, hiatus hernia, reflux oesophagitis, regurgitation and all cases of epigastric and retrosternal distress where the underlying cause is gastric reflux.

Dosage and administration *Adults, children over 12*: 10–20 ml (dosage measure provided) after meals and at bedtime.

Children under 12: 5–10 ml after meals and at bedtime. Infants not recommended. See Infant Gaviscon. If desired, the standard dose of Liquid Gaviscon may be taken diluted with not more than an equal quantity of water, well stirred.

Contra-indications, warnings, etc There are no specific contra-indications, and no unwanted effects have been reported.

As Gaviscon's mode of action is almost entirely physical, overdosage presents virtually no hazard, and no ill-effects have been reported. The only likely consequence is abdominal distension, which is best treated conservatively.

Pharmaceutical precautions Store in a cool place.

Legal category GSL.

Package quantities Amber bottles of 500 ml.

Further information On ingestion Gaviscon reacts with gastric acid to produce in the stomach a floating viscous gel of higher pH than normal gastric contents, this effectively impedes reflux. In severe cases the gel itself may be refluxed into the oesophagus, where it protects the inflamed mucosa, thus allowing healing to take place and preventing further inflammation.

The sodium content of a dose of 10 ml liquid is 145 mg (6.3 mmol) this may be of importance when a highly restricted salt diet is required as in some renal and cardiovascular conditions.

Product licence number 0044/0058.

Product licence held by Reckitt & Colman Pharmaceutical Division.

GAVISCON® TABLETS

Presentation White, mint-flavoured tablet engraved on both sides with the word 'Gaviscon' and a sword symbol. Each tablet contains Alginate Acid BPC 500 mg, Magnesium Trisilicate BP 25 mg, Dried Aluminium Hydroxide Gel BP 100 mg, Sodium Bicarbonate PhEur 170 mg in an inert base including: Sucrose PhEur and Mannitol BP.

Uses Gaviscon alleviates the painful conditions resulting from the reflux of gastric acid and bile into the oesophagus by suppressing the reflux itself. It is indicated in heartburn, including heartburn of pregnancy, dyspepsia associated with gastric reflux, hiatus hernia, reflux oesophagitis, regurgitation and all cases of epigastric and retrosternal distress where the underlying cause is gastric reflux.

Dosage and administration *Adults, children over 12:* 1 or 2 tablets after meals and at bedtime.

Children under 12: 1 tablet after meals and at bedtime. Infants not recommended. See Infant Gaviscon.

Tablets should be thoroughly chewed (they can be broken and chewed a little at a time) and may be followed by a drink of water.

Contra-indications, warnings, etc There are no specific contra-indications, and no unwanted effects have been reported.

As Gaviscon's mode of action is almost entirely physical, overdosage presents virtually no hazard, and no ill-effects have been reported. The only likely consequence is abdominal distention which is best treated conservatively.

Pharmaceutical precautions Nil.

Legal category GSL.

Package quantities Carton containing 3 tubes of 20 tablets.

Further information On ingestion, Gaviscon reacts with gastric acid to produce in the stomach a floating viscous gel of higher pH than normal gastric contents; this effectively impedes reflux. In severe cases the gel itself may be refluxed into the oesophagus, where it protects the inflamed mucosa, thus allowing healing to take place and preventing further inflammation.

Care should be taken when treating diabetic patients, owing to the sugar content of the tablets. The sodium content of a tablet is 46.5 mg (2.05 mmol).

Product licence number 0044/0021.

Product licence held by Reckitt & Colman Pharmaceutical Division.

GAVISCON® GRANULES

Presentation Brown, chocolate-flavoured granules. One sachet of granules contains Alginate Acid BPC 481 mg, Sodium Alginate BPC 521 mg, Magnesium

Trisilicate BP 52 mg, Dried Aluminium Hydroxide Gel BP 208 mg, Sodium Bicarbonate PhEur 177 mg in an inert base including Sucrose PhEur.

Uses Gaviscon alleviates the painful conditions resulting from the reflux of gastric acid and bile into the oesophagus by suppressing the reflux itself. It is indicated in heartburn, including heartburn of pregnancy, dyspepsia associated with gastric reflux, hiatus hernia, reflux oesophagitis, regurgitation, and all cases of epigastric and retrosternal distress where the underlying cause is gastric reflux.

Dosage and administration *Adults, children over 12:* 1 sachet after meals and at bedtime.

Children under 12: $\frac{1}{2}$ sachet (1 level 5 ml spoonful granules) after meals and at bedtime. Infants: Not recommended. See Infant Gaviscon.

Granules should be thoroughly chewed and may be followed by a drink of water.

Contra-indications, warnings, etc There are no specific contra-indications and no unwanted effects have been reported. As Gaviscon's mode of action is almost entirely physical, overdosage presents virtually no hazard, and no ill-effects have been reported. The only likely consequence is abdominal distention which is best treated conservatively.

Pharmaceutical precautions Nil.

Legal category GSL.

Package quantities Cartons of 10 sachets.

Further information On ingestion, Gaviscon reacts with gastric acid to produce in the stomach a floating viscous gel of higher pH than normal gastric contents; this effectively impedes reflux. In severe cases the gel itself may be refluxed into the oesophagus, where it protects the inflamed mucosa, thus allowing healing to take place and preventing further inflammation.

Care should be taken when treating diabetic patients owing to the sugar content of the granules. The sodium content of a sachet is 122 mg (5.3 mmol).

Product licence number 0044/5008.

Product licence held by Reckitt & Colman Pharmaceutical Division.

INFANT GAVISCON®

Presentation Infant Gaviscon is a fine white powder, packed in a sachet and sterilised. Each sachet contains Alginate Acid BPC 924 mg, Magnesium Trisilicate BP 50 mg, Dried Aluminium Hydroxide Gel BP 200 mg and Sodium Bicarbonate PhEur 340 mg, in a base containing colloidal silica (Aerosil) and Mannitol BP.

Uses Infant Gaviscon helps to prevent gastric regurgitation in infants, where competence of the cardiac sphincter has not been fully established.

Its indications are gastric regurgitation, gastro-oesophageal reflux and reflux associated with hiatus hernia in infants and young children.

Dosage and administration *Young children:* The contents of 1 sachet mixed with half a tumbler of water after each meal. Infants: $\frac{1}{2}$ –1 sachet mixed with the made-up feed immediately before use. Any unused powder should be discarded.

Contra-indications, warnings, etc Not to be used in premature infants, or in situations where excessive water-loss is likely, e.g. fever or high room-temperature. Care should be taken when treating infants with gastroenteritis or known or suspected renal disease or impairment, as the sodium content (93 mg, or 4 mmol per sachet) may add to the risk of hyponatraemia.

As Infant Gaviscon's mode of action is almost entirely physical there are virtually no systemic unwanted effects resulting from overdosage. Overdosage may lead to gastric distension, which is best treated conservatively. Gross overdosage has been reported as causing an intragastric mass.

Pharmaceutical precautions Nil.

Legal category GSL.

Package quantities Carton of 10 sachets.

Further information Infant Gaviscon thickens a water or milk feed, and in the stomach reacts with acid gastric contents to form a viscous gel which suppresses gastro-oesophageal reflux.

Product licence number 0044/5007.

Product licence held by Reckitt & Colman Pharmaceutical Division.

PERCUTOL* ▼

Presentation A cream-coloured ointment containing glyceryl trinitrate 2% w/w in a lanolin-petrolatum base.

Uses Prophylaxis of angina pectoris.

Dosage and administration Magnitude and duration of effect is directly related to the amount of ointment applied, consequently the dosage should be titrated against the clinical presentation of the patient. One inch of ointment contains 16.64 mg glyceryl trinitrate. The ointment may be applied every 3-4 hours or less frequently as required (see further information). The usual dose is 1 to 2 inches, as squeezed from the tube, although some patients may require more. The optimum dosage is best determined by starting with an application of $\frac{1}{2}$ " ointment on the first day and increasing the dose by $\frac{1}{2}$ " increments on each successive day, until headache occurs; then reducing this length by $\frac{1}{2}$ ".

Measurement and application of Percutol is easily accomplished with the aid of the specially designed Applirule sheets supplied with the ointment. The ointment is squeezed from the tube along the graduated line on the Applirule. Using the Applirule sheet, apply the ointment, without rubbing, to any convenient part of the body preferably chest, thigh or arm and press firmly with the palm of the hand onto the skin, so as to thinly spread the ointment to cover the area beneath the Applirule.

The Applirule is then secured in place over the ointment with dressing tape or a suitable dressing.

Contra-indications, warnings, etc

Contra-indications: May be contra-indicated in patients with marked anaemia. Should not be employed in patients with known idiosyncrasies to nitrates.

Side effects: A hypotensive headache is a sign of overdosage. Occasionally elderly patients may have no untoward symptoms while recumbent but may develop postural hypotension with faintness upon suddenly rising.

Pharmaceutical precautions Keep the tube tightly closed and store in a cool place.

Legal category P.

Package quantities Tubes of 30 g.

Further information When the ointment is spread on the skin, the active ingredient (GTN) is continuously absorbed through the skin into the circulation, thus exerting a prolonged vasodilator effect.

Recent work shows a highly significant increase in exercise duration at both 5 and 8 hours after application of 2% glyceryl trinitrate ointment.¹

A controlled study to determine the best sites for application showed the chest to be the most appropriate.²

As with other vasodilators chronic therapy should not be discontinued abruptly. the frequency of application and the dosage should gradually be reduced (over a period of 4-6 weeks).

Product licence number 0044/0067.

Product licence held by Reckitt & Colman Pharmaceutical Division.

PRIPSEN*

Presentation Pripsen is a cream-coloured powder presented in a dual sachet pack. The powder forms a fine red suspension in milk or water.

Each individual sachet contains 4 g Piperazine Phosphate BP and standardised senna equivalent to 15.3 mg total sennosides calculated as sennoside B.

Uses Pripsen is a potent anthelmintic recommended for the eradication of threadworm and roundworm.

Dosage and administration

Adults and children over 6: 1 sachet. Repeat after 14 days.

Children aged 1-6 years: $\frac{2}{3}$ sachet (2 level 5 ml spoonsful). Repeat after 14 days.

Infants - 3 months to 1 year: $\frac{1}{3}$ sachet (1 level 5 ml spoonful). Repeat after 14 days.

Pripsen should be stirred into a small glass of milk or water and drunk immediately.

When treating roundworms, additional single prophylactic doses at monthly intervals may be necessary to eliminate the risk of reinfection.

Contra-indications, warnings, etc Pripsen should not be used in patients with severe bilateral renal dysfunction.

As doses are normally separated by at least 14 days the rare neurotoxic side-effects of piperazine (transient visual disturbance and vertigo), which are due to cumulative blood-levels, are unlikely to occur and have not been reported.

Although Pripsen has not been associated with any reports of teratogenicity, in common with most drugs, its use in the first trimester of pregnancy is not advised.

Overdose: Effects of overdosage will most likely be due to the piperazine content. Treatment by gastric lavage and supportive measures is indicated.

1. Davidov M.E. Cutaneous administration of nitroglycerin in patients with angina pectoris. *Angiology* 32(1) 16-20. 1981.
2. Hansen M.S. Application site for nitroglycerin ointment. *Am. J. Cardiol.* 42 1061. 1978.

Pharmaceutical precautions Any unused powder should be discarded.

Legal category P.

Package quantities Carton of 12 dual-sachets.

Further information Pripsen has an effective cure rate of virtually 100%, the piperazine paralysing the worms which are then evacuated before recovery by the efficient laxative action of standardised senna. Threadworms may be still in the larval stage when Pripsen is first administered so the follow-up dose should be taken after 14 days to eliminate this reinfestation.

Pripsen is ideal for mass administration where cross-infestation is likely.

Product licence number 0063/5004.

Product licence held by Westminster Laboratories Ltd.

SENOKOT*

Presentation *Tablets*: Small brown tablets engraved on one side only with the word Senokot and a sword symbol. One tablet contains standardised senna equivalent to 7.5 mg total sennosides calculated as sennoside B.

Granules: Brown chocolate-flavoured granules. One 5 ml level spoonful (2.73 g) contains standardised senna equivalent to 15 mg total sennosides calculated as sennoside B.

Syrup: Brown, fruit-flavoured syrup. One 5 ml spoonful contains standardised senna extract equivalent to 7.5 mg total sennosides calculated as sennoside B.

Uses In the management of constipation, including: Simple constipation, whether self-induced or environmental, e.g. neglect of the call to stool or poor sanitary conditions.

Constipation in old age, especially where maintenance treatment is required.

Constipation in pregnancy and the puerperium.

Idiopathic slow-transit constipation.

Constipation in the irritable bowel syndrome.

Conservative treatment of haemorrhoids.

Avoidance of straining after surgery and in cerebral and cardiovascular disease.

Dosage and administration The correct dose of Senokot is the smallest required to produce a comfortable soft-formed motion. It varies between individuals, but is generally found within the following ranges:

Adults: 2 to 4 tablets, or 1 to 2 level 5 ml spoonfuls of granules or 2 to 4 × 5 ml spoonfuls of syrup.

Children over 6 years: Half the adult dosages.

Children 2–6 years: Senokot syrup $\frac{1}{2}$ to one 5 ml spoonful for preference.

New users should start with the lowest doses and, if necessary increase it by half the initial dose each day until a comfortable formed motion is produced. If no bowel action has occurred after three days' progressively increased dosage a further medical examination should be considered.

Senokot is best taken as a single dose, at bedtime by adults and in the morning by children. The tablets can be taken with a drink, the granules can be stirred into hot milk, sprinkled on food, or eaten as they are.

Contra-indications, warnings, etc Senokot like all laxatives, should not be given when any undiagnosed

acute or persistent abdominal symptoms are present. Temporary mild griping may occur during adjustment of dosage. In case of gross accidental overdosage, where diarrhoea is severe, conservative measures are usually sufficient: generous amounts of fluid especially fruit drinks should be given.

Pharmaceutical precautions The tablets and granules should be kept in closed airtight containers, and the syrup in amber bottles as supplied. Store in a cool place.

Legal category P.

Package quantities *Tablets*: Foils of 24, tins of 50, 100, 200, 1,000.

Granules: Tins of 100 and 500 g.

Syrup: Bottles of 100 and 500 ml.

Further information The physiological action of the natural anthrone glycosides in Senokot is virtually colon-specific. The active glycosides are protected by a natural sugar moiety which safeguards their transport to the large bowel, where bacterial action breaks the sugar-anthrone bond and releases the active fraction. Peristalsis is then stimulated via the submucosal and myenteric nerve plexuses.

Being colon-specific, Senokot does not affect the vital nutritional functions of the upper gastro-intestinal tract.

Diabetic patients should use the tablets as these have a low sugar content.

Clinical studies have shown that breast fed infants of mothers taking Senokot did not show any side effects to the drug.

Product licence numbers

Tablets 0063/5000

Granules 0063/5002

Syrup 0063/5003

Product licences held by Westminster Laboratories Ltd.

SOLPRIN*

Presentation White tablets engraved on both sides with a sword symbol. Each tablet contains Aspirin BP 300 mg, and when dissolved in water provides a palatable solution of calcium acetylsalicylate.

Uses As an analgesic, antipyretic and anti-inflammatory, for the relief of pain in headache, toothache, neuralgia, sciatica and period pains, and the reduction of inflammation in rheumatism and associated conditions.

Dosage and administration *Adults*: 1–3 tablets dissolved in water. The dose may be repeated after four hours; maximum 12 tablets daily in divided doses (in acute rheumatic conditions up to 24 tablets daily in divided doses).

Children 6–12 years: 1 tablet dissolved in water, repeated after four hours if necessary; maximum 80 mg/kg body weight daily in divided doses.

Contra-indications, warnings, etc Unwanted effects are those of soluble aspirin. Solprin should not be given to patients suffering from active peptic ulceration or haemophilia or known to be allergic to aspirin.

There is clinical and epidemiological evidence of the safety of aspirin in pregnancy, but it may prolong labour and contribute to maternal and neonatal bleeding and is best avoided at term.

Aspirin may precipitate bronchospasm, and induce attacks of asthma in susceptible subjects; it may also

induce gastro-intestinal haemorrhage, occasionally major.

Aspirin may enhance the effects of anticoagulants and inhibit the action of uricosurics.

For overdosage, the usual procedures for aspirin overdosage should be followed, including general supportive measures and gastric lavage if necessary.

Pharmaceutical precautions Nil.

Legal category GSL.

Package quantities 500 tablets in foil.

Further information Solprin is aspirin in a soluble form. Because the aspirin is taken in solution, effective blood levels and the relief of pain and inflammation may be achieved more rapidly than with ordinary aspirin; further, it is less likely to cause gastric upsets.

Product licence number 0044/5000.

Product licence held by Reckitt & Colman Pharmaceutical Division.

TEMGESIC* INJECTION

Presentation Temgesic Injection is a colourless liquid containing 0.3 mg/ml buprenorphine, as the hydrochloride, in a 5% dextrose solution, adjusted to pH range 3.5–5.5. Clear glass snap-ampoules of 1 ml (0.3 mg) or 2 ml (0.6 mg).

Uses As a strong analgesic for the relief of moderate or severe pain.

Dosage and administration *Adults:* The recommended dosage is 1 to 2 ml (0.3–0.6 mg buprenorphine), by i.m. or slow i.v. injection, every six to eight hours or as required. Temgesic is not at present recommended for children.

Contra-indications, warnings, etc There are no absolute contra-indications; however, care should be taken when treating patients with impaired respiratory function as Temgesic may rarely affect respiration. Because buprenorphine has antagonist properties, it may precipitate mild withdrawal symptoms in narcotic addicts. Temgesic may cause some drowsiness; this could be potentiated by other centrally-acting agents, including alcohol. Ambulant patients should be warned not to drive or operate machinery if affected.

Since buprenorphine is metabolised in the liver, the intensity and duration of its action may be affected in patients with impaired liver function.

Until further information is available, Temgesic should be used with caution in patients receiving monoamine oxidase inhibitors, and is not recommended for use during pregnancy.

Overdosage: Temgesic has a wide safety margin, and in clinical practice doses well in excess of those recommended have been used without untoward effect. Should respiratory depression occur to a clinically undesirable degree, supportive measures should be used to maintain adequate ventilation and oxygenation. The effects of buprenorphine are not readily reversible by such narcotic reversing agents as levallorphan, though naloxone may be partially effective; in the unlikely event of a profound respiratory depression occurring, doxapram may be used to stimulate respiration. In post-

operative patients, a component of respiratory depression may be the residual effect of previously administered narcotics, and naloxone should be given in the first instance, before the use of doxapram is considered.

Side-effects: Drowsiness, or sleep from which the patient can easily be aroused, may occur particularly in the post-operative period. Improved mood or mild euphoria have occasionally been observed and respiratory depression has been observed rarely. In common with other strong analgesics, nausea, vomiting, dizziness and sweating have been reported which may be more frequent in ambulant patients. Constipation attributable to Temgesic has not been reported.

Pharmaceutical precautions Temgesic Injection, though stable, should be kept cool and protected from light.

Legal category POM.

Package quantities Pack of 10 ampoules (1 ml or 2 ml).

Further information Temgesic Injection contains 50 mg dextrose per ml, but no sodium, potassium, or preservative).

Dependence Liability: The human and animal studies conducted indicate that buprenorphine has a substantially lower dependence profile than conventional centrally-acting analgesics.

Product licence numbers

Temgesic Injection 1 ml 0044/0056

Temgesic Injection 2 ml 0044/0057

Product licence held by Reckitt & Colman Pharmaceutical Division.

TEMGESIC* SUBLINGUAL ▼

Presentation Temgesic Sublingual tablet is a white, biconvex tablet engraved on one side with a sword-symbol, containing 0.2 mg buprenorphine, as the hydrochloride.

Uses As a strong analgesic for the relief of moderate to severe pain.

Dosage and administration 1–2 tablets (0.2–0.4 mg buprenorphine) to be dissolved under the tongue, every 6 to 8 hours or as required.

The recommended starting dose for moderate to severe pain of the type typically presenting in general practice is one tablet eight hourly.

The tablet should not be chewed or swallowed. Temgesic Sublingual is not at present recommended for children.

Contra-indications, warnings, etc There are no absolute contra-indications for Temgesic Sublingual; however, care should be taken when treating patients with impaired respiratory function as Temgesic may rarely affect respiration.

Because buprenorphine has antagonist properties, it may precipitate mild withdrawal symptoms in narcotic addicts.

Temgesic may cause some drowsiness; this could be potentiated by other centrally-acting agents, including alcohol. Ambulant patients should be warned not to drive or operate machinery if affected.

Since buprenorphine is metabolised in the liver, the intensity and duration of its action may be affected in patients with impaired liver function.

Until further information is available. Temgesic should be used with caution in patients receiving monoamine oxidase inhibitors, and is not recommended for use during pregnancy.

Overdosage: Overdosage by the sublingual route is unlikely. The expected symptoms would be drowsiness, nausea and vomiting. If tablets are swallowed, overdosage is less likely because the absorbed active ingredient is rapidly metabolised by the liver. Gastric lavage should be carried out and supportive measures instituted. The effects of buprenorphine are not readily reversible by such narcotic reversing agents as levallorphan, though naloxone may be partially effective; in the unlikely event of a profound respiratory depression occurring doxapram may be used to stimulate respiration.

Side-effects: No serious toxic reactions have been observed where Temgesic Sublingual has been given in normal therapeutic doses and side-effects are generally of a minor nature.

In common with other strong analgesics, nausea, vomiting, dizziness, sweating and drowsiness have been reported and may be more frequent in ambulant patients. Clinically significant respiratory depression has been observed rarely, and only in the post-operative period.

The psychotomimetic effects sometimes observed with other antagonist-analgesics have not been encountered with Temgesic Sublingual.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Carton of 50 tablets, blister-packs of 10 tablets each.

Further information Temgesic Sublingual has been formulated to allow the active ingredient to be absorbed through the buccal mucosa within minutes.

The tablets must not be chewed or swallowed as this will reduce the efficacy.

Dependence liability: No manifestations of physical dependence have been produced when Temgesic Sublingual has been withdrawn from patients receiving large doses of Temgesic Sublingual over long periods.

Product licence number

Temgesic Sublingual 0044/0063.

Product licence held by Reckitt & Colman Pharmaceutical Division.

TIMODINE*

Presentation Pale yellow cream containing (w/w):

Nystatin BP	100,000	i.u./g
Hydrocortisone PhEur	0.5%	
Benzalkonium Chloride Solution BP	0.2%	
Dimethicone 350 BPC	10.0%	

Uses For the treatment of dermatoses, including intertrigo, eczema, seborrhoeic dermatitis, "housewife's eczema" and pruritus ani and vulvae, in which *Candida albicans* is a factor. For the treatment of severe napkin rash involving *Candida albicans*.

Dosage and administration

Dermatoses: Sufficient Timodine should be applied to cover the lesion in a thin layer. It should then be massaged into the skin until the cream disappears. The treatment should be repeated three times a day until the lesion has healed.

Napkin Rash: After removal of the soiled napkin, the affected area should be cleaned and dried and a thin layer of Timodine applied. The treatment should be repeated after every napkin change until the lesion has healed.

Contra-indications, warnings, etc

Contra-indications: Sensitivity to benzalkonium chloride or nystatin.

Precaution: Keep away from the eyes.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Side-effects: None have been reported.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Tubes of 30 g.

Further information Timodine is particularly indicated in the treatment of dermatoses occurring in sites, such as the skin folds, in which the special environmental conditions present predispose to maceration and chafing, leading to secondary infection with *Candida albicans* and bacteria, and causing additional inflammation and persistent pruritus.

Product licence number 1839/0001.

Product licence held by Lloyd-Hamol Ltd.

TRANSVASIN*

Presentation Creamy-white, water-miscible cream containing (w/w):

Ethyl nicotinate	2.0%
Hexyl nicotinate	2.0%
Tetrahydrofurfuryl salicylate	14.0%
Benzocaine PhEur	2.0%

Uses For the relief of rheumatic and muscular pain and the treatment of sprains and strains.

Dosage and administration *Directions for use:* Massage gently into the affected area until the cream is entirely absorbed.

Transvasin should be applied at least twice daily until the pain abates.

Contra-indications, warnings, etc

Contra-indications: Sensitivity to salicylates, nicotines or benzocaine.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Tubes of 30 g.

Further information Transvasin is a rubefacient, and within a few minutes of application a sensation of warmth is felt, followed by a reddening of the skin. This erythema does not indicate intolerance.

Product licence number 1839/5001.

Product licence held by Lloyd-Hamol Ltd.

* Trade Mark

Riker Laboratories

Morley Street

Loughborough

Leics LE11 1EP



ALU-CAP*

Presentation Opaque green/red hard gelatin capsule, size 0, marked 'RIKER'. Each capsule contains 475 mg Dried Aluminium Hydroxide Gel BP as a white powder.

Uses Alu-Cap is recommended for use as a phosphate-binding agent in the management of renal failure. It may also be used as an antacid.

In the gut, aluminium hydroxide adsorbs phosphate ions. This reduces absorption of phosphate into the body, and thereby reduces serum phosphate levels. In patients with renal failure, the problem of high serum phosphate levels may be partially solved by a diet low in phosphorus. However, a more liberal diet is feasible when a phosphate-binding agent, such as aluminium hydroxide, is used.

Aluminium hydroxide gel is a slow-acting antacid. It is used to provide symptomatic relief in gastric hyperacidity. In addition, the antipeptic and demulcent activity of aluminium hydroxide helps to protect inflamed gastric mucosa against further irritation by gastric secretions.

Dosage and administration *For phosphate-binding:*

Adults and children: The dosage must be selected in accordance with individual patient requirements, and may range from 4 to 20 capsules of Alu-Cap daily (approximately 2–10 g dried aluminium hydroxide gel), taken with meals.

As an antacid: **Adults:** One Alu-Cap four times daily and on retiring. Alu-Cap is not suitable for antacid therapy in children.

Contra-indications, warnings, etc

Side-effects: Aluminium hydroxide is astringent and may cause constipation.

Precautions: Serum phosphate levels should be monitored in all patients receiving phosphate binders, to prevent the development of a phosphate depletion syndrome.

Aluminium hydroxide may form complexes with certain antibiotics (tetracyclines); concomitant administration may result in reduced absorption of the antibiotic.

Contra-indications: Patients with hypophosphataemia.

Overdosage: Symptoms and treatment: A single massive dose of aluminium hydroxide is unlikely to have harmful sequelae, as aluminium is not absorbed systemically to any great extent. Gastric lavage should be administered, followed by a mild aperient if required.

Pharmaceutical precautions No special storage precautions are required.

Legal category P.

Package quantities Bottles of 100 capsules.

Further information Nil.

Product licence number 0068/0052.

CALCISORB*

Presentation Creamy-white to beige fibrous powder. The active ingredient is the sodium salt of the phosphate ester of cellulose. Each dose of 5 g is supplied in sachet form and contains approximately 4.7 g of the active ingredient and 0.3 g of moisture.

Uses Sodium cellulose phosphate is an ion-exchange compound with a particular affinity for divalent cations. The product binds calcium ions in the lumen of the stomach and intestine and thus prevents hyperabsorption of dietary calcium. Calcium bound by cellulose phosphate is no longer available for absorption and is therefore excreted in the faeces.

Each 5 g dose will bind approximately 250 mg of calcium.

Calcisorb is used to diminish calcium absorption from the diet: 1) in the treatment of hypercalciuria and recurrent formation of renal stones; 2) in osteopetrosis; 3) as a basis of a test for calcium absorption.

Other possible uses are: 1) treatment of idiopathic hypercalcaemia of infancy; 2) treatment of hypercalcaemic sarcoidosis; 3) treatment of vitamin D intoxication.

Dosage and administration

Adults: 15 g daily, divided as three 5 g doses with meals.

Children: 10 g daily, divided as three doses with meals.

The required dose should be dispersed in water and taken orally. Alternatively the powder may be sprinkled onto food.

Contra-indications, warnings, etc Renal failure. Congestive heart failure and other conditions in which a low sodium intake is essential.

Side-effects are rare. Isolated cases of diarrhoea have been reported. One patient with mild renal disease developed a moderate magnesium deficiency. This was readily corrected by halving the dose.

No signs of calcium deficiency have been reported during the continuous use of cellulose phosphate for up to 11 years. This theoretical hazard is particularly relevant to pregnancy, but in view of the absence of data on the effect of cellulose phosphate on calcium levels in pregnant women it is recommended that treatment is discontinued during pregnancy and lactation. Likewise growing children should be prescribed Calcisorb only at the discretion of a senior physician and under his direct supervision.

Pharmaceutical precautions Since cellulose phosphate is an ester, some hydrolysis occurs on storage, the rate increasing with temperature. Calcisorb should therefore be kept in a refrigerator for long-term storage.

For short-term storage by the patient, i.e. of the order of one month, refrigeration is unnecessary. The product is supplied with a minimum expiry date of two years from manufacture.

Legal category P.

Package quantities Supplied in packs of 100 sachets.

Further information Calcisorb should be used in conjunction with a low calcium diet in which dairy products in particular are severely restricted.

Product licence number 0068/5900

DISALCID*

Presentation Grey and orange hard gelatin capsule, size 0, marked DS on one half and RIKER on the other.

Each 'Disalcid' capsule contains salsalate 500 mg.

Uses Disalcid is indicated in the treatment of chronic inflammatory conditions of joints, tendons, muscles and connective tissue – for example, osteoarthritis, rheumatoid arthritis, tendinitis, bursitis, fibrositis and polymyalgia.

Salsalate is an ester which after absorption is slowly hydrolysed to two molecules of free salicylic acid. Its insolubility in gastric juice renders it very unlikely to cause the gastric irritation, erosion and haemorrhage associated with acetylsalicylic acid. Moreover, its prolonged biological half-life is a real therapeutic advantage at night and in the relief of morning stiffness.

Dosage and administration *Adults:* 4 capsules daily in divided doses. Where a greater anti-inflammatory effect is required dosage may be increased to 2 capsules three or four times daily.

The last dose should be taken at bedtime. Disalcid should be taken immediately before or with food.

Children: Disalcid has not yet been evaluated in children. No dosage recommendation can therefore be made for children under the age of 12.

Contra-indications, warnings, etc

Side-effects: Allergic reactions may occur rarely with salsalate, as with other salicylates. If tinnitus and deafness occur they are usually signs of overdosage and are reversible by reducing dosage.

Caution: Although Disalcid is relatively free from the risk of gastric erosion usually associated with anti-inflammatory agents, caution should be observed in patients with active peptic ulcer.

Disalcid should be used with caution in patients with renal impairment.

Disalcid may enhance the activity of anticoagulants and hypoglycaemic agents.

Contra-indications: Disalcid is contra-indicated in patients with known hypersensitivity to salicylic acid or its derivatives.

Overdosage: Symptoms: Overdosage with Disalcid produces the usual symptoms of salicylism: tinnitus and deafness, vertigo, headache, sweating, hyperventilation and confusion are likely to occur.

Treatment: The stomach should be emptied by lavage with sodium bicarbonate or water.

Patients suffering from severe intoxication should in addition have forced alkaline diuresis by intravenous infusions of sodium bicarbonate solution. Haemodialysis or peritoneal dialysis may be needed in extreme cases, especially in the presence of cardiac or renal impairment.

Pharmaceutical precautions Disalcid should be stored in a cool, dry place. The container should be kept tightly closed.

Legal category POM.

Package quantities *Disalcid Capsules:* Bottles of 100.

Further information Nil.

Product licence number 0068/0089.

DORBANEX* DORBANEX* FORTE

Presentation Dorbanex is available in three forms – as capsules and two strengths of liquid.

Each yellow size 1 capsule, marked 'RIKER' contains:

Danthron BP	25 mg
Poloxamer 188	200 mg

Dorbanex Liquid is peach flavoured and orange coloured. Each 5 ml spoonful contains:

Danthron BP	25 mg
Poloxamer 188	200 mg

Dorbanex Forte is peach flavoured and orange coloured. Each 5ml spoonful contains:

Danthron BP	75 mg
Poloxamer 188	1,000 mg

Uses Dorbanex is indicated whenever a laxative needs to be prescribed for acute or chronic constipation. It is particularly useful in: painful defaecation associated with anal fissures, ulcers and haemorrhoids; restoring normal bowel habit in children and the elderly; post-operative patients and those confined to bed; pregnancy and the puerperium; preparation of patients for surgery and radiography; the prevention of faecal impaction; drug-induced constipation.

Dorbanex Forte is indicated for the patient with chronic, intractable constipation, or who may have become resistant to laxative treatment at normal dosage.

Poloxamer increases the penetration of water into faecal material, thus preventing the faecal mass from drying and hardening excessively. Faecal softening plus the surface activity of poloxamer has a useful lubricant effect on the gut content.

Poloxamer is not absorbed from the gut and does not directly stimulate peristalsis. It is excreted almost completely in the faeces.

Danthron is a synthetic anthraquinone compound, chemically related to emodin, the laxative principle of cascara, and to other anthraquinones which occur naturally in senna, rhubarb and aloes. It acts on the nerve endings of the myenteric plexus to stimulate the muscle of the large intestine.

Onset of effect is between six and twelve hours after administration.

Dosage and administration *Dorbanex Capsules:* *Adults:* One or two capsules.

Children: One capsule.

Before or after surgery or before radiography: 2 to 4 capsules.

Dorbanex Liquid: Adults: One or two 5 ml spoonfuls.

Children: A half to one 5 ml spoonful, as required.

Before or after surgery or before radiography: Two to four 5 ml spoonfuls.

Dorbanex Forte: Adults: One 5 ml spoonful, or as directed by the physician.

Dorbanex Forte is not recommended for children under 12 years.

Treatment should be taken at bedtime.

Contra-indications, warnings, etc

Side-effects: Danthron may cause temporary harmless pink or red colouring of the urine and perianal skin and, in prolonged use or high dosage, of the mucosa of the large intestine.

Caution: In some incontinent patients and in babies or children wearing napkins, Dorbanex may cause staining of the buttocks which may proceed to superficial sloughing of the skin. For this reason Dorbanex is not recommended for the treatment of infants and children in napkins, and should be used with caution in all incontinent patients.

Contra-indications: In common with other gastro-intestinal evacuants, Dorbanex should not be given when acute, painful conditions of the abdomen are present, or the cause of constipation is suspected to be intestinal obstruction.

Overdosage: Patients should be given plenty of fluids. An anticholinergic preparation such as atropine methonitrate would help to offset the excessive intestinal motility.

Pharmaceutical precautions No special storage precautions required.

Diluents: Tragacanth Mucilage BPC or Syrup BP should be used as diluents if required.

Attention is drawn to the fact that it is not possible to dilute Dorbanex Forte to fulfil prescriptions for Dorbanex because of the different ratio of the ingredients.

Legal category.

Capsules P.

Liquid P.

Forte P.

Package quantities *Dorbanex Capsules:* Packs of 30 and 500.

Dorbanex Liquid: Bottles of 250 ml and 1,000 ml.

Dorbanex Forte: Bottles of 250 ml and 1,000 ml.

Further information Nil.

Product licence numbers

Dorbanex Capsules 0068/5067

Dorbanex Liquid 0068/5033

Dorbanex Forte 0068/5007

DUO-AUTOHALER*

Presentation Duo-Autohaler is a breath-actuated, pressurised aerosol for inhalation therapy. The vial contains a creamy-white suspension of isoprenaline hydrochloride 8 mg/ml and phenylephrine bitartrate 12 mg/ml in aerosol propellant, and delivers 400 measured doses, each containing 160 mcg isoprenaline hydrochloride and 240 mcg phenylephrine bitartrate.

Uses Duo-Autohaler is a potent bronchodilator, and is indicated for the immediate and prolonged relief of bronchospasm in bronchial asthma and chronic bronchitis.

Duo-Autohaler works differently from other inhalation aerosols in that it is operated by the intake of breath. This

means that each dose is delivered into the lungs at the right time in the breathing cycle, and that the amount of the dose inhaled is removed from the patient's control.

Isoprenaline is a directly acting sympathomimetic amine which activates both β_1 and β_2 adrenergic receptors. It has virtually no affinity for α -receptors. As a result it is a bronchodilator which also produces vasodilation in all blood vessels, including those of the pulmonary system. Pulse rate and cardiac output are increased, the degree of cardiac stimulation being proportional to the blood level. Isoprenaline is quickly eliminated from the blood and therefore has no cumulative effect. It inhibits histamine release in the lungs and has a beneficial effect on cilia and mucus flow.

By inhalation, isoprenaline has a rapid onset of bronchodilatation. Cardiac stimulation does not usually occur and the maximum possible bronchodilatation is produced at doses below those which result in significant tachycardia. Appreciable cardiac stimulation occurs only at the upper end of the therapeutic dose range.

Phenylephrine acts primarily on α -receptors. It complements and modifies the action of isoprenaline in several respects. It augments bronchodilatation. It delays the absorption of isoprenaline from the lungs and helps to prolong the bronchodilator activity. Phenylephrine also tends to offset cardiovascular effects of isoprenaline.

Paradoxically, the improved ventilation produced by bronchodilators is often accompanied by impairment of oxygenation of venous blood as it passes through the lungs, with consequent falls in arterial oxygen levels. This results from the non-selective relaxation of smooth muscle both of bronchioles and the pulmonary blood vessels. Phenylephrine opposes this effect and Duo-Autohaler is thus less likely to cause falls in the arterial oxygen tension than isoprenaline alone.

Dosage and administration Each puff from Duo-Autohaler delivers a measured dose of 160 mcg isoprenaline hydrochloride and 240 mcg phenylephrine bitartrate.

One, two or at the most three puffs should be sufficient to provide relief in most cases. It should not be necessary for the patient to take further treatment for at least 30 minutes, or more than eight treatments in any 24-hour period.

Children: Duo-Autohaler should be administered to children only under the supervision of a responsible adult.

Instructions for use: To obtain full benefit from Duo-Autohaler, the patient should follow these simple steps:

1. Shake the unit with the mouthpiece cover closed. Then open the mouthpiece cover downwards.

2. Breathe out as much as possible, then close the lips tightly round the mouthpiece. Keep the teeth apart and the tongue flat (to allow the flow of medicament into the lungs).

3. Suck in air through the mouthpiece as rapidly and deeply as possible. When the unit operates a click will be heard. Continue to breathe in after the click until the lungs are full. Hold the breath for a few seconds. Then take the inhaler away from the mouth and breath out slowly through pursed lips. If no click is heard, repeat step three, making sure that the lips are well sealed around the mouthpiece.

4. The unit must be reset before another dose can be taken by closing the mouthpiece cover upwards. It is important to keep the cover closed when the unit is not in use.

Contra-indications, warnings, etc

Side-effects: Overdosage may cause dry mouth, palpitations or nervousness.

Contra-indications: Duo-Autohaler should be used with caution in the presence of cardiac disease, hypertension or hyperthyroidism.

Overdosage: *Acute poisoning in non-asthmatics:* No cases have been reported. In the absence of details of such practical experience, the following guidance is based on theoretical considerations.

Symptoms: The toxic effects of isoprenaline (namely those of tachycardia, palpitations, peripheral vasodilatation and fall in blood pressure) are likely to be counterbalanced by the vasoconstrictor action of phenylephrine.

Treatment: General symptomatic therapy.

Chronic poisoning in asthmatics: No cases have been reported.

Excessive use of Duo-Autohaler during an attack of asthma indicates lack of response. This is a grave sign suggestive of status asthmaticus. It is recommended that 100 mg hydrocortisone be given immediately by intravenous injection, and the patient admitted to hospital without delay. Beta-blocking drugs should not be used.

Pharmaceutical precautions Duo-Autohaler should be stored in a cool place, protected from frost and sunlight. The shelf-life of Duo-Autohaler is three years.

The Duo-Autohaler vial is pressurised and therefore no attempt should be made to puncture it or to dispose of it by burning.

Legal category POM.

Package quantities Duo-Autohaler is supplied as complete units for which replacement cartridges are available. Each vial contains 400 doses.

Further information Nil.

Product licence number 0068/5012.

DUROPHET*

Presentation *7.5 mg strength:* Opaque white/white size 3 capsules printed 'RIKER'. Each capsule contains amphetamine 3.75 mg, dexamphetamine 3.75 mg, as ion-exchange resin complexes.

12.5 mg strength: Opaque white/charcoal grey size 3 capsules printed 'RIKER'. Each capsule contains amphetamine 6.25 mg, dexamphetamine 6.25 mg, as ion-exchange resin complexes.

20.0 mg strength: Opaque charcoal grey/charcoal grey size 3 capsules printed 'RIKER'. Each capsule contains amphetamine 10.0 mg, dexamphetamine 10.0 mg, as ion-exchange resin complexes.

Uses Durophet is an appetite-depressant and is indicated in all types of simple obesity.

Durophet contains laevo- and dextro-amphetamine in the ratio 1:3 as the anorectic agent. The amphetamines are present as ion-exchange resin complexes from which they are released in the gut over a period of about 10 hours. The extended absorption reduces the chance of side-effects and simplifies dosage. Each capsule provides 10–14 hours smooth anorectic effect.

Dosage and administration *Adults:* One capsule at breakfast. Administration can be delayed until mid-morning if an effect persisting well into the evening is required.

Children: Durophet is not recommended for children.

Contra-indications, warnings, etc

Side-effects: Dryness of the mouth, hyperactivity and other signs of mild central nervous stimulation may occur in some patients.

Cautions and contra-indications: Durophet is contra-indicated in patients under treatment with monoamine oxidase (MAO) inhibitors. It should be used with caution in severe hypertension and cardiovascular disease, and in patients hypersensitive to sympathomimetic agents.

Overdosage: *Symptoms:* These would be, initially, insomnia and irritability, but larger doses may give rise to fatigue, mental depression, an increase in blood pressure, fever, cardiovascular reactions, respiratory failure and cyanosis, disorientation, hallucinations, convulsions and coma.

Treatment: The stomach should be emptied by emesis or stomach tube and washed out with water if the preparation has been ingested within the last three or four hours.

If respiration is irregular or cyanosis is present, artificial respiration or oxygen should be given. The patient should be kept quiet and warm. For marked excitement, chlorpromazine 1–1.5 mg per kg body weight may be given intramuscularly or intravenously. Alternatively, a short-acting barbiturate, such as quinalbarbitone sodium or cyclobarbitone, should be given by mouth, or, if necessary, thiopentone sodium should be administered by intravenous injection. Providing renal function is adequate, elimination of amphetamine may be assisted by acidification of the urine with ammonium chloride in conjunction with an adequate fluid intake.

Pharmaceutical precautions No special storage precautions are required.

Legal category POM: MDA.

Package quantities

Capsules 7.5 mg: Bottles of 30.

Capsules 12.5 mg: Bottles of 30.

Capsules 20.0 mg: Bottles of 30.

Further information Nil.

Product licence numbers

Capsules 7.5 mg 0068/5064

Capsules 12.5 mg 0068/5065

Capsules 20.0 mg 0068/5066

HUMAN ALBUMIN MICROSPHERES

Presentation Each Albumin Microsphere 99m Tc (instant microspheres) labelling vial contains 5 mg 3M Human Albumin Microspheres. The labelling vial and a radioactive warning label are the components of a single Albumin Microsphere 99m Tc Labelling Unit. The vial is a dry, sterile, pyrogen-free unit containing the microspheres, together with the necessary reagents for rapid and efficient labelling of the microspheres with 99m technetium. As manufactured, each vial contains 5 mg Albumin Microspheres, 6 mg Poloxamer 188 and tin (less than 50 mcg tin/mg microspheres).

Uses 3M Human Albumin Microspheres, labelled with 99m technetium are intended for gamma scintillation imaging of the lungs following intravenous administration or when injected into the dorsal pedal veins for combined radionuclide venography and lung scanning.

3M Human Albumin Microspheres are indicated as an adjunct to other diagnostic procedures whenever information about pulmonary circulation is required. The main uses are in the diagnosis of pulmonary embolism, chronic obstructive lung disease such as emphysema and chronic bronchitis, pathological conditions which impede pulmonary blood flow such as carcinoma and pulmonary abscess and other pulmonary diseases such as pneumonia and tuberculosis.

Combined radionuclide venography and imaging of the lungs is indicated as an adjunct to other diagnostic procedures where deep venous thrombosis in the lower extremities is suspected.

Dosage and administration The recommended adult dose range of 99m Tc-labelled Albumin Microspheres for lung scanning is 1–4 mCi (0.2–2 mg Albumin Microspheres) and for radionuclide venography it is 4–7 mCi (0.8–3.5 mg Albumin Microspheres).

In choosing the amount of 99m Tc radioactivity to be used in the preparation of the 99m Tc-labelled Albumin Microspheres, the labelling efficiency, number of patients, administered radioactive dose and radio-active decay must be taken into account. The recommended amount of 99m Tc radioactivity to be added to the labelling vial is 30 mCi. Assuming an average 99m Tc uptake of 95 per cent this will yield 5 mg of 99m Tc-labelled Albumin Microspheres with a specific activity of approximately 6 mCi/mg at the time of labelling and approximately 2 mCi/mg eight hours later.

The 99m Tc-labelled microspheres should be used within eight hours of labelling.

Lung imaging procedure: The suspension of 99m Tc-labelled Albumin Microspheres is administered by intravenous injection over a 10–20 second period using a plastic syringe.

Venography procedure: The following sequence is recommended for optimum imaging.

Camera area of view	Fraction of total dose (each foot)
Inferior Vena Cava and Iliac veins	1/4
Iliac and Femoral veins	1/8
Femoral and Popliteal veins	1/8

The procedure is completed with a lung scan.

For optimum results, patient studies should be completed within 60 minutes after administration of Albumin Microspheres.

Contra-indications, warnings, etc

Side-effects: Transient facial flushing and dyspnoea may occur in some patients. Less frequently, transient nausea, perspiration, and cyanosis may be encountered and, rarely, severe respiratory distress. The possibility of hypersensitivity reactions should be borne in mind after the administration of Albumin Microspheres, especially in patients who receive additional doses a number of weeks after the initial dose; these may be treated with corticosteroids, adrenaline and antihistamines.

Contra-indications: The safety of Albumin Microspheres in patients with a known right to left shunt has not been established and its use in such patients is contra-

indicated. The use of radiopharmaceuticals is contra-indicated in pregnant women, nursing mothers, or patients under 18 years of age unless exceptional circumstances exist.

Warning: The contents of the 3M Human Albumin Microspheres are not radioactive. However after 99m technetium is added, adequate shielding of the resulting preparation must be maintained.

Since 99m Tc is excreted in breast milk, breast feeding is not advised during treatment with Albumin Microspheres.

Overdosage: Not applicable.

Pharmaceutical precautions Instructions for the radioactive labelling of the Albumin Microspheres are included with each five unit kit of 3M Albumin Microspheres.

The shelf-life of Human Albumin Microspheres is one year.

Legal category POM.

Package quantities The complete product consists of the following items: Five 3M Microspheres (instant microspheres) Labelling Vials. Package insert. Technetium-99m labelling instructions.

Further information Nil.

Product licence number 0068/0041.

INTRALGIN®

Presentation Intralgin contains Benzocaine BP 2 per cent w/w and salicylamide 5 per cent w/w in an alcoholic vehicle. Intralgin is a clear, pleasant-smelling preparation – non-greasy and non-staining.

Uses Intralgin is indicated for the relief of muscle pain from strains, sprains and injuries, and pain associated with fibrositis, lumbago and non-articular rheumatism.

Intralgin combines two ingredients to relieve muscular aches and pains by absorption through the skin into the muscle.

Benzocaine is a widely used, well-tolerated local anaesthetic, acting rapidly on nerve endings. The action of the analgesic, salicylamide, is similar to that of salicylates.

The use of isopropyl alcohol as a vehicle for the medicaments contributes significantly to the action of Intralgin. Isopropyl alcohol because of its penetrative properties facilitates the percutaneous absorption of benzocaine and salicylamide so that they reach underlying tissue to relieve pain rapidly. Vigorous massage is not needed with 'Intralgin', unlike traditional rubs which rely for effect on erythema or counter-irritation.

Dosage and administration Intralgin Gel should be applied liberally and rubbed gently into the skin until penetration is complete. Vigorous massage is unnecessary.

For more rapid absorption the painful area should be warmed before applying 'Intralgin'.

Contra-indications, warnings, etc

Side-effects: Local sensitivity reactions to the benzocaine constituent have occasionally been reported.

Caution: If irritation or itching occurs due to hypersensitivity, Intralgin should be discontinued and a soothing cream applied.

Overdosage: Not applicable.

Pharmaceutical precautions The tube should be kept tightly closed and kept away from direct heat.

Legal category P.

Package quantities Tubes of 50 g.

Further information Nil.

Product licence number 0068/5076.

ISO-AUTOHALER*

Presentation Iso-Autohaler is a breath-actuated, pressurised aerosol for inhalation therapy. The vial contains a creamy-white suspension of Isoprenaline Sulphate BP 4 mg/ml in aerosol propellant, and delivers 400 measured doses, each containing 80 mcg Isoprenaline Sulphate BP.

Uses Iso-Autohaler is a potent bronchodilator, and is indicated for the relief of bronchospasm in bronchial asthma and chronic bronchitis.

Iso-Autohaler works differently from other inhalation aerosols in that it is operated by the intake of breath. This means that each dose is delivered into the lungs at the right time in the breathing cycle, and that the amount of the dose inhaled is removed from the patient's control.

Isoprenaline is a directly acting sympathomimetic amine which activates both the β_1 and β_2 adrenergic receptors. It has virtually no affinity for α -receptors. As a result it is a bronchodilator which also produces vasodilatation in all blood vessels, including those of the pulmonary system. Pulse rate and cardiac output are increased, the degree of cardiac stimulation being proportional to the blood level. Isoprenaline is quickly eliminated from the blood and therefore has no cumulative effect. It inhibits histamine release in the lungs and has a beneficial effect on cilia and mucus flow.

By inhalation, isoprenaline has a rapid onset of bronchodilatation. Cardiac stimulation does not usually occur and the maximum possible bronchodilatation is produced at doses below those which result in significant tachycardia. Appreciable cardiac stimulation occurs only at the upper end of the therapeutic dose range.

Dosage and administration Each puff from Iso-Autohaler delivers a measured dose of 80 mcg isoprenaline sulphate.

One, two or at the most three puffs should be sufficient to provide relief in most cases. It should not be necessary for the patient to take further treatment for at least 30 minutes, or more than eight treatments in any 24-hour period.

Children: Iso-Autohaler should be administered to children only under the supervision of a responsible adult.

Instructions for use: To obtain full benefit from Iso-Autohaler, the patient should follow these simple steps:

1. Shake the unit with the mouthpiece cover closed. Then open the mouthpiece cover downwards.

2. Breathe out as much as possible, then close the lips tightly round the mouthpiece. Keep the teeth apart and the tongue flat (to allow the flow of medicament into the lungs).

3. Suck in air through the mouthpiece as rapidly and deeply as possible. When the unit operates a click will be heard. Continue to breathe in after the click until the lungs are full. Hold the breath for a few seconds. Then take the inhaler away from the mouth and breathe out

slowly through pursed lips. If no click is heard, repeat step 3, making sure that the lips are well sealed around the mouthpiece.

4. The unit must be reset before another dose can be taken by closing the mouthpiece cover upwards. It is important to keep the cover closed when the unit is not in use.

Contra-indications, warnings, etc

Side-effects: Overdosage may cause dry mouth, palpitations or nervousness.

Contra-indications: Iso-Autohaler should be used with caution in the presence of cardiac disease, hypertension or hyperthyroidism.

Overdosage: Acute poisoning in non-asthmatics: No cases have been reported. In the absence of details of such practical experience, the following guidance is based on theoretical considerations.

Symptoms of acute isoprenaline poisoning are likely to be mainly cardiovascular effects, e.g. tachycardia, palpitations, peripheral vasodilation and a fall in blood pressure.

Treatment: General symptomatic therapy.

Chronic poisoning in asthmatics: Some cases have been reported, but no details of treatment have been given, other than withdrawal of the aerosol.

Excessive use during an attack of asthma indicates lack of response. This is a grave sign suggestive of status asthmaticus. It is recommended that 100 mg hydrocortisone be given immediately by intravenous injection, and the patient admitted to hospital without delay. Beta blocking drugs should not be used.

Pharmaceutical precautions Iso-Autohaler should be stored in a cool place, protected from frost and sunlight. The shelf-life of Iso-Autohaler is three years.

The Iso-Autohaler vial is pressurised and therefore no attempt should be made to puncture it or to dispose of it by burning.

Legal category POM.

Package quantities Iso-Autohaler is supplied as complete units for which replacement cartridges are available. Each vial contains 400 doses.

Further information Nil.

Product licence number 0068/5017.

LERGOBAN*

Presentation Creamy-white, circular, bi-convex tablets, 0.25 inch (6.4 mm) in diameter. The markings are 'LB' on one side and 'RIKER' on the other. Each Lergoban Tablet contains Diphenylpyraline Hydrochloride BP 5 mg.

Uses Lergoban is indicated in: allergic rhinitis, allergic conjunctivitis, angioneurotic oedema, hay fever, urticaria, allergic skin conditions and irritation.

Diphenylpyraline is an antihistamine with the general properties of antihistamine compounds, but with a low incidence of side-effects. In Lergoban its therapeutic usefulness is greatly increased by the long-acting presentation. Lergoban Tablets consist of a porous plastic matrix in which the diphenylpyraline is dispersed. In the gastro-intestinal tract, the active ingredient is gradually leached from the pores of the matrix and absorbed systemically. The release rate is not affected by

changes in pH, digestive enzymes, viscosity, surface tension or electrolyte concentration. The small plastic skeleton is insoluble and is excreted unchanged in the faeces.

The duration of effect from each dose of Lergoban is about 10 hours, so that only two doses every 24 hours are required.

Dosage and administration *Adults:* One or two 5 mg tablets every 12 hours, or as directed by the physician.

Children: Older children may be given one 5 mg tablet every 12 hours.

Lergoban is not recommended for children under 10 years.

Contra-indications, warnings, etc

Side-effects: Although side-effects are less likely with this sustained release tablet, slight drowsiness and dizziness, flushing, headache, anorexia and dryness of the mouth may occur.

Contra-indications: None.

Caution: Doses greater than those recommended may cause sedation and drowsiness. Patients undergoing treatment with an antihistamine should be warned of this possibility if they are in control of vehicles or machinery, where loss of attention may lead to accidents.

In some patients, the action of antihistamines may be potentiated by alcohol or other CNS depressants.

Overdosage: In adults, overdosage of antihistamines usually causes sedation, varying from drowsiness to deep sleep. Conversely in children, antihistamines often act as cerebral stimulants and may cause convulsions and hyperpyrexia. Stimulation may also occur in some adults.

Treatment: If the drug has recently been taken, the stomach should be emptied by gastric lavage, using a tube greater than 7 mm in diameter. Excitement may be controlled with diazepam given by mouth; the ECG should be monitored.

Pharmaceutical precautions No special storage precautions are required.

Legal category P.

Package quantities Bottles of 50 and 200 tablets.

Further information Nil.

Product licence number 0068/5002.

MEDIHALER-DUO*

Presentation Medihaler-duo is a pressurised aerosol for inhalation therapy. The vial contains a creamy-white suspension of isoprenaline hydrochloride 8 mg/ml and phenylephrine bitartrate 12 mg/ml in aerosol propellant, and delivers 400 measured doses each containing 160 mcg isoprenaline hydrochloride and 240 mcg phenylephrine bitartrate.

Uses Medihaler-duo is a potent bronchodilator and is indicated for the immediate and prolonged relief of bronchospasm in bronchial asthma and chronic bronchitis.

Isoprenaline is a directly acting sympathomimetic amine which activates both β_1 and β_2 adrenergic receptors. It has virtually no affinity for α -receptors. As a result it is a bronchodilator which also produces

vasodilatation in all blood vessels, including those of the pulmonary system. Pulse rate and cardiac output are increased, the degree of cardiac stimulation being proportional to the blood level. Isoprenaline is quickly eliminated from the blood and therefore has no cumulative effect. It inhibits histamine release in the lungs and has a beneficial effect on cilia and mucus flow.

By inhalation, isoprenaline has a rapid onset of bronchodilatation. Cardiac stimulation does not usually occur and the maximum possible bronchodilatation is produced at doses below those which result in significant tachycardia. Appreciable cardiac stimulation occurs only at the upper end of the therapeutic dose range.

Phenylephrine acts primarily on α -receptors. It complements and modifies the action of isoprenaline in several respects. It augments bronchodilatation. It delays the absorption of isoprenaline from the lungs and helps to prolong the bronchodilator activity. Phenylephrine also tends to offset the cardiovascular effects of isoprenaline.

Paradoxically, the improved ventilation produced by bronchodilators is often accompanied by impairment of oxygenation of venous blood as it passes through the lungs, with consequent falls in arterial oxygen levels. This results from the non-selective relaxation of smooth muscle both of bronchioles and the pulmonary blood vessels. Phenylephrine opposes this effect and Medihaler-duo is thus less likely to cause falls in the arterial oxygen tension than isoprenaline alone.

Dosage and administration Each puff from Medihaler-duo delivers a measured dose of 160 mcg isoprenaline hydrochloride and 240 mcg phenylephrine bitartrate. One, two or at the most three puffs should be sufficient to provide relief in most cases. It should not be necessary for the patient to take further treatment for at least 30 minutes or more than eight treatments in any 24-hour period.

Correct technique is essential if the patient is to obtain full benefit from each treatment. Probably the most reliable way of ensuring this is for the doctor to show the patient how to use 'Medihaler-duo' by personal demonstration, using a Demonstration Unit containing no active medicament. These units are available on request.

Children: Medihaler-duo should be administered to children only under the supervision of a responsible adult.

Instructions for use: With the dust cap removed, Medihaler-duo should be shaken to disperse the particles of medicament in the propellant.

The mouthpiece should then be placed well into the mouth and the lips closed firmly around it. (When the adapter is held at the correct angle, the spray will go to the back of the throat and down into the lungs.) The patient should now breathe out fully through the adapter.

As soon as the patient starts to breathe in, the vial should be pressed firmly down into the adapter. This releases a dose.

The adapter should now be taken from the mouth and the inspired breath held for as long as possible to avoid exhaling particles of medicament.

Before taking a further inhalation, the patient should wait at least one minute to allow the full effect of the puff to become apparent.

Contra-indications, warnings, etc

Side-effects: Overdosage may cause dry mouth, palpitations or nervousness.

Contra-indications: Medihaler-duo should be used with caution in the presence of cardiac disease, hypertension or hyperthyroidism.

Overdosage: Acute poisoning in non-asthmatics: No cases have been reported. In the absence of details of such practical experience, the following guidance is based on theoretical considerations.

Symptoms: The toxic symptoms of isoprenaline (namely those of tachycardia, palpitations, peripheral vasodilatation and fall in blood pressure) are likely to be counterbalanced by the vasoconstrictor action of phenylephrine.

Treatment: General symptomatic therapy.

Chronic poisoning in asthmatics: No cases have been reported. However, excessive use of Medihaler-duo during an attack of asthma indicates lack of response. This is a grave sign suggestive of status asthmaticus. It is recommended that 100 mg hydrocortisone be given immediately by intravenous injection, and the patient admitted to hospital without delay. Beta blocking drugs should not be used.

Pharmaceutical precautions Medihaler-duo should be stored in a cool place, protected from frost and sunlight. The shelf-life of Medihaler-duo is three years.

As the Medihaler vial is pressurised, no attempt should be made to puncture it or to dispose of it by burning.

Legal category POM.

Package quantities Standard pack (complete unit): vial contains 400 doses.

Further information Nil.

Product licence number 0068/5070.

MEDIHALER-EPI*

Presentation Medihaler-epi is a pressurised aerosol for inhalation therapy. The vial contains a creamy-white suspension of Adrenaline Acid Tartrate BP 14 mg/ml in aerosol propellant, and delivers 400 measured doses, each containing 280 mcg Adrenaline Acid Tartrate BP.

Uses Medihaler-epi is a potent bronchodilator, and is indicated for the relief of bronchospasm in bronchial asthma, chronic bronchitis and drug sensitivity reactions.

Adrenaline is a sympathomimetic amine which activates both α - and β -adrenergic receptors. As a result, it causes vasoconstriction, bronchodilatation, relieves mucosal congestion and is a cardiac stimulant.

By inhalation adrenaline relaxes bronchial smooth muscle and constricts bronchial mucosal vessels, relieving congestion and oedema. However, tolerance to adrenaline can develop after repeated use and the action of adrenaline in reducing bronchial secretion may make mucus more viscid.

Dosage and administration Each puff from Medihaler-epi delivers a measured dose of 280 mcg adrenaline acid tartrate. One, two or at the most three puffs should be sufficient to provide relief in most cases. It should not be necessary for the patient to take further treatment for at least 30 minutes or more than eight treatments in any 24-hour period.

Correct technique is essential if the patient is to obtain full benefit from each treatment. Probably the most reliable way of ensuring this is for the doctor to show the

patient how to use Medihaler-epi by personal demonstration, using a Demonstration Unit containing no active medicament. These units are available on request.

Children: Medihaler-epi should be administered to children only under the supervision of a responsible adult.

Instructions for use: With the adapter dust cap removed, Medihaler-epi should be shaken to disperse the particles of medicament in the propellant.

The mouthpiece should then be placed well into the mouth and the lips closed firmly around it. (When the adapter is held at the correct angle, the spray will go right to the back of the throat and down into the lungs.) The patient should now breathe out fully through the adapter.

As soon as the patient starts to breathe in, the vial should be pressed firmly down into the adapter. This releases a dose.

The adapter should now be taken from the mouth and the inspired breath held for as long as possible to avoid exhaling particles of medicament.

Before taking a further inhalation, the patient should wait at least one minute to allow the full effect of the puff to become apparent.

Contra-indications, warnings, etc

Side-effects: Overdosage may cause dry mouth, palpitations or nervousness.

Contra-indications: Medihaler-epi should be used with caution in the presence of cardiac disease, hypertension or hyperthyroidism.

Prolonged use of adrenaline may lead to the development of tolerance (adrenaline 'fastness'). When this occurs, isoprenaline is a most effective alternative.

Overdosage: Acute poisoning in non-asthmatics: No cases have been reported. The following guidance is based on acute adrenaline poisoning following parenteral administration.

Symptoms: Restlessness, palpitations, rapid pulse, tremor, weakness, dizziness, headache, coldness of extremities; elevated blood pressure, tachycardia; the symptoms are rapid in onset and of short duration.

Treatment: It is essential to administer immediately intravenous injections of quick-acting sympatholytics, e.g. phentolamine or piperoxan.

Chronic poisoning in asthmatics: Some cases have been reported, but no details of treatment have been given, other than withdrawal of the aerosol.

Excessive use of Medihaler-epi during an attack of asthma indicates lack of response. This is a grave sign suggestive of status asthmaticus. It is recommended that 100 mg hydrocortisone be given immediately by intravenous injection, and the patient admitted to hospital without delay. Beta-blocking drugs should not be used.

Pharmaceutical precautions Medihaler-epi should be stored in a cool place, protected from frost and sunlight. The shelf-life of Medihaler-epi is three years.

As the Medihaler vial is pressurised, no attempt should be made to puncture it or to dispose of it by burning.

Legal category POM.

Package quantities Standard pack (complete unit): vial contains 400 doses.

Further information Nil.

Product licence number 0068/5060.

MEDIHALER-ISO* MEDIHALER-ISO* FORTE

Presentation Medihaler-iso and Medihaler-iso Forte are pressurised aerosols for inhalation therapy.

The Medihaler-iso vial contains a creamy-white suspension of Isoprenaline Sulphate BP 4 mg/ml in aerosol propellant and delivers 400 measured doses, each containing 80 mcg Isoprenaline Sulphate BP.

The Medihaler-iso Forte vial contains a creamy-white suspension of Isoprenaline Sulphate BP 20 mg/ml in aerosol propellant, and delivers 400 measured doses, each containing 400 mcg Isoprenaline Sulphate BP.

Uses Medihaler-iso and Medihaler-iso Forte are potent bronchodilators, and are indicated for the relief of bronchospasm in bronchial asthma and chronic bronchitis.

Isoprenaline is a directly acting sympathomimetic amine which activates both β_1 and β_2 adrenergic receptors. It has virtually no affinity for α -receptors. As a result it is a bronchodilator which also produces vasodilatation in all blood vessels, including those of the pulmonary system. Pulse rate and cardiac output are increased, the degree of cardiac stimulation being proportional to the blood level. Isoprenaline is quickly eliminated from the blood and therefore has no cumulative effect. It inhibits histamine release in the lungs and has a beneficial effect on cilia and mucus flow.

By *inhalation*, isoprenaline has a rapid onset of bronchodilatation. Cardiac stimulation does not usually occur and the maximum possible bronchodilatation is produced at doses below those which result in significant tachycardia. Appreciable cardiac stimulation occurs only at the upper end of the therapeutic dose range.

Dosage and administration Each puff from Medihaler-iso delivers a measured dose of 80 mcg isoprenaline sulphate; and from Medihaler-iso Forte, 400 mcg isoprenaline sulphate. One, two or at the most three puffs should be sufficient to provide relief in most cases. It should not be necessary for the patient to take further treatment for at least 30 minutes, or more than eight treatments in any 24-hour period.

Correct technique is essential if the patient is to obtain full benefit from each treatment. Probably the most reliable way of ensuring this is for the doctor to show the patient how to use Medihaler by personal demonstration, using a Demonstration Unit containing no active medicament. These units are available on request.

Children: Medihaler-iso should be administered to children only under the supervision of a responsible adult. Medihaler-iso Forte is not recommended for children.

Instructions for use: With the adapter dust cap removed, Medihaler should be shaken to disperse the particles of medicament in the propellant.

The mouthpiece should then be placed well into the mouth and the lips closed firmly around it. (When the adapter is held at the correct angle, the spray will go right to the back of the throat and down into the lungs.) The patient should now breathe out fully through the adapter.

As soon as the patient starts to breathe in, the vial should be pressed firmly down into the adapter. This releases a dose.

The adapter should now be taken from the mouth and the inspired breath held for as long as possible to avoid exhaling particles of medicament.

Before taking a further inhalation, the patient should

wait at least one minute to allow the full effect of the puff to become apparent.

Contra-indications, warnings, etc

Side-effects: Overdosage may cause dry mouth, palpitations or nervousness.

Contra-indications: Medihaler-iso and Medihaler-iso Forte should be used with caution in the presence of cardiac disease, hypertension or hyperthyroidism.

Overdosage: *Acute poisoning in non-asthmatics:* No cases have been reported. In the absence of details of such practical experience, the following guidance is based on theoretical considerations.

Symptoms of acute isoprenaline poisoning are likely to be mainly cardiovascular effects, e.g. tachycardia, palpitations, peripheral vasodilation and a fall in blood pressure.

Treatment: General symptomatic therapy.

Chronic poisoning in asthmatics: Some cases have been reported, but no details of treatment have been given, other than withdrawal of the aerosol.

Excessive use during an attack of asthma indicates lack of response. This is a grave sign suggestive of status asthmaticus. It is recommended that 100 mg hydrocortisone be given immediately by intravenous injection, and the patient admitted to hospital without delay. Beta blocking drugs should not be used.

Pharmaceutical precautions Medihaler-iso and Medihaler-iso Forte should be stored in a cool place, protected from frost and sunlight. The shelf-life of Medihaler-iso and Medihaler-iso Forte is three years.

As the Medihaler vial is pressurised, no attempt should be made to puncture it or to dispose of it by burning.

Legal category POM.

Package quantities Standard pack (complete unit): vial contains 400 doses.

Further information Nil.

Product licence numbers

Medihaler-iso	0068/5082
Medihaler-iso Forte	0068/5072

NORFLEX*

Presentation *Injection:* Each 2 ml ampoule contains Orphenadrine Citrate BP 30 mg/ml.

Tablets: White, circular, bi-convex tablets, 8.8 mm diameter, marked 'N/X' on one side and 'RIKER' on the reverse. Each tablet contains Orphenadrine Citrate BP 100 mg in a slow-release base.

Uses Norflex is indicated for the relief of acute skeletal muscle spasm associated with muscle injury, sprains and strains, prolapsed intervertebral disc, 'whiplash' injuries, fractures before and after reduction and immobilisation, acute torticollis and hiccough.

Orphenadrine acts centrally by blocking reticular facilitation, i.e. it blocks preferentially those pathways whose hyperactivity leads to an exaggeration of motor function such as spasticity, rigidity or muscle spasm.

Norflex is a potent skeletal muscle relaxant which provides relief of acute muscle spasm and associated pain. It relaxes only muscle in spasm without impairment of normal muscle tone or voluntary movement. Action is rapid in onset, particularly in the case of Norflex Injection, and relatively prolonged. The effect of orphenadrine on

skeletal muscle spasm has been demonstrated objectively by means of electromyography.

Dosage and administration *Parenteral*: 60 mg (one 2 ml ampoule) administered intramuscularly or intravenously. Further 60 mg doses may be given at 12-hour intervals, if required.

Note: An intravenous injection should be administered over a period of about five minutes.

Oral: 2 tablets daily, 1 in the morning and 1 in the evening. This may be increased to 3 tablets daily if required.

Norflex is not recommended for children under 12 years.

Contra-indications, warnings, etc

Side-effects: Dry mouth, nausea, blurring of vision, dizziness and restlessness may occur in some patients susceptible to the parasympatholytic action of orphenadrine. These symptoms rapidly disappear following reduction of dosage or cessation of treatment. Some patients may experience a transient feeling of light-headedness or dizziness following an injection of Norflex.

Caution: Norflex should be used with caution in patients with tachycardia.

Contra-indications: Contra-indications to Norflex result from the parasympatholytic action of orphenadrine. Norflex should not be given to patients with glaucoma, urinary retention (e.g. due to prostatic hypertrophy or obstruction of the bladder neck) and myasthenia gravis.

Overdosage: Symptoms of orphenadrine citrate overdosage: Excitement, confusion and delirium leading to coma, convulsions, tachycardia. Dilated pupils and urinary retention may occur.

Treatment: Gastric lavage should be carried out immediately regardless of the estimated ingested dose. Convulsions and delirium respond to relatively large doses of diazepam, preferably by mouth. Adequate hydration of the patient is important.

Pharmaceutical precautions No special storage precautions are required.

Legal category POM.

Package quantities *Ampoules (30 mg/ml)*: 3 × 2 ml. *Tablets*: Bottles of 100.

Further information Nil.

Product licence numbers

Norflex Tablets 0068/5008
Norflex Injection 0068/5078

NORGESIC*

Presentation A white or almost white, circular, compressed tablet 12.8 mm diameter. Markings are 'N/G' on one side and 'RIKER' on the other. Each tablet contains Orphenadrine Citrate BP 35 mg and Paracetamol BP 450 mg.

Uses Norgesic is indicated for the relief of painful skeletal muscle spasm associated with chronic low back pain, sprains and strains, prolapsed intervertebral disc, muscle injury, non-articular rheumatism (fibrositis, myositis and myalgia), 'whiplash' injuries, acute torticollis, tension headache, dysmenorrhoea, other acute or chronic painful muscular conditions.

Orphenadrine acts centrally by blocking reticular

facilitation, i.e. it blocks preferentially those pathways whose hyperactivity leads to an exaggeration of motor function such as spasticity, rigidity or muscle spasm. Orphenadrine relaxes only muscle in spasm without impairment of normal muscle tone or voluntary movement. Action is rapid in onset and relatively prolonged. The effect of orphenadrine on skeletal muscle spasm has been demonstrated objectively by means of electromyography.

Paracetamol is a well-tolerated analgesic and antipyretic. Its analgesic action is rapid in onset (within 30 minutes) and lasts for three to four hours. It has been found to be particularly effective for the relief of pain in muscles and joints.

Paracetamol does not produce gastric upset or bleeding. Hepatic and renal necrosis have been associated with the ingestion of paracetamol in amounts greatly in excess of normal therapeutic dosage.

Dosage and administration *Adults*: Two tablets three times a day.

Norgesic is not recommended for children under 12 years old.

Contra-indications, warnings, etc

Side-effects: Dry mouth, nausea, blurring of vision, dizziness and restlessness may occur in some patients susceptible to the parasympatholytic action of orphenadrine. These symptoms disappear rapidly following reduction of dosage or withdrawal of treatment.

Contra-indications: Contra-indications to Norgesic result from the parasympatholytic action of orphenadrine. Norgesic should not be given to patients with glaucoma, urinary retention (e.g. due to prostatic hypertrophy or obstruction of the bladder neck) or myasthenia gravis. It should be used with caution in patients with tachycardia.

Overdosage: Symptoms of orphenadrine citrate overdosage are excitement, confusion, and delirium leading to coma. Convulsions, tachycardia, dilated pupils and urinary retention may occur.

Paracetamol overdosage may cause acute liver damage but symptoms may not appear for up to several days after ingestion.

Treatment: Gastric lavage should be carried out immediately, regardless of the estimated ingested dose. Convulsions and delirium respond to relatively large doses of diazepam, preferably by mouth. Adequate hydration of the patient is important. It is recommended that the patient be referred to a hospital where early and regular monitoring of plasma paracetamol levels can be carried out. If instituted sufficiently early, treatment with N-acetylcysteine, L-methionine or L-cysteamine will minimise liver damage.

Pharmaceutical precautions No special storage precautions are required.

Legal category POM.

Package quantities Bottles of 100 and 500 tablets.

Further information Nil.

Product licence number 0068/5059.

NUELIN*

Presentation White, circular, biconvex tablet with breakline, 9 mm in diameter, marked NL/125 on one side and 'RIKER' on the other.

Each Nuelin tablet contains Theophylline BP 125 mg in microcrystalline form.

Uses Nuelin is indicated for the relief of bronchospasm.

Theophylline is well established in the treatment of bronchospasm. In Nuelin, the theophylline is present as microfine particles to give a very high rate of dissolution which results in rapid and predictable absorption.

Dosage and administration *Adults:* One tablet three or four times daily; this can be increased to two tablets three or four times daily depending on response.

Children: 7–12 years (20–35 kg): Half or 1 tablet three or four times daily.

The difficulty of dividing the tablet accurately makes Nuelin unsuitable for use in children under the age of seven.

Nuelin tablets are soluble in water.

Contra-indications, warnings, etc

Side-effects: Nausea or other gastric distress may occur rarely. Palpitations and insomnia have been reported occasionally.

Contra-indications: There are no known contra-indications to theophylline therapy.

Overdosage: Symptoms: Characterised by nausea, vomiting and gastro-intestinal irritation. Tachycardia and hypotension may also occur.

Treatment: Gastric lavage and general supportive measures are recommended.

Pharmaceutical precautions The tablets should be stored at a temperature not exceeding 30°C. The container should be kept tightly closed.

Legal category P.

Package quantities Bottles of 100 tablets.

Further information Nil.

Product licence number 0068/0064.

NUELIN* LIQUID

Presentation Clear, light brown, pleasantly flavoured liquid. Each 5 ml dose of Nuelin Liquid contains theophylline sodium glycinat 120 mg equivalent to Theophylline Hydrate BP 60 mg.

Uses Nuelin Liquid is indicated for the relief of bronchospasm. Nuelin in tablet form (microcrystalline theophylline 125 mg) is established as a highly effective bronchodilator. Nuelin Liquid is designed to offer comparable relief of bronchospasm with the same low incidence of side-effects, for patients who prefer a liquid presentation. Each 10 ml of Nuelin Liquid approximates to one 125 mg Nuelin tablet.

Dosage and administration *Adults:* 10–20 ml (two to four 5 ml spoonfuls) three or four times daily.

Children: 7–12 years: One-and-a-half or two 5 ml spoonfuls three or four times daily.

2–6 years: One or one-and-a-half 5 ml spoonfuls three or four times daily.

Under 2 years: It is recommended that dosage is calculated at 5 mg/kg theophylline hydrate per dose (0.4 ml/kg Nuelin Liquid) and given three or four times daily. Nuelin Liquid may be diluted with Syrup BP if required.

Contra-indications, warnings, etc

Contra-indications: There are no known contra-indications to theophylline therapy.

Side-effects: Nausea or other gastric distress may occur rarely. Palpitations and insomnia have been reported occasionally.

Overdosage: Symptoms: Nausea, vomiting and gastro-intestinal irritation.

Treatment: Gastric lavage and general supportive measures are recommended.

Pharmaceutical precautions No special storage precautions are required.

The shelf-life of Nuelin Liquid is two years.

Legal category P.

Package quantities Bottles of 500 ml.

Further information Each 5 ml spoonful of Nuelin Liquid contains 0.38 mEq sodium (8.7 mg Na).

Product licence number 0068/0084.

NUELIN* SA

Presentation *Nuelin SA:* White, biconvex, round tablets, 9 mm in diameter and marked NLS 175 on one side and RIKER on the other.

Each Nuelin SA tablet contains 175 mg anhydrous theophylline in a slow release formulation which gives a particularly smooth release of medicament over a prolonged period.

Nuelin SA-250: White, biconvex, round tablets with breakline, 11 mm in diameter and marked NLS 250 on one side and RIKER on the other. Each Nuelin SA-250 tablet contains 250 mg anhydrous theophylline in a slow release formulation.

Uses Nuelin SA and Nuelin SA-250 tablets are indicated for the treatment and prophylaxis of bronchospasm.

Because effective plasma levels are maintained for up to twelve hours from a single dose, less frequent dosing is required than with conventional theophylline preparations.

Dosage and administration *Nuelin SA: Adults:* One tablet twice daily, increasing to two tablets twice daily if necessary.

Children: 6 to 12 years: one tablet twice daily.

Nuelin SA-250: Adults: One tablet twice daily, increasing to two tablets twice daily if necessary.

Children: 6 to 12 years: Half or one tablet twice daily.

Nuelin SA and Nuelin SA-250 tablets are not recommended for children under six years.

Nuelin SA tablets should be swallowed whole and not crushed or chewed.

Nuelin SA-250 tablets are scored and may be halved but should not be crushed or chewed.

Contra-indications, warnings, etc

Side-effects: The side-effects commonly associated with xanthine derivatives such as nausea, gastric irritation, palpitations and insomnia are much diminished when a sustained action preparation such as Nuelin SA is used.

Caution: In the case of an acute asthmatic attack in a patient receiving a sustained action theophylline preparation, great caution must be taken when administering

intravenous aminophylline. Half the recommended loading dose of aminophylline (generally 6 mg/kg) should be given i.e. 3 mg/kg, cautiously.

Contra-indications: There are no known contra-indications to theophylline therapy.

Overdosage: Symptoms: Nausea, vomiting and gastric irritation. Tachycardia and hypotension may also occur.

Treatment: Gastric lavage and general supportive measures are recommended.

Pharmaceutical precautions No special storage precautions are required.

Legal category P.

Package quantities *Nuelin SA:* Bottles of 100 tablets.
Nuelin SA-250: Bottles of 100 tablets.

Further information Nil.

Product licence numbers

Nuelin SA 0068/0092
Nuelin SA-250 0068/0093

NUMOTAC*

Presentation White to creamy-white, circular bi-convex tablets 7.15 mm diameter, marked 'NT' on one side and 'RIKER' on the other. Each tablet contains isoetharine hydrochloride 10 mg in a porous plastic matrix.

Uses Numotac is indicated for the relief of bronchospasm in chronic bronchitis, bronchial asthma and pulmonary emphysema.

Isoetharine is a sympathomimetic amine with a marked bronchodilator action. It is rapidly absorbed from the gastro-intestinal tract and has a relatively fast onset of action.

A notable feature of isoetharine is that at normal dosage levels it acts selectively on the β_2 -receptors of bronchial muscle and has little effect on the β_1 cardiac receptors. Cardiac side-effects are therefore reduced to negligible levels, and occur only at higher doses or in hypersensitive patients.

Numotac contains isoetharine hydrochloride embedded in a porous plastic matrix. By this means, the release of isoetharine is controlled, giving Numotac a duration of action of between four and six hours. This formulation reduces the possibility of side-effects associated with uneven blood levels.

Dosage and administration *Adults:* One or two tablets three or four times daily.

For patients who have not previously been prescribed oral bronchodilator therapy or who are known to be sensitive to the action of sympathomimetic amines, treatment should be started on the lower dosages (3 or 4 tablets daily). Dosage may then be adjusted upwards, if necessary, to achieve optimum response.

Clinical and pharmacological studies have shown that 'Numotac' acts for between four and six hours. In susceptible patients administration at shorter intervals may give rise to side-effects. When this occurs dosage should be adjusted accordingly.

Children: The 10 mg tablet should not be broken, and this dose is not recommended for children aged 12 years or under.

Contra-indications, warnings, etc

Side-effects: With higher doses, or in persons sensitive

to sympathomimetic amines, tachycardia, palpitations, tremor or vertigo may occur.

Cautions and contra-indications: Numotac should be used with caution in the presence of cardiac disease, or hypertension. The use of Numotac is contra-indicated in thyrotoxicosis.

Overdosage: Symptoms: The blood pressure may fall and cause dizziness and fainting. Other symptoms may include headache, nervousness, tremor and weakness.

Treatment: General symptomatic treatment. If the drug has recently been taken, the stomach should be emptied by gastric lavage, using a tube greater than 8 mm in diameter.

Pharmaceutical precautions No special storage precautions are required.

Legal category POM.

Package quantities Bottles of 100 and 500 tablets.

Further information Nil.

Product licence number 0068/5054.

PENTOXYLON*

Presentation Reddish-brown, circular, bi-convex tablets marked 'P/X' on one side and 'RIKER' on the other. Diameter 8.0 mm. Each Pentoxylon Tablet contains Rauwiloid brand of alkaloid hydrochlorides of *Rauwolfia serpentina* 1 mg and pentaerythritol tetranitrate 10 mg.

Uses Pentoxylon is indicated for the prophylaxis of angina pectoris.

Pentaerythritol tetranitrate (PETN) is an organic nitrate which produces a prolonged dilatation of the coronary blood vessels, consequently reducing the incidence and severity of angina attacks.

Rauwiloid produces a moderate fall in blood pressure (more particularly in cases where it is raised), bradycardia and a general feeling of well-being.

Dosage and administration *Adults:* One or two tablets four times daily between meals.

Pentoxylon is not recommended for children.

Contra-indications, warnings, etc

Side-effects: Occasional headache may occur due to the pentaerythritol tetranitrate. Some nasal stuffiness and looseness of the bowel may occur. There might also be a slight increase in appetite and an increase in weight. As with other Rauwolfia preparations, the possibility of mental depression must be considered. However, serious mental depression has not been reported as a result of Rauwiloid therapy.

Contra-indications: There are no absolute contra-indications to the use of Pentoxylon. It should, however, be administered with caution to patients who have a history of depression or peptic ulcer.

Overdosage: Symptoms: Mild overdosage can produce nasal congestion, gastro-intestinal upset such as vomiting and diarrhoea, drowsiness, apathy, fatigue, headache, vertigo, hallucinations.

Higher doses may cause flushing, insomnia, vasodilatation, bradycardia, severe depression, sodium retention, oedema, peptic ulceration.

After a single massive dose most of the effects are not encountered. Instead, the patient becomes sleepy and eventually comatose. Coma may last for several days.

Treatment: In the acutely poisoned patient, who is not in a coma, an emetic should be administered, or gastric lavage performed, even several hours after ingestion of the alkaloid. A saline cathartic should be left in the stomach. Nasal congestion, excessive salivation, gastro-intestinal upsets and other parasympathetic side-effects may be controlled by small doses of atropine.

Epigastric pain and peptic ulcer may be treated with local antacid therapy.

Unless the blood pressure becomes very low, vasopressor drugs which may prove inactive (e.g. ephedrine) or which may lead to exaggerated cardiovascular response (e.g. adrenaline or noradrenaline) should be avoided. Blankets and external application of mild heat should be used to maintain normal body temperature. If coma with hypotension occurs, conservative supportive therapy should be employed. In general, supportive measures that do not involve extensive drug therapy are probably safest, and are expected to suffice in most cases.

In cases of methaemoglobinaemia and syncope, intravenous injection of methylene blue (1–2 mg/kg body weight) can be given.

Pharmaceutical precautions No special storage precautions are required.

Legal category POM.

Package quantities Bottle of 100 tablets.

Further information Nil.

Product licence number 0068/5073.

PEPTARD*

Presentation Creamy-white, circular, biconvex tablet, 7 mm in diameter. The markings are 'RIKER' on one side, and letters 'PTD' on the other. Each Peptard tablet contains 1-hyoscyamine sulphate 200 mcg.

Uses Peptard is indicated for the treatment of peptic ulcer, irritable colon, hyperhidrosis and conditions in which the oral administration of an antispasmodic/antisecretory agent is beneficial.

Naturally occurring atropine consists of a racemic mixture of hyoscyamine isomers of which the l-isomer has the greater physiological activity. With l-hyoscyamine it is possible to adjust the dose more readily to obtain a selective action on the gastro-intestinal tract with fewer anticholinergic side-effects than with atropine.

l-Hyoscyamine reduces the volume of gastric secretion and total acid output. Secretion during both psychic and gastric phases is reduced, but not abolished. A decrease in pepsin output contributes to the overall effects.

In Peptard, the slow release of l-hyoscyamine sulphate from the plastic matrix provides more even blood levels and response.

Dosage and administration *Adults:* In general, two or three tablets (400–600 mcg) twice daily.

Children: Older children (over 10 years) one or two tablets twice daily.

Individual cases may be increased, for example, with peptic ulcer therapy, up to 3 mg a day in three divided doses.

The tablets should be swallowed whole.

Contra-indications, warnings, etc

Side-effects: At the optimum effective dose, the only side-effects that have occurred are dry mouth, slight visual disturbance and occasional hesitancy of micturition.

Contra-indications: Peptard should not be given to patients with, or suspected of suffering from glaucoma or with obstruction of the neck of the urinary bladder, pyloric stenosis or myasthenia gravis.

Overdosage – Symptoms: The main symptoms of toxicity are dryness of mucous membranes and intense thirst, dilation of pupils and blurred vision, a hot, dry skin, with or without a rash, hyperpyrexia, tachycardia, palpitations and elevated blood pressure, urinary urgency and hesitation; and restlessness, excitement and confusion.

Treatment: If the drug has recently been taken, the stomach should be emptied by gastric lavage, using a tube greater than 7 mm in internal diameter. Symptomatic treatment should be given.

Pharmaceutical precautions The tablets should be stored at room temperature.

The shelf-life of Peptard is two years.

Legal category POM.

Package quantities Bottles of 100 tablets.

Further information Nil.

Product licence number 0068/0054.

PHOLTEX*

Presentation Each 5 ml dose contains Pholcodine BP 15 mg and phenyltoloxamine 10 mg as ion-exchange resin complexes in a pleasantly flavoured, orange-coloured, thixotropic vehicle.

Uses For prolonged antitussive action.

Pholtex is well accepted by children and is valuable in the treatment of whooping cough and the cough associated with measles.

Pholtex contains the cough depressant pholcodine, the action of which is potentiated and reinforced by the antihistamine phenyltoloxamine. Both are presented as ion-exchange resin complexes to give smooth and prolonged effect.

Phenyltoloxamine complements the action of pholcodine not only because it potentiates the activity of the cough depressant but also because of its antihistaminic and antispasmodic actions which help to relieve associated symptoms.

The cough-depressant action of Pholtex is maintained for up to 10 hours with a single 5 ml dose. Consequently, a dose taken on retiring and another on rising should provide effective relief of cough throughout the day and night in most cases.

Dosage and administration *Adults:* One 5 ml dose two or three times daily.

Children: Half to full adult dosage, according to age.

Pholtex contains no sugar and is therefore suitable for cough treatment in diabetic patients.

Contra-indications, warnings, etc

Side-effects: In common with all preparations which contain antihistamines, Pholtex may cause drowsiness, although this is very unlikely to occur in the recommended dosage.

Contra-indications: None.

Overdosage: The symptoms of antihistamine over-dosage would probably predominate. These include nausea and vomiting, diarrhoea, colic and epigastric pain. Overdosage may cause sedation, but large doses could cause convulsions and hyperpyrexia, particularly in children.

Treatment: The stomach should be emptied by aspiration and lavage. The respiration may require assistance. The patient, particularly if a child, should be kept quiet.

Pharmaceutical precautions No special storage precautions are required.

Diluents: Tragacanth Mucilage BPC or Syrup BP should be used as diluents if required.

Legal category P.

Package quantities Bottles of 100 ml and 1,000 ml.

Further information Nil.

Product licence number 0068/5030.

PULMADIL* INHALER

PULMADIL* AUTO

Presentation Pulmadil Inhaler is a pressurised aerosol or bronchodilator inhalation therapy. The vial contains a suspension of rimiterol hydrobromide 10 mg/ml in aerosol propellant and delivers to the patient 300 measured doses each containing 200 mcg rimiterol hydrobromide.

Pulmadil Auto is a breath-actuated, pressurised aerosol or bronchodilator inhalation therapy. The vial contains a suspension of rimiterol hydrobromide 10 mg/ml in aerosol propellant and delivers to the patient 300 measured doses each containing 200 mcg rimiterol hydrobromide.

Uses Pulmadil is indicated for the relief of bronchospasm in bronchial asthma and chronic bronchitis.

Rimiterol hydrobromide is a sympathomimetic agent which has a rapid and highly selective action on β_2 -adrenergic receptors in bronchial muscle. At therapeutic dose levels it has virtually no effect on β_1 -adrenergic receptors. Cardiac stimulation is therefore reduced to negligible levels and occurs only at high doses or in hypersensitive patients. The plasma half life of rimiterol in man is less than five minutes.

Dosage and administration One to three puffs should provide relief in most cases. This treatment dose should not be repeated in less than thirty minutes. No more than eight treatments should be taken in any 24-hour period.

Children: Pulmadil Inhaler and Pulmadil Auto should be administered to children only under the supervision of a responsible adult.

Instructions for use: Pulmadil Inhaler: With the dust cap removed, Pulmadil Inhaler should be shaken to disperse the particles of medicament in the propellant.

The mouthpiece should then be placed well into the mouth and the lips closed firmly around it. The patient should now breathe out fully through the adapter.

As soon as the patient starts to breathe in, the vial should be pressed firmly down into the adapter. This releases a dose. The adapter should now be taken from the mouth and the breath held for as long as possible to avoid exhalation of particles of medicament.

Before taking a further inhalation, the patient should

wait at least one minute to allow the full effect of the first to become apparent.

Pulmadil Auto: To obtain full benefit from Pulmadil Auto the patient should follow these simple steps:

1. Shake the unit with the mouthpiece cover closed. Then open the mouthpiece cover downwards.

2. Breathe out as much as possible, then close the lips tightly round the mouthpiece. Keep the teeth apart and the tongue flat (to allow the flow of medicament into the lungs).

3. Suck in air through the mouthpiece as rapidly and deeply as possible. When the unit operates a click will be heard. *Continue to breathe in after the click* until the lungs are full. Hold the breath for a few seconds. Then take the inhaler away from the mouth and breathe out slowly through pursed lips. If no click is heard, repeat step 3, making sure that the lips are well sealed round the mouthpiece.

4. *The unit must be reset before another dose can be taken*, by closing the mouthpiece cover upwards. It is important to keep the cover closed when it is not in use.

Contra-indications, warnings, etc *Side-effects:* No side-effects of any significance have been reported.

Contra-indications: There are no known contra-indications, but 'Pulmadil' should be administered with care to patients with thyrotoxicosis.

Overdosage: As rimiterol is rapidly eliminated from the blood it carries little risk of accumulation even if used excessively. No cases of overdosage have been reported and the following guidance is based on theoretical considerations.

Symptoms: The blood pressure may fall and cause dizziness and fainting. Anxiety, tremor and tachycardia may be present.

Treatment: General symptomatic therapy.

Excessive use in asthmatics: Excessive use of any bronchodilator aerosol can indicate lack of response. This is a grave sign suggestive of status asthmaticus. It is recommended that 100 mg of hydrocortisone be given intravenously immediately and the patient admitted to hospital without delay.

Pharmaceutical precautions Pulmadil Inhaler and Pulmadil Auto should be stored in a cool place, protected from frost and direct sunlight.

As the Pulmadil vial is pressurised, no attempt should be made to puncture or dispose of it by burning.

The shelf-life of both Pulmadil preparations is three years.

Legal category POM.

Package quantities Pulmadil Inhaler is supplied as a complete standard pack, comprising a vial delivering 300 doses and an adapter.

Pulmadil Auto is supplied as a complete unit for which replacement cartridges are available. Each cartridge deliver 300 doses.

Further information Nil.

Product licence number 0068/0030.

RAUWILOID*

Presentation Dark cream circular, bi-convex tablets, diameter 8 mm, marked 'RD' on one side and 'RIKER' on the other. Each tablet contains 2 mg alseroxylon fraction

(selected alkaloid hydrochlorides) of *Rauwolfia serpentina*.

Uses Rauwiloid is indicated for the treatment of mild to moderate hypertension.

When a more pronounced fall in blood pressure is needed, Rauwiloid can be combined with other anti-hypertensive agents, such as the thiazide diuretics. Rauwiloid reduces blood pressure by interfering with transmission at sympathetic nerve endings, and depleting the myocardium of its catecholamines (chiefly noradrenaline).

The antihypertensive activity of Rauwiloid is complemented by mild bradycardic and tranquillising effects.

Rauwiloid causes a slow but prolonged release of serotonin and catecholamines from stores in various parts of the body. This release leads eventually to the depletion of noradrenaline at the post-ganglionic nerve endings of the sympathetic nervous system, in the blood-vessel walls, and in other organs such as the heart and spleen. Depletion of noradrenaline results in a generalised reduction of sympathetic transmission. Since the sympathetic system is the pathway for vasoconstrictor impulses, vasomotor tone is reduced. This reduction is particularly noticeable in vascular areas such as the skin and splanchnic circulation, and the resulting peripheral vasodilatation produces a lowering of blood pressure.

Dosage and administration Initially, two tablets (4 mg) daily. This may be taken as a single dose at night or in divided doses. When the blood pressure is stable at the lower level a maintenance dose of one tablet daily may be sufficient.

Onset of antihypertensive effect is graded and may not be apparent for four weeks or more after the start of treatment.

Contra-indications, warnings, etc

Side-effects: Nasal stuffiness, drowsiness and a slight looseness of the bowel (although diarrhoea is rare) may occur. There might also be a slight increase in appetite and an increase in weight. As with other *Rauwolfia* preparations, the possibility of mental depression must be considered. However, serious mental depression has not been reported as a result of Rauwiloid therapy.

Contra-indications: There are no absolute contra-indications to the use of Rauwiloid. It should, however, be administered with caution to patients who have a history of depression or peptic ulcer.

Overdosage: Symptoms: Mild overdosage can produce nasal congestion, gastro-intestinal upsets such as vomiting and diarrhoea, drowsiness, apathy, fatigue, headache, vertigo, hallucinations.

Higher doses may cause flushing, insomnia, vasodilatation, bradycardia, severe depression, sodium retention, oedema, peptic ulceration.

After a single massive dose most of the above effects are not encountered. Instead, the patient becomes sleepy and eventually comatose. Coma may last for several days.

Treatment: In the acutely poisoned patient, who is not in a coma, an emetic should be administered, or gastric lavage performed, even several hours after ingestion of the alkaloid. A saline cathartic should be left in the stomach. Nasal congestion, excessive salivation, gastro-intestinal upsets and other parasympathetic side-effects may also be controlled by small doses of atropine.

Epigastric pain and peptic ulcer may be treated with local antacid therapy.

Unless the blood pressure becomes very low, vasopressor drugs which may prove inactive (e.g. ephedrine) or which may lead to exaggerated cardiovascular response (e.g. adrenaline or noradrenaline) should be avoided. Blankets and external application of mild heat should be used to maintain normal body temperature.

Pharmaceutical precautions No special storage precautions are required.

Legal category POM.

Package quantities Bottles of 60 and 500 tablets.

Further information Nil.

Product licence number 0068/5010.

RAUWILOID* + VERILOID*

Presentation Light reddish-brown, circular, biconvex tablets, 8.0 mm diameter, marked R/V on one side and 'RIKER' on the other. Each tablet contains Rauwiloid brand of alkaloid hydrochlorides of *Rauwolfia serpentina* 1 mg, and standardised alkaloids of *Veratrum viride* equivalent to 3 mg of 100% potency material.

Uses Rauwiloid + Veriloid is indicated for moderate to severe essential hypertension.

Rauwiloid reduces blood pressure by interfering with transmission at sympathetic nerve endings, depleting the myocardium of its catecholamines (chiefly noradrenaline).

Rauwiloid also has mild bradycardic and tranquillising effects.

Rauwiloid causes a slow but prolonged release of serotonin and catecholamines from stores in various parts of the body. This release leads eventually to depletion of noradrenaline at the post-ganglionic nerve endings of the sympathetic nervous system in the blood-vessel walls, and in other organs such as the heart and spleen. Depletion of noradrenaline results in a generalised reduction of sympathetic transmission. Since the sympathetic system is the pathway for vasoconstrictor impulses, vasomotor tone is reduced. This reduction is particularly noticeable in vascular areas such as the skin and splanchnic circulation, and the resulting peripheral vasodilatation produces a lowering of blood pressure.

Veriloid produces a complementary antihypertensive effect, accompanied by bradycardia. This is brought about by inhibition of the vasomotor centre and stimulation of the vagus. Veriloid does not affect ganglionic or adrenergic responses. Heart, kidney and liver functions are unimpaired.

Dosage and administration Initially, one tablet three times daily at minimum intervals of four hours and preferably after meals. After two weeks, this may be increased, if necessary, by stages to a maximum of eight tablets daily, although the average requirement of Rauwiloid + Veriloid is one tablet four times daily.

Contra-indications, warnings, etc

Side-effects: Postural hypotension, gastric disturbance or emesis may occur from higher doses.

Contra-indications: Rauwiloid + Veriloid is contra-indicated in patients receiving quinidine.

Because of the *Rauwolfia* constituent, Rauwiloid + Veriloid should be administered with caution to patients with a history of depression or peptic ulcer.

Overdosage: Overdosage with Rauwiloid + Veriloid is

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68/5069.

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in ileostomy and colos-
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and other dry ischaemic

cid compounds are mild

antiseptics and can reduce the destructive effect of
bacteria on debilitated tissue.

Administration *Directions for use:* Shake the canister.
The affected part should be sprayed sparingly, keeping
the nozzle about six to nine inches from the skin. To
obtain an adequate and evenly distributed film, the
canister should be kept moving during application.

Contra-indications, warnings, etc

Side-effects: None reported.

Contra-indications: Rikospray Balsam should not be
applied over areas of obvious infection. It is not intended
for use by inhalation.

Overdosage: Not applicable.

Pharmaceutical precautions The shelf life of Riko-
spray Balsam is five years.

As the Rikospray Balsam canister is pressurised, it
should not be punctured, incinerated or exposed to heat,
including the sun, even when empty.

Legal category GSL.

Package quantities Canisters of 150 g.

Further information Nil.

Product licence number 0068/5028.

RIKOSPRAY* SILICONE

Presentation White suspension in a pressurised
aerosol container. The application of Rikospray Silicone
delivered to the skin contains:

Aluminium dihydroxyallantoinate	0.5% w/w
Cetylpyridinium Chloride BP	0.02% w/w
Dimethicone 1,000 BP to	100%

Uses Rikospray Silicone is indicated in: the prevention
and treatment of bedsores, particularly in incontinent
patients; the prevention and treatment of napkin rash;
colostomy hygiene.

Rikospray Silicone delivers a spray which coats the
skin with a film of virtually 100% silicone. The silicone
compounds are well known for their water-repellent and
protective properties. The protective film is instantly
impervious to water, urine or faeces.

Aluminium dihydroxyallantoinate is an amphoteric
substance which is insoluble in water and alcohol. It
combines the astringent and bacteriostatic activity of
aluminium with the healing properties of allantoin, and
is also a mild antiperspirant. No irritant or sensitising
properties have been reported from its use.

Cetylpyridinium chloride possesses bactericidal
properties.

Administration *Directions for use:* Before applying
Rikospray Silicone, the affected area should be washed
thoroughly and the skin dried carefully.

The canister should be shaken before use, and then
held about six to nine inches from the skin. Rikospray
Silicone should be applied sparingly to cover the entire
area. This should be done twice daily for at least one
week, then application once daily will often be sufficient.

Contra-indications, warnings, etc

Side-effects: None reported.

Contra-indications: None.

Overdosage: Not applicable.

Pharmaceutical precautions The shelf life of Rikospray Silicone is five years.

As the Rikospray Silicone canister is pressurised, it should not be punctured, incinerated or exposed to heat, including the sun, even when empty.

Legal category GSL.

Package quantities Canisters of 200 g.

Further information Nil.

Product licence number 0068/5080.

THEODROX*

Presentation White to creamy-white, circular, bi-convex tablets, 12.0 mm diameter, marked TX on one side and 'RIKER' on the other. Each tablet contains Dried Aluminium Hydroxide Gel BP 260 mg and Aminophylline BP 195 mg.

Uses Theodrox is indicated in the prophylaxis of bronchospasm in asthma and chronic bronchitis.

Aminophylline is a combination of theophylline and ethylenediamine. It has properties very similar to those of theophylline but is more soluble. It relaxes involuntary muscle and relieves bronchial spasm. In common with other xanthine compounds, aminophylline has a diuretic action.

Administered orally, aminophylline can cause gastric irritation. However, in Theodrox this possibility is reduced by the simultaneous administration of aluminium hydroxide gel, which counteracts gastric acidity and retards the breakdown of aminophylline to theophylline in the stomach. By this means, larger doses of aminophylline can be given with less risk of side-effects such as nausea and vomiting.

Dosage and administration *Adults:* 1 tablet three times daily and one at night.

Theodrox is not recommended for children.

Contra-indications, warnings, etc

Side-effects: Occasionally, nausea or vomiting may occur in some patients.

Caution: Theodrox should be administered with caution to patients with peptic ulcer.

Overdosage: *Symptoms:* Nausea and vomiting.

Treatment: If necessary the stomach should be emptied by aspiration and lavage.

Pharmaceutical precautions No special storage precautions are required.

Legal category P.

Package quantities Bottles of 100 tablets.

Further information Nil.

Product licence number 0068/5011.

THIAVER*

Presentation Oval, pale blue tablets, with a break line on one side and 'RIKER' on the other. Each tablet contains standardised alkaloids of *Veratrum viride* equivalent to 4 mg of 100% potency material, and epithiazide 4 mg.

Uses Thiaver is an antihypertensive preparation, which is indicated in all grades of benign, essential hypertension.

The total antihypertensive effect of Thiaver results from the combined actions of the *Veratrum viride* alkaloids (which have a centrally mediated antihypertensive action) and epithiazide (which has a diuretic/antihypertensive effect).

The main pharmacological action of the *Veratrum viride* alkaloids is the antihypertensive effect accompanied by bradycardia. This is brought about by inhibition of the vasomotor centre and stimulation of the vagus. The *Veratrum viride* alkaloids do not affect ganglionic or adrenergic responses. Heart, kidney and liver functions are unimpaired.

Epithiazide is an antihypertensive thiazide diuretic with pharmacological properties broadly resembling those of the thiazides in general. Its use in Thiaver complements the antihypertensive action of the *Veratrum viride* alkaloids and is associated with negligible potassium loss.

Dosage and administration One tablet, two or three times daily.

Maximum response to treatment may not be achieved until after one or two weeks.

Thiaver is not recommended for children.

Contra-indications, warnings, etc

Side-effects: Mild gastro-intestinal disturbances, e.g. nausea, dizziness, headache, malaise, weakness and fatigue may occasionally occur.

Caution: Both epithiazide and the *Veratrum viride* alkaloids potentiate the action of other antihypertensive agents.

As a precautionary measure, patients with a tendency to hypokalaemia (e.g. patients with severe cardiac, renal or hepatic disease, or on corticosteroids or digitalis therapy) should receive regular electrolyte determinations.

Also, as diabetes mellitus and gout may occur with thiazide therapy, if either condition is suspected, blood glucose or blood uric acid determinations should be undertaken.

Overdosage: Overdosage with Thiaver is unlikely, because vomiting usually occurs.

Overdosage with *Veratrum viride* alkaloids: Symptoms include substernal and epigastric burning, severe nausea and vomiting, cold sweats, shallow respiration and vertigo.

Treatment: The stomach should be emptied by aspiration and lavage with warm water.

Excessive hypotension with bradycardia or cardiac arrhythmias may be treated by intramuscular injection of 500 mcg atropine sulphate.

The patient should be supine with the feet raised.

Pharmaceutical precautions The bottles are supplied with a charcoal sachet and this should not be removed.

Legal category POM.

Package quantities Bottles of 100 tablets.

Further information Nil.

Product licence number 0068/5068.

lar, bi-convex tablets, on one side and 'RIKER' and 'Calcium Carbonate' on the other. Each contains 100 mg of Neomycin Acid USNF (glycine).

the relief of hyperacidity, gastritis, and indigestion following administration of drugs. It acts as an antacid and prolongs the action of drugs.

Titralac tablet closely

Adults: One or two

tablets before meals at hourly intervals. The tablets should be allowed to dissolve in the mouth as desired.

Indicated for children.

js, etc

s No special storage

of 100 and 500 tablets.

68/5004.

erosol canister contains

1000 units

1000 units

1000 units

110 g

sterile.

Indicated for the prevention and treatment of surgery, at any stage of

absorbed from broken or abraded skin. It should not be used on large areas of skin due to burns, sunburn, inflammatory dermatoses, or pruritis and minor skin

in, bacitracin and polymyxin B. It provides an almost complete barrier against the common pathogenic bacteria and infected skin. It is non-toxic and non-touch application; it is indicated during manufacture of spray which is evenly

Neomycin is a broad-spectrum antibiotic, primarily bactericidal rather than bacteriostatic. It is not inactivated by pus, exudates, gastro-intestinal secretions, bacterial growth products or enzymes. Hypersensitivity reactions are uncommon.

Bacitracin is effective against most Gram-positive organisms. However, it is not destroyed by Gram-negative bacteria and can be of value in the control of mixed infections.

Polymyxin B is selectively bactericidal to Gram-negative bacteria (particularly *Pseudomonas aeruginosa*, *Escherichia coli*, *Aerobacter aerogenes*, *Haemophilus influenzae*, Friedlander's bacillus and the dysentery group) but exerts no action on *Proteus*. Topical applications of polymyxin B have been found effective in the prophylaxis and treatment of infection in granulating surfaces.

Dosage and administration *Directions for use:* The canister should be shaken before and between applications, and held six to nine inches from the skin.

The spray should be applied sparingly to cover the affected area and should be kept clear of the eyes.

Important: During use, the canister should not be inverted or inclined at an angle greater than 45°.

Application of Tribiotic Spray should be limited in adults to a maximum of one canister per day for no more than seven days. Patients with renal impairment are particularly vulnerable to neomycin ototoxicity and the dose should be appropriately reduced.

Dosage should not exceed 15 mg neomycin/kg body weight/day in children. Each 1 second spray contains approximately 15 mg neomycin.

Greater caution should be exercised when treating infants.

Occasionally, blockage may occur from agglomeration of the powder in the outlet of the actuating button. This can easily be cleared with a sterile hypodermic needle (No. 15-17).

Use in pregnancy: Due to lack of sufficient information, the product should not be administered during the first trimester of pregnancy or during lactation unless the clinical need outweighs the possible risk.

Contra-indications, warnings, etc

Contra-indications: Because of the risk of systemic absorption Tribiotic Spray is not recommended for the treatment of burns. The only other contra-indication is allergic sensitivity to one or more of the constituents.

Precautions: The quantity of neomycin absorbed after topical administration is usually small. However, if high doses are applied, sufficient absorption can occur to cause permanent loss of hearing; the maximum recommended dose should not therefore be exceeded. Nephrotoxicity, resulting in ototoxicity may also occur. Care should be taken in patients with a hearing loss.

The concurrent use with other aminoglycoside antibiotics is not recommended and caution should be exercised in case of cross hypersensitivity to other aminoglycoside antibiotics.

The possibility of resistant organisms should be considered.

Neomycin has inherent neuromuscular blocking activity and may potentiate the action of similar agents, causing respiratory depression.

Overdosage: Overdosage only occurs with chronic use rather than acute.

Pharmaceutical precautions

Storage: Store in a cool place. The shelf-life of Tribiotic Spray is three years.

Container: As the Tribiotic Spray canister is pressurised, it should not be punctured, incinerated or exposed to heat, including the sun, even when empty.

Legal category POM.

Package quantities Canister of 110 g.

Further information Nil.

Product licence number 0068/5075.

VERILOID*

Presentation Veriloid contains standardised alkaloids of *Veratrum viride* equivalent to 2 mg of 100% potency material. The tablets are yellow, circular, bi-convex, 6.4 mm diameter, a break line on one side and 'RIKER' on the other.

Uses Veriloid is an oral antihypertensive preparation and is indicated in moderate to severe hypertension.

The main pharmacological action of the *Veratrum viride* alkaloids is the antihypertensive effect accompanied by bradycardia. This is brought about by inhibition of the vasomotor centre and stimulation of the vagus. Veriloid does not affect ganglionic or adrenergic responses. Heart, kidney and liver functions are unimpaired.

Dosage and administration 9–15 mg daily doses, at intervals of six to eight hours.

Veriloid is not recommended for children.

Contra-indications, warnings, etc

Side-effects: Postural hypotension, gastric distress or emesis may result from high doses of Veriloid.

Contra-indications: Veriloid is contra-indicated in patients receiving quinidine.

Overdosage: Serious overdosage with Veriloid because vomiting usually occurs before toxic effects are reached.

Symptoms include substernal and epigastric severe nausea and vomiting, cold sweats, shallow respiration and vertigo.

Treatment: The stomach should be emptied by vomiting and lavage with warm water.

Excessive hypotension with bradycardia and arrhythmias may be treated by intramuscular injection of 500 mcg atropine sulphate. The patient should be kept warm with the feet raised.

Pharmaceutical precautions No special precautions are required.

Legal category POM.

Package quantities Bottles of 100 tablets.

Further information Nil.

Product licence number 0068/5063.

*Trade Mark

A. H. Robins Company Limited
Redkiln Way
Horsham
West Sussex RH13 5QP

A·H·ROBINS

ALLBEE* WITH C
ALLBEE* WITH C ELIXIR

'resentation *Allbee with C*: Yellow and green, size 1 capsule monogrammed AHR in black:

thiamine Mononitrate USP	15.0 mg
riboflavine PhEur	10.0 mg
pyridoxine Hydrochloride PhEur	5.0 mg
nicotinamide PhEur	50.0 mg
calcium Pantothenate PhEur	10.0 mg
ascorbic Acid PhEur	300.0 mg

Allbee with C Elixir: Citrus-flavoured, yellow-coloured liquid: each 5 ml contains:

thiamine Mononitrate USP	6.0 mg
riboflavine Phosphate (sodium salt) BPC	4.0 mg
pyridoxine Hydrochloride PhEur	2.0 mg
nicotinamide PhEur	20.0 mg
ascorbic Acid PhEur	120.0 mg

Uses Vitamin B and C deficiencies.

Dosage and administration *Oral*: Allbee with C capsules:

Adults: 1 to 3 capsules daily.

Children: 1 capsule daily.

Allbee with C Elixir:

Adults: 5 to 10 ml two or three times daily.

Children: 5 to 10 ml daily.

Contra-indications, warnings, etc When Allbee with C is co-prescribed with levodopa, care should be exercised as the pyridoxine may antagonise the therapy. Yellow colouration of urine is normal on recommended dosage.

Pharmaceutical precautions Store in a dry place.

Legal category GSL.

Package quantities

Capsules: Bottles of 100 and 500 capsules

Elixir: Bottles of 500 ml

Further information Allbee with C Elixir contains ethanol (96%) 5.0% v/v.

Product licence numbers

Capsules 0100/5001

Elixir 0100/0044

DIMOTANE* L.A.
DIMOTANE* TABLETS
DIMOTANE* ELIXIR

'resentation *Dimotane L.A.*: Sugar-coated, peach-coloured tablet monogrammed AHR in black. Each tablet contains Brompheniramine Maleate USP 12.0 mg (one-third of active ingredient in coating for immediate release; two-thirds of active ingredient in delayed-release core).

Dimotane Tablets: Scored, peach-coloured compressed tablet stamped AHR. Each tablet contains Brompheniramine Maleate USP 4.0 mg.

Dimotane Elixir: Cola-flavoured, pale yellow-green-coloured liquid. Each 5 ml contains Brompheniramine Maleate USP 2.0 mg.

Uses Antihistaminic in the treatment of allergic conditions and reactions such as hay fever and urticaria.

Dosage and administration *Oral*: Dimotane L.A:

Adults: 1 to 2 tablets night and morning.

Children: 6–12 years: 1 tablet at night on retiring, a further tablet may be taken in the morning if necessary.

Dimotane tablets:

Adults: 1 to 2 tablets three or four times daily.

Children: 6–12 years: $\frac{1}{2}$ to 1 tablet three or four times daily.

Dimotane Elixir:

Adults: 10 to 20 ml three or four times daily.

Children: 6–12 years: 5 to 10 ml three or four times daily.

3–6 years: 5 ml three or four times daily.

Under 3 years: 0.4–1 mg/kg per 24 hours in four divided doses or at the discretion of the physician.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to the active ingredients. Coma or pre-coma states. Known brain damage or epilepsy.

Precautions and warnings: Drowsiness may occur. Patients receiving Dimotane should not drive nor operate machinery unless it has been shown that their physical and mental capacity remains unaffected. May potentiate the effects of CNS depressants including alcohol. The effects of anti-cholinergic drugs may also be potentiated. May act as a cerebral stimulant in children and occasionally in adults. If this occurs, it is possible that insomnia, nervousness, hyperpyrexia and tremors may occur and, very rarely, epileptiform convulsions. Therefore children taking Dimotane should not be left unattended for long periods. This product should not be used during pregnancy unless considered essential by the physician.

Treatment of overdose: Gastric lavage together with appropriate supportive therapy dependent upon individual response to the various constituents of the preparation.

Pharmaceutical precautions Protect from light.

Legal category P.

Package quantities

Dimotane L.A.: Bottles of 100 and 500 tablets

Dimotane: Bottles of 100 tablets

Dimotane Elixir: Bottles of 500 ml

Further information

Dimotane Elixir contains Ethanol (96%) BP 3.2% v/v.
Dimotane Tablets, Dimotane LA and Dimotane Elixir are tartrazine free. These products contain the following quantities of sucrose:

Dimotane LA: 132 mg per tablet

Dimotane Tablets: No sucrose

Dimotane Elixir: 2050 mg per 5 ml.

Product licence numbers

Dimotane Tablets 0100/5004

Dimotane Elixir 0100/5005

Dimotane LA 0100/5006

DIMOTANE* EXPECTORANT

Presentation Raspberry-flavoured, pale pink-coloured liquid. Each 5 ml contains:

Guaiphenesin BPC	100.0 mg
Phenylephrine Hydrochloride BP	5.0 mg
Phenylpropanolamine Hydrochloride BP	5.0 mg
Brompheniramine Maleate USP	2.0 mg

Uses Treatment of cough to facilitate expectoration. Dimotane Expectorant has been formulated to combine the expectorant properties of guaiphenesin together with decongestants, and an antihistamine.

Dosage and administration Oral:

Adults: 5 to 10 ml three or four times daily.

Children: 6–12 years: 5 ml three or four times daily

3–6 years: 2.5 to 5 ml three or four times daily

Under 3 years: At the discretion of the physician.

Suggested dosage 1.0 to 2.5 ml three or four times daily.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to the active ingredients. Coma or pre-coma states. Known brain damage or epilepsy. Use in patients with acute ischaemic heart disease, thyrotoxicosis, glaucoma, or urinary retention. Patients currently receiving, or who have within two weeks received, monoamine oxidase inhibitors or tricyclic antidepressants. Patients receiving other sympathomimetic drugs.

Precautions and warnings: Drowsiness may occur. Patients receiving Dimotane Expectorant should not drive nor operate machinery unless it has been shown that their physical and mental capability remains unaffected. May potentiate the effects of CNS depressants including alcohol. The effects of anticholinergic drugs may also be potentiated. May act as a cerebral stimulant in children and occasionally in adults. If this occurs it is possible that insomnia, nervousness, hyperpyrexia or tremor may occur and, very rarely, epileptiform convulsions. Therefore children taking Dimotane Expectorant should not be left unattended for long periods. Should be used with caution in patients receiving digitalis, adrenergic blockers or anti-hypertensive agents. This product should not be used during pregnancy unless considered essential by the physician.

Treatment of overdose: Gastric lavage together with appropriate supportive therapy dependent upon individual response to the various constituents of the preparation.

Pharmaceutical precautions Avoid prolonged storage at low temperatures.

Legal category P.

Package quantities Bottles of 500 ml and 2 litres.

Further information Recommended diluent: Syrup BP.

Dimotane Expectorant contains: Ethanol (96%) BP 3.6% v/v.

This product contains 2500 mg sucrose per 5 ml.

Product licence number 0100/5007.

DIMOTANE* EXPECTORANT DC

Presentation Raspberry-flavoured, bright pink-coloured liquid. Each 5 ml contains:

Guaiphenesin BPC	100.0 mg
Phenylephrine Hydrochloride BP	5.0 mg
Phenylpropanolamine Hydrochloride BP	5.0 mg
Brompheniramine Maleate USP	2.0 mg
Hydrocodone Bitartrate USP	1.8 mg

Uses Treatment of severe cough. In Dimotane Expectorant DC the antitussive effect of hydrocodone bitartrate is included to control the harsh irritating cough, whilst the expectorant action of guaiphenesin together with decongestants aids the removal of bronchial debris. The antihistamine brompheniramine maleate controls any associated allergy.

Dosage and administration Oral:

Adults: 5 to 10 ml three or four times daily

Children – 6–12 years: 5 ml three or four times daily

3–6 years: 2.5 to 5 ml three or four times daily

1–3 years: At the discretion of the physician. Suggested dosage 1.0 to 2.5 ml three or four times daily.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to the active ingredients. Coma or pre-coma states. Known brain damage or epilepsy. Use in patients with acute ischaemic heart disease, thyrotoxicosis, glaucoma, or urinary retention. Patients currently receiving, or who have within two weeks received, monoamine oxidase inhibitors or tricyclic antidepressants. Patients receiving other sympathomimetic drugs.

Precautions and warnings: Drowsiness may occur. Patients receiving Dimotane Expectorant DC should not drive nor operate machinery unless it has been shown that their physical and mental capability remains unaffected. May potentiate the effects of CNS depressant including alcohol. The effects of anticholinergic drug may also be potentiated. May act as a cerebral stimulant in children and occasionally in adults. If this occurs it is possible that insomnia, nervousness, hyperpyrexia or tremor may occur and very rarely epileptiform convulsions. Therefore children taking Dimotane Expectorant DC should not be left unattended for long periods. Should be used with caution in patients receiving digitalis, adrenergic blockers or anti-hypertensive agents. Prolonged use of this product may induce dependence. This product should not be used during pregnancy unless considered essential by the physician.

Treatment of overdose: Gastric lavage together with appropriate supportive therapy dependent upon individual response to the various constituents of the preparation.

Pharmaceutical precautions Avoid prolonged storage at low temperatures.

gal category POM, MDA.

ckage quantities Bottles of 500 ml.

irther information Dimotane Expectorant DC con-
ns: Ethanol (96%) BP 3.6% v/v.

commended diluent: Syrup BP. This product contains
75 mg sucrose and 1667 mg glucose per 5 ml.

oduct licence number 0100/5008.

MOTANE* WITH CODEINE MOTANE* WITH CODEINE PAEDIATRIC

esentation *Dimotane with Codeine:* Raspberry-
voured, bright pink-coloured liquid. Each 5 ml
ntains:

iaiphenesin BPC	100.0 mg
enylephrine Hydrochloride BP	5.0 mg
enylpropanolamine Hydrochloride BP	5.0 mg
ompheniramine Maleate USP	2.0 mg
deine Phosphate PhEur	10.0 mg

motane with Codeine Paediatric: Raspberry-fla-
ured, bright pink-coloured liquid. Each 5 ml contains:

iaiphenesin BPC	50.0 mg
enylephrine Hydrochloride BP	2.5 mg
enylpropanolamine Hydrochloride BP	2.5 mg
ompheniramine Maleate USP	1.0 mg
deine Phosphate PhEur	3.0 mg

ies For cough associated with colds and other similar
nditions of the upper respiratory tract. Dimotane with
deine and Dimotane with Codeine Paediatric have
en formulated to combine the expectorant properties
guaiphenesin together with decongestants and an
tihistamine. Codeine phosphate has been included in
e formulation to ensure control of irritating cough.

osage and administration *Oral: Dimotane with
deine:*

lults: 5 to 10 ml four times daily

ildren – 6–12 years: 5 ml four times daily

Under 6 years: At the discretion of the physician.
motane with Codeine Paediatric is recommended.

motane with Codeine Paediatric:

ildren – 6–12 years: 5 to 10 ml four times daily

3–5 years: 5 ml four times daily

1–3 years: Dose at the discretion of the physician.
ggested dosage 2.5 to 5.0 ml four times daily.

Under 1 year: Not to be used.

ontra-indications, warnings, etc

ontra-indications: Hypersensitivity to the active ingre-
nts. Coma or pre-coma states. Known brain damage
epilepsy. Use in patients with acute ischaemic heart
ease, thyrotoxicosis, glaucoma, or urinary retention.
tients currently receiving, or who have within two
eks received, monoamine oxidase inhibitors or tri-
clic antidepressants. Patients receiving other sym-
thomimetic drugs.

ecautions and warnings: Codeine is a narcotic anal-
sic. Drowsiness may occur. Patients receiving Dimo-
ne with Codeine should not drive nor operate machin-
/ unless it has been shown that their physical and
ental capability remains unaffected. May potentiate
e effects of CNS depressants including alcohol. The
ects of anticholinergic drugs may also be potentiated.

May act as a cerebral stimulant in children and occa-
sionally in adults. If this occurs it is possible that
insomnia, nervousness, hyperpyrexia or tremor may
occur and very rarely epileptiform convulsions. Therefore
children taking Dimotane with Codeine should not be
left unattended for long periods. Should be used with
caution in patients receiving digitalis, adrenergic blockers
or anti-hypertensive agents. This product should not be
used during pregnancy unless considered essential by
the physician.

Treatment of overdosage: Gastric lavage together with
appropriate supportive therapy dependent upon individ-
ual response to the various constituents of the
preparation.

Pharmaceutical precautions Avoid prolonged stor-
age at low temperatures.

Legal category P.

Package quantities Bottles of 500 ml and 2 litres.

Further information *Recommended diluent:* Syrup
BP.

Dimotane with Codeine contains: Ethanol (96%) BP
3.6% v/v.

This product contains 825 mg sucrose and 1,000 mg
glucose per 5 ml.

Dimotane with Codeine Paediatric contains: Ethanol
(96%) BP 3.6% v/v.

This product contains 2,750 mg sucrose per 5 ml.

Product licence numbers

Dimotane with Codeine	0100/0042
Dimotane with Codeine Paediatric	0100/0046

DIMOTAPP* LA DIMOTAPP* ELIXIR DIMOTAPP* ELIXIR PAEDIATRIC

Presentation *Dimotapp LA:* Sugar-coated, choco-
late-coloured tablet monogrammed AHR in white. Each
tablet contains:

Brompheniramine Maleate USP	12.0 mg
Phenylephrine Hydrochloride BP	15.0 mg
Phenylpropanolamine Hydrochloride BP	15.0 mg

(one-third of active ingredients in coating for immediate
release; two-thirds of active ingredients in delayed-
release core).

Dimotapp Elixir: Grape-flavoured, pale red-brown col-
oured liquid. Each 5 ml contains:

Brompheniramine Maleate USP	4.0 mg
Phenylephrine Hydrochloride BP	5.0 mg
Phenylpropanolamine Hydrochloride BP	5.0 mg

Dimotapp Elixir Paediatric: Grape-flavoured, pale red-
brown coloured liquid. Each 5 ml contains:

Brompheniramine Maleate USP	1.0 mg
Phenylephrine Hydrochloride BP	2.5 mg
Phenylpropanolamine Hydrochloride BP	2.5 mg

Uses Anti-histaminic, nasal decongestant in the man-
agement of upper respiratory tract disorders, including
congestion, hypersecretion, rhinitis and sinusitis.

Dosage and administration *Oral:*

Dimotapp LA:

Adults: 1 to 2 tablets night and morning.

Dimotapp Elixir:

Adults: 5 to 10 ml three or four times daily

Children – 6–12 years: 5 ml three or four times daily
2–6 years: 2.5 ml to 5 ml three or four times daily.

Dimotapp Elixir Paediatric:

Children – 6–12 years: 10 ml three or four times daily
2–6 years: 2.5 to 10 ml three or four times daily

Under 2 years: At discretion of physician. Suggested dosage 2.5 ml three or four times daily.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to the active ingredients. Coma or pre-coma states. Known brain damage or epilepsy. Use in patients with acute ischaemic heart disease, thyrotoxicosis, glaucoma, or urinary retention. Patients currently receiving, or who have within two weeks received, monoamine oxidase inhibitors or tricyclic antidepressants. Patients receiving other sympathomimetic drugs. Dimotapp L.A. contains 3.0 mg of wheat flour per tablet and should be avoided by patients requiring a wheat-gluten-free diet (coeliac disease, dermatitis herpetiformis).

Precautions and warnings: Drowsiness may occur. Patients receiving Dimotapp should not drive nor operate machinery unless it has been shown that their physical and mental capability remains unaffected. May potentiate the effects of CNS depressants including alcohol. The effects of anticholinergic drugs may also be potentiated. May act as a cerebral stimulant in children and occasionally in adults. If this occurs it is possible that insomnia, nervousness, hyperpyrexia or tremor may occur and very rarely epileptiform convulsions. Therefore children taking Dimotapp should not be left unattended for long periods. Should be used with caution in patients receiving digitalis, adrenergic blockers or anti-hypertensive agents. This product should not be used during pregnancy unless considered essential by the physician.

Treatment of overdose: Gastric lavage together with appropriate supportive therapy dependent upon individual response to the various constituents of the preparation.

Pharmaceutical precautions Discolouration of tablets may occur when exposed to prolonged strong sunlight.

Legal category P.

Package quantities *Dimotapp L.A.*: Bottles of 100 and 500 tablets

Dimotapp Elixir: Bottles of 500 ml and 2 litres

Dimotapp Elixir Paediatric: Bottles of 500 ml

Further information Dimotapp Elixir and Dimotapp Elixir Paediatric contain Ethanol (96%) BP 2.5% v/v, Dimotapp L.A. contains sucrose 135 mg per tablet. The recommended diluent is Syrup BP.

Dimotapp offers the advantages of controlling the congestion and hypersecretion associated with sinusitis and rhinitis. The combination of phenylephrine hydrochloride and phenylpropanolamine hydrochloride in the formulations means that the problem of overdrying and rebound congestion is avoided, thus allowing the mucosa to return to its normal moist state.

Product licence numbers

Dimotapp L.A.	0100/5009
Dimotapp Elixir	0100/5010
Dimotapp Elixir Paediatric	0100/0063

DIMOTAPP* P ▼

Presentation A white, round, flat bevelled edge tablet embossed **AHR** containing:
 DPP

Brompheniramine Maleate USP	2.0 mg
Phenylephrine Hydrochloride BP	5.0 mg
Phenylpropanolamine Hydrochloride BP	5.0 mg
Paracetamol PhEur	325.0 mg

Uses Analgesic antihistaminic nasal decongestant the management of upper respiratory tract disorder such as sinusitis and rhinitis with associated pain.

Dosage and administration Oral:

Adults: 1 to 2 tablets three times daily.

Children: 6–12 years $\frac{1}{2}$ to 1 tablet three times daily

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to the active ingredients. Coma or pre-coma states. Known brain damage or epilepsy. Use in patients with acute ischaemic heart disease, thyrotoxicosis, glaucoma, or urinary retention. Patients currently receiving, or who have within two weeks received, monoamine oxidase inhibitors or tricyclic antidepressants. Patients receiving other sympathomimetic drugs.

Precautions and warnings: Drowsiness may occur. Patients receiving Dimotapp P should not drive nor operate machinery unless it has been shown that the physical and mental capability remains unaffected. May potentiate the effects of CNS depressants including alcohol. The effects of anticholinergic drugs may also be potentiated. May act as a cerebral stimulant in children and occasionally in adults. If this occurs it is possible that insomnia, nervousness, hyperpyrexia or tremor may occur and very rarely epileptiform convulsions. Therefore children taking Dimotapp P should not be left unattended for long periods. Should be used with caution in patients receiving digitalis, adrenergic blockers, or anti-hypertensive agents. This product should not be used during pregnancy unless considered essential by the physician.

Treatment of overdose: Gastric lavage together with appropriate supportive therapy dependent upon individual response to the various constituents of the preparation. Dimotapp P contains paracetamol. N-acetylcysteine I.V. or L-methionine orally should be administered as soon as possible following overdose.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Bottles of 100 and 500 tablets

Further information Dimotapp P offers the advantages of controlling the congestion and hypersecretion associated with sinusitis and rhinitis whilst at the same time controlling associated pain. The combination of phenylephrine hydrochloride and phenylpropanolamine hydrochloride in the formulation means that the problem of overdrying and rebound congestion is avoided, thus allowing the mucosa to return to its normal moist state.

Product licence number 0100/0057.

DOPRAM* INFUSION DOPRAM* INJECTION

Presentation *Dopram Infusion*: Clear colourless solution. Each 500 ml bottle contains:

oxapram Hydrochloride USP 2 mg per ml in 5%
Dextrose Injection BP.

opram Injection: Clear colourless solution. Each 5 ml
ampoule contains:

oxapram Hydrochloride USP 20 mg per ml

uses Respiratory stimulant.

acute respiratory failure: Dopram prevents and reverses
apnoea during administration of oxygen.

Following anaesthesia: Dopram reduces the incidence
of postoperative chest complications, and increases the
rate of recovery from inhalational anaesthesia. In addition
Dopram reduces respiratory depression associated with
analgesic therapy. Dopram aids the differential diagnosis
of postoperative apnoea.

dosage and administration For intravenous use
only. There is no recommended dosage schedule for
children.

For the treatment of respiratory failure: 0.5 mg per
minute to 4.0 mg per minute of Dopram Infusion
dependent upon the condition and response of the
patient. Whenever possible the condition of the patient
should be monitored by frequent measurement of blood
gas tensions.

Following anaesthesia: Usual dosage 1.0–1.5 mg/kg
body weight of Dopram Injection which may be repeated
at one hour intervals. Alternatively, Dopram Infusion
may be given at a rate of 2–3 mg per minute. Appropriate
adjustments to the administration rate should be made
according to the response of the patient.

opram Infusion: (a) Treatment of respiratory failure. To
prevent or reverse the depression of ventilation which
occurs in some hypoxic patients during oxygen
administration.

(b) Following anaesthesia. To stimulate ventilation in
the post operative period as an aid to the reduction of
post operative pulmonary complications.

To permit the use of effective doses of narcotic
analgesics without associated problems of respiratory
depression.

opram Injection: Following anaesthesia. To stimulate
ventilation in the post operative period as an aid to the
reduction of post operative pulmonary complications.

To permit the use of effective doses of narcotic
analgesics without associated problems of respiratory
depression.

To aid differential diagnosis and treatment of post
operative apnoea.

To increase the rate of recovery from anaesthesia
when this would be beneficial.

contra-indications, warnings, etc

contra-indications: Severe hypertension, status asth-
maticus, coronary artery disease, thyrotoxicosis.

precautions and warnings: Dopram should be adminis-
tered concurrently with oxygen to patients with severe
reversible airways obstruction or severely decreased
lung compliance, due to the increased work of breathing
in these patients. Although Dopram has been adminis-
tered safely to patients suffering from epilepsy, great care
should be employed when such patients are treated with
Dopram. Clinical data suggest that there may be
interaction between doxapram and aminophylline which
manifested by agitation and increased skeletal muscle
activity. Care should thus be taken when these two
drugs are used concomitantly. Dopram should also be
administered with great care to patients being treated

concurrently with monoamine oxidase inhibitors. Animal
studies have shown that the action of doxapram, in
common with a large number of drugs, is potentiated
after pre-treatment with a monoamine oxidase inhibitor.

In patients presenting with bronchoconstriction, Do-
pram should always be used in conjunction with
bronchodilator drugs in order to reduce the amount of
respiratory effort. Although studies in rats and rabbits
have not revealed any teratogenic effects of doxapram,
absolute safety in human pregnancy has not yet been
confirmed.

On recommended dosage a moderate increase in
blood pressure, a slight increase in heart rate, dizziness
and perineal warmth have been reported. Other side-
effects have been reported in the post anaesthetic period
but these are also commonly observed during recovery
from anaesthesia, and include muscle fasciculation,
hyperactivity, sweating, confusion, cough, dyspnoea,
laryngospasm, bronchospasm, sinus tachycardia, bra-
dycardia, extrasystoles, nausea and/or vomiting and
salivation.

Treatment of overdosage: Gross overdosage may result
in hypertension, tachycardia, and increased skeletal
muscle activity. The hypertension may be treated with
an appropriate α -adrenergic blocking agent and the
increase in skeletal muscle activity controlled with
intravenous barbiturates.

Pharmaceutical precautions Dopram is incompati-
ble with alkaline solutions such as aminophylline,
frusemide and thiopentone sodium. Store at room
temperature. Do not refrigerate Dopram Injection.

Legal category POM.

Package quantities

Dopram Infusion: Pack of 4 bottles each containing
500 ml

Dopram Injection: Pack of 5 ampoules each contain-
ing 5 ml

Further information The principal pharmacological
action of Dopram is an increase in minute volume
produced primarily by an increase in tidal volume and to
a lesser extent by changes in respiratory rate. Neuro-
pharmacological studies have shown that the primary
sites of action of Dopram are the peripheral chemore-
ceptors. It is considered that this site of action of Dopram
is responsible for its relative specificity of action: it is
only following large doses of Doxapram Hydrochloride
that non-specific central nervous system stimulation
occurs.

Product licence numbers

Dopram Infusion: 0100/5019

Dopram Injection: 0100/5018

FEAC* ▼

Presentation A two-layered biconvex tablet, film-
coated vermilion and monogrammed FEAC in white.
Each tablet contains:

Ascorbic Acid PhEur	150.0 mg
Nicotinamide PhEur	25.0 mg
Pyridoxine Hydrochloride PhEur	2.5 mg
Riboflavin PhEur	5.0 mg
Thiamine Mononitrate USP	7.5 mg

Dried Ferrous Sulphate BP 150.0 mg
(Equivalent to 45 mg elemental iron)

The vitamin constituents are contained in one layer in an immediate release form; the ferrous sulphate is contained in the controlled-release layer.

Uses For the treatment and prevention of iron deficiency anaemia accompanied by vitamin B and C deficiencies.

Dosage and administration *Oral:*

Adults: 1 tablet twice daily.

Contra-indications, warnings, etc

Contra-indications: There are no contra-indications.

Precautions and warnings: When FEAC is co-prescribed with levodopa, care should be exercised as the pyridoxine may antagonise the therapy. Iron chelates with tetracyclines and may impair absorption of both agents. Yellow colouration of urine is normal on recommended dosage. Nausea, gastrointestinal irritation and constipation may occasionally occur.

Treatment of overdosage: In the event of overdosage in adults (or children) 2 g desferrioxamine in water for injection should be given intra-muscularly and the stomach washed out with a 1% solution of sodium bicarbonate. 5 g desferrioxamine in 50–100 ml water should then be given by mouth or stomach tube preventing further absorption of iron.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Bottles of 100 tablets.

Further information Nil.

Product licence number 0100/0049.

RHEUMOX* 600 RHEUMOX* CAPSULES

Presentation *Rheumox 600 Tablets:* Pale orange, film-coated, capsule shaped tablets both sides scored with a breakline and one side printed RHEUMOX 600, containing Azapropazone Dihydrate 600 mg.

Rheumox Capsules: Two-tone orange size 1 capsule, monogrammed AHR Rheumox containing Azapropazone Dihydrate 300 mg.

Uses Rheumox is a non-steroidal anti-inflammatory analgesic agent indicated in the treatment of rheumatoid arthritis, ankylosing spondylitis, osteoarthritis and painful musculoskeletal conditions. Rheumox is also indicated in attacks of acute gouty arthritis and in the long term prophylaxis of gout and the control of hyperuricaemia.

Dosage and administration Rheumatoid arthritis, ankylosing spondylitis, osteoarthritis and painful musculoskeletal conditions.

Rheumox 600 Tablets: Oral – One 600 mg tablet night and morning.

Rheumox Capsules: Oral – One 300 mg capsule four times daily or two 300 mg capsules night and morning.

Older patients: Azapropazone is principally excreted unchanged by the kidney. In patients over 65 whose renal function may be reduced, it is therefore suggested that the starting dose be 300 mg in the morning and 600 mg to be taken last thing at night. In patients much

older than this, a suitable starting regimen is 600 mg night or 300 mg twice daily. This dosage can be subsequently adjusted since some elderly patients have excellent renal function.

Acute gout: 2,400 mg in divided doses during the first 24 hours followed by 1,800 mg per day until the attack is resolving after which 1,200 mg per day is used until symptoms have disappeared.

Chronic gout: Azapropazone reduces serum urate levels by enhancing urate excretion. The usual dosage for this purpose is 600 mg night and morning (either Rheumox 600 or Rheumox Capsules may be used). In patients over 65 the dosage should be 900 mg daily as described above and in some cases this may be reduced to 600 mg daily provided that adequate control of gouty symptoms and serum urate are maintained.

Paediatric dosage has not yet been established.

Contra-indications, warnings, etc

Contra-indications: Rheumox increases the plasma concentration of phenytoin and should not be given to patients taking this drug.

Rheumox potentiates the action of warfarin in many patients and should not be used with this or other oral anticoagulants. If it is essential that Rheumox be given to a patient already taking an oral anticoagulant, the dosage should not be done until the dose of the anticoagulant has been reduced to a very low level. Rheumox can then be introduced and the dose of the anticoagulant increased until the required effect is produced. Prothrombin determinations should be carried out daily throughout this procedure. Rheumox is not recommended in the presence of a peptic ulcer or where there is a history of blood dyscrasia. Patients on long term treatment should be regularly reviewed.

Precautions and warnings: Patients with a history of peptic ulcer have been treated safely with Rheumox but in this situation constant supervision is recommended. In some, ulceration may recur. Data at present available does not indicate that interaction occurs with drugs such as sulphonamides and oral hypoglycaemic agents but adjustments of the dosage of these drugs may be necessary in some instances.

Specific renal function tests in man and long term administration to animals have not revealed any adverse effects of Rheumox on the kidney but since its clearance is predominantly renal it is not recommended for use in patients with overt renal dysfunction. Animal reproduction studies did not result in foetal abnormalities but safety in human pregnancy cannot be assumed and its use should be avoided in pregnancy whenever possible.

Skin rashes occur occasionally and a proportion of these are photo-allergic reactions. Fluid retention and gastro-intestinal upsets also occur occasionally. Gastrointestinal bleeding has been reported as has angio-neurotic oedema.

Treatment of overdosage: If overdosage should occur two specific courses of action are suggested on theoretical grounds. Firstly, since Rheumox is poorly soluble in gastric juice, stomach lavage should recover any gastric residue of the drug, provided of course that it is done early enough.

Secondly, since Rheumox is predominantly excreted unchanged by the kidney, forced alkaline diuresis is theoretically indicated.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities *Rheumox 600 Tablets*: Amber glass bottles of 100 and 500 tablets.

heumox Capsules: Amber glass bottles of 100 and 500 capsules.

Further information Nil.

Product licence numbers

heumox 600 Tablets: 0100/0059

heumox Capsules: 0100/0037

OBAXIN* 750

Presentation Scored white compressed capsule-shaped tablet embossed AHR containing:

methocarbamol USP 750 mg.

Uses Treatment of skeletal muscle spasm.

Dosage and administration *Oral*:

Adults: 2 tablets four times daily.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to methocarbamol. Coma or pre-coma states. Known brain damage or epilepsy. Use in presence of tachycardia, glaucoma, prostatic hypertrophy or bladder neck obstruction. Myasthenia gravis.

Precautions and warnings: This product may cause drowsiness and patients receiving it should not drive nor operate machinery unless their physical and mental capability remain unaffected – especially if other medication capable of causing drowsiness is also being taken. This product may potentiate the effects of other central nervous system depressants and stimulants including alcohol, barbiturates, anaesthetics and appetite suppressants.

The effects of anti-cholinergics, e.g. atropine and some psychotropic drugs may be potentiated by methocarbamol.

Robaxin may give rise to manifestations of allergy including skin rash, urticaria and angioneurotic oedema. This product may very rarely give rise to restlessness, anxiety, vertigo, tremor, confusion and convulsions. Lightheadedness and dizziness have been reported. Nausea and vomiting have also been reported during use of Robaxin.

In accordance with established medical practice this product should not be used during pregnancy unless considered essential by the physician.

Treatment of overdosage: Gastric lavage with appropriate supportive therapy for 24 hours as methocarbamol is excreted within that time.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Bottles of 100 tablets.

Further information Nil.

Product licence number 0100/5026.

OBAXIN* INJECTABLE

Presentation 10 ml sterile ampoules each containing:

methocarbamol USP 1.0 g

Vehicle 50% aqueous polyethylene glycol 300.

Uses Treatment of acute skeletal muscle spasm.

Dosage and administration 10–30 ml dependent on the severity of the condition and therapeutic response. Should not exceed 30 ml per day for more than three consecutive days, except in the treatment of tetanus.

Rate of administration:

Intravenous: Administer by slow intravenous injection or infusion directly into the vein at a maximum rate of 3 ml per minute.

Intramuscular: Not more than 5 ml into each gluteal region.

Diluent: May be added to an intravenous drip of sterile isotonic saline, or sterile 5% dextrose. Dilution should not be greater than 10 ml per 250 ml.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to methocarbamol. Coma or pre-coma states. Known brain damage or epilepsy. Use in presence of tachycardia, glaucoma, prostatic hypertrophy or bladder neck obstruction. Myasthenia gravis.

Precautions and warnings: This product may cause drowsiness and patients receiving it should not drive nor operate machinery unless their physical and mental capability remain unaffected – especially if other medication capable of causing drowsiness is also being taken. This product may potentiate the effects of other central nervous system depressants and stimulants including alcohol, barbiturates, anaesthetics and appetite suppressants. The effects of anti-cholinergics e.g. atropine and some psychotropic drugs may be potentiated by methocarbamol.

Robaxin may give rise to manifestations of allergy including skin rash, urticaria and angioneurotic oedema. This product may very rarely give rise to restlessness, anxiety, vertigo, tremor, confusion and convulsions. Lightheadedness and dizziness have been reported. Nausea and vomiting have also been reported during use of Robaxin.

Robaxin Injectable should be used with extreme caution in patients with impaired renal function, as the solvent used may cause raised urea levels and acidosis.

In accordance with established medical practice this product should not be used during pregnancy unless considered essential by the physician.

Treatment of overdosage: Appropriate supportive therapy for 24 hours as methocarbamol is excreted within that time.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Boxes containing 5 ampoules.

Further information Nil.

Product licence number 0100/5027.

ROBAXISAL* FORTE

Presentation A two-layer, pink and white compressed tablet scored and stamped AHR, containing:

Methocarbamol USP 400 mg

Acetylsalicylic Acid PhEur 325 mg

Uses In the management of pain and skeletal muscle spasm associated with musculoskeletal disorders such as lumbago, fibrositis, sprains, strains etc.

Dosage and administration *Oral:*

Adults: 2 tablets four times daily.

Safety in children 12 years of age and below has not been established.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to methocarbamol or aspirin. Coma or pre-coma states. Known brain damage or epilepsy. Use in presence of tachycardia, glaucoma, prostatic hypertrophy or bladder neck obstruction. Myasthenia gravis.

Precautions and warnings: This product may cause drowsiness and patients receiving it should not drive nor operate machinery unless their physical and mental capability remain unaffected – especially if other medication capable of causing drowsiness is also being taken. This product may potentiate the effects of other central nervous system depressants and stimulants including alcohol, barbiturates, anaesthetics and appetite suppressants. The effects of anti-cholinergics e.g. atropine and some psychotropic drugs may be potentiated by methocarbamol.

Robaxial Forte may give rise to manifestations of allergy including skin rash, urticaria and angioneurotic oedema. This product may very rarely give rise to restlessness, anxiety, vertigo, tremor, confusion and convulsions. Light-headedness and dizziness have been reported. Nausea and vomiting have also been reported during the use of Robaxial Forte. Patients currently on anti-coagulant therapy should have blood coagulation parameters regularly monitored.

In accordance with established medical practice this product should not be used during pregnancy unless considered essential by the physician.

Treatment of overdose: Supportive therapy for 24 hours, as methocarbamol is excreted within that time. If salicylate intoxication occurs, especially in children, the hyperpnoea may be controlled with sodium bicarbonate. Judicious use of 5% CO₂ with 95% O₂ may be of benefit. Abnormal electrolyte patterns should be corrected with appropriate fluid therapy.

Pharmaceutical precautions Nil.**Legal category** POM.

Package quantities Bottles of 100 and 500 tablets.

Further information Nil.

Product licence number 0100/5028.

ROBINUL*

Presentation Scored pink compressed tablet stamped AHR containing:

2
Glycopyrrolate USP 2.0 mg

Uses Treatment of peptic ulcer and gastro-intestinal hypermotility.

Dosage and administration *Oral:*

Adults: $\frac{1}{2}$ –2 tablets two or three times daily.

Contra-indications, warnings, etc

Contra-indications: Glaucoma and pyloric stenosis.

Precautions and warnings: Care is required when treating patients with known or suspected prostatic disease. Blurred vision, dry mouth, tachycardia, drowsiness and mild abdominal discomfort may occur. Patients receiving glycopyrrolate should not drive nor operate

machinery unless it has been shown not to affect the physical or mental ability. Do not use during pregnancy as safety in this condition has not been established. Reproduction studies in rats and rabbits revealed no teratogenic effects from glycopyrrolate. However, diminished rates of conception and of survival at weaning were observed in rats, in a dose related manner. Studies in dogs suggest that this may be due to diminished seminal secretion which is evident at high doses of glycopyrrolate. The significance of this for man is not clear.

Treatment of overdose: Gastric lavage or induced emesis is advised. Catheterisation may be necessary.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Bottles of 100 tablets.

Further information Nil.

Product licence number 0100/5029.

ROBINUL* INJECTION ▼

Presentation 3 ml and 1 ml ampoule (snap-open ampoule) of isotonic aqueous solution containing in each 1 ml:

Glycopyrrolate USP 0.2 mg

Uses *Properties:* Robinul (glycopyrrolate) is a quaternary ammonium anticholinergic agent. The quaternary ammonium moiety renders Robinul highly ionised at physiological pH and it thus penetrates the blood brain and placental barriers poorly. The effect of Robinul on secretory organs is particularly marked and prolonged, and good control of salivary and pharyngeal secretion can be obtained with doses which do not produce marked changes in heart rate. Gastric secretions are similarly, reduced by Robinul.

Indications: 1. To protect against the peripheral muscarinic actions of anticholinesterases such as neostigmine and pyridostigmine, used to reverse neuromuscular blockade produced by nondepolarising muscle relaxants.

2. As a preoperative antimuscarinic agent to reduce salivary, tracheobronchial and pharyngeal secretions and to reduce the acidity of the gastric contents.

3. As a preoperative or intra-operative antimuscarinic to attenuate or prevent intraoperative bradycardia associated with the use of suxamethonium or due to cardiac vagal reflexes.

Dosage and administration *Premedication – Adults* 0.2 mg to 0.4 mg intravenously or intramuscularly before the induction of anaesthesia. Alternatively, a dose of 0.004 to 0.005 mg/kg up to a maximum of 0.4 mg may be used. Larger doses may result in profound and prolonged antisialogogue effect which may be unpleasant for the patient.

Children: 0.004 to 0.008 mg/kg up to a maximum of 0.2 mg intravenously or intramuscularly before the induction of anaesthesia. Larger doses may result in profound and prolonged antisialogogue effect which may be unpleasant for the patient.

Intraoperative use – Adults: In those situations where intraoperative use is indicated, a single dose of 0.2 to 0.4 mg (or 0.004 to 0.005 mg/kg up to a maximum of 0.4 mg) by intravenous injection should be used. This dose may be repeated if necessary.

Children: In those situations where intraoperative use is indicated, a single dose of 0.004 to 0.008 mg/kg or up to a maximum of 0.2 mg by intravenous injection should be used. This dose may be repeated if necessary.

Reversal – Adults: 0.2 mg intravenously per 1 mg neostigmine or the equivalent dose of pyridostigmine. Alternatively, a dose of 0.01–0.015 mg/kg intravenously with 0.5 mg/kg neostigmine or equivalent dose of pyridostigmine. Robinul may be administered simultaneously on the same syringe with the anticholinesterase; greater cardiovascular stability results from this method of administration.

Children: 0.01 mg/kg intravenously with 0.05 mg/kg pyridostigmine or the equivalent dose of pyridostigmine. Robinul may be administered simultaneously on the same syringe with the anticholinesterase; greater cardiovascular stability results from this method of administration.

Contra-indications, warnings, etc

Contra-indications: Apart from established hypersensitivity to glycopyrrolate, there are no absolute contra-indications to Robinul.

Precautions and warnings: Reproduction studies in rats and rabbits revealed no teratogenic effects from glycopyrrolate. Safety in human pregnancy and lactation has not been established. However, diminished rates of conception and of survival at weaning were observed in rats, in a dose-related manner. Studies in dogs suggest that this may be due to diminished seminal secretion which is evident at high doses of glycopyrrolate. The significance of this for man is not clear.

Because of the increase in heart rate produced by the administration of anticholinergics, use with caution in patients with coronary artery disease; congestive heart failure; cardiac arrhythmias; hypertension; thyrotoxicosis. This product should be used very cautiously in pyrexial patients due to inhibition of sweating.

Large doses of quaternary ammonium anticholinergic compounds have been shown to block end plate nicotinic receptors. This should be considered before using glycopyrrolate in patients with myasthenia gravis.

It is known that the administration of anticholinergic agents during inhalation anaesthesia can result in ventricular arrhythmias.

Side-effects: Robinul may produce the following effects which are extensions of its fundamental pharmacological actions, dry mouth, difficulty in micturition, disturbances of visual accommodation, tachycardia, palpitation, inhibition of sweating.

Treatment of overdosage: Since glycopyrrolate is a quaternary ammonium agent symptoms of overdosage are peripheral rather than central in nature. To combat peripheral anticholinergic effects a quaternary ammonium anticholinesterase such as neostigmine methyl sulphate may be given in a dose of 1.0 mg for each 0.5 mg of glycopyrrolate known to have been administered by the parenteral route.

Pharmaceutical precautions Robinul Injection has been shown to be physically compatible with the following agents commonly used in anaesthetic practice: fluorophanol, Lorazepam, Droperidol and Fentanyl Citrate, Levorphanol Tartrate, Pethidine Hydrochloride, Morphine Sulphate, Neostigmine, Promethazine and Pyridostigmine.

Robinul Injection has been shown to be physically compatible with the following agents commonly used in anaesthetic practice:

Diazepam, Dimenhydrinate, Methohexitone Sodium, Pentazocine, Pentobarbitone Sodium, Thiopentone Sodium.

Robinul Injection should be stored at ambient temperature.

Legal category POM.

Package quantities Packs of 10 ampoules each containing 1 ml or 3 ml.

Further information Robinul Injection has been used successfully as an adjunct to reversal by neostigmine when atropine has been used as the preoperative anticholinergic.

The use of Robinul Injection as a preoperative anticholinergic is associated with less effect on the cardiovascular system, compared to atropine.

The use of Robinul Injection as an adjunct to reversal by neostigmine of non depolarising muscle relaxants is associated with less initial tachycardia and better protection against the cholinergic effects of neostigmine compared to reversal with a mixture of neostigmine and atropine.

Product licence number 0100/0054.

ROBINUL* POWDER

Presentation A white, crystalline powder Glycopyrrolate USP

Uses Iontophoretic treatment of the plantar and palmar skin for idiopathic hyperhidrosis.

Dosage and administration A 0.05% solution in distilled water of Glycopyrrolate USP is applied to palmar or plantar skin. When treating the foot or hand sufficient solution to cover the palm or sole is placed in a non-metallic container and the anode, of sheet metal larger in area than the part being treated, is placed in the solution. The sole or palm is separated from the anode by 5 mm of plastic foam or a layer of lint or sponge sheet.

In all cases an electrical circuit is completed by placing another limb in lukewarm tap water containing the cathode, similarly shielded from direct contact with the skin.

Recommended average conditions are 90 volts DC at 10–20 mA for adults and 2–10 mA for children, for 12 minutes at each site, depending on the patient's skin tolerance, body weight and size. Only one site should be treated at a time, and only two sites in any one day. Treatments should not be repeated within seven days, but may be repeated later varying the precise conditions according to the recurrence and severity of hyperhidrosis. See also Warnings section below.

Contra-indications, warnings, etc

Contra-indications: Glaucoma. Do not use during pregnancy.

Precautions and warnings: Glycopyrrolate may cause tachycardia. Since this drug may cause drowsiness, patients receiving glycopyrrolate should not drive nor operate machinery immediately after treatment unless it has been shown not to affect their physical or mental ability. It should be used with great caution in patients with cardiovascular disease, thyrotoxicosis and obstructive disorders of the lower urinary tract. Patients with mycotic or other skin infection should not be treated.

Dryness of mouth, blurred vision and mild abdominal discomfort may occur. Exercise care in patients with

prostatic hypertrophy. Due to the effect of anti-cholinergics on mucous secretions, it is advisable not to treat people with chronic bronchitis. Occasionally difficulty in eating may occur and micturition may be temporarily affected for some hours after treatment. A mild tingling feeling may occur in the immersed areas during treatment and any recent cuts or cracks in the skin may smart when the current is increased at the start of iontophoresis. The latter can be avoided by covering the lesion with a thin smear of petroleum jelly. Avoid over-exertion especially in hot weather, until any side effects have disappeared.

The product should only be used by specialist units experienced in iontophoretic technique.

The electrodes and treated skin areas *must* be placed in non-metallic containers and separated carefully by layers of, for example, sponge or lint. Direct contact between electrodes and skin must be avoided otherwise burns may result.

The current must be very slowly increased from zero mA and decreased to zero mA at the beginning and end of the treatment period respectively to avoid any Faradic discharge between the electrode and skin on removal of the patient's limb from the container of solution. Instruct patient that contact must not be broken during treatment.

Do not use during pregnancy as safety in this condition has not been established. Reproduction studies in rats and rabbits revealed no teratogenic effects from glycopyrrolate. However, diminished rates of conception and of survival at weaning were observed in rats, in a dose related manner. Studies in dogs suggest that this may be due to diminished seminal secretion which is evident at high doses of glycopyrrolate. The significance of this for man is not clear.

Pharmaceutical precautions Robinul Power is supplied in amber-glass bottles containing 5 grams. The powder is slightly hygroscopic and the container should not be left open. For use by iontophoresis the powder should be dissolved in freshly distilled or deionised water to the recommended concentration.

Prior to use a stock solution (e.g. 0.1% or 0.5% w/v) may be made up with freshly boiled and cooled distilled or deionised water. This stock solution should be stored in a refrigerator to minimise possible microbial growth and should be kept in thoroughly clean amber-glass, capped containers. Glycopyrrolate does hydrolyse very slowly at pH 7 and room temperature and it is recommended that stock solutions be kept for no more than 14 days. Do not keep solutions once used for iontophoretic treatment. The solution must not be alkaline, otherwise the glycopyrrolate will hydrolyse more rapidly.

Legal category POM.

Package quantities Supplied in amber-glass bottles containing 5 grams Glycopyrrolate USP.

Further information Further recommendations concerning treatment are given in the package insert.

Product licence number 0100/0052.

ROBITUSSIN*

Presentation Raspberry-flavoured, dark red-coloured liquid. Each 5 ml contains:

Guaiphenesin BP 100 mg

Uses Treatment of cough.

Dosage and administration *Oral:*

Adults: 5 to 10 ml every two to three hours.

Children: 3-12 years: 5 ml every two to three hours.

Under 3 years: 2.5 to 5 ml every two to three hours.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Avoid prolonged storage at low temperatures.

Legal category P.

Package quantities Bottles of 125 ml and 500 ml.

Further information *Recommended diluent:* Syru BP.

Robitussin contains Ethanol (96%) BP 3.6% v/v.

This product contains 2,500 mg sucrose per 5 ml.

Product licence number 0100/5031.

ROBITUSSIN* AC

Presentation Raspberry-flavoured, light amber-coloured liquid. Each 5 ml contains:

Guaiphenesin BP 100.0 mg

Pheniramine Maleate BP 7.5 mg

Codeine Phosphate PhEur 10.0 mg

Uses For the relief of cough especially when associated with allergy.

Dosage and administration *Oral:*

Adults: 5 to 10 ml four times daily.

Children - 6-12 years: 5 ml four times daily.

Under 6 years: At the discretion of the physician.

Contra-indications, warnings, etc

Contra-indications: Use in patients hypersensitive to the active ingredients. Coma or pre-coma states. Known brain damage or epilepsy.

Precautions and warnings: May cause drowsiness. Patients receiving Robitussin AC should not drive or operate machinery unless it has been shown that the physical and mental capability remains unaffected. May potentiate the effects of anti-cholinergic drugs and CNS depressants including alcohol. May act as a cerebral stimulant in children and occasionally in adults. If this occurs, it is possible that insomnia, nervousness, hyperpyrexia, and tremors may occur and very rarely epileptiform convulsions. In accordance with established medical practice this product should not be used during pregnancy unless considered essential by the physician.

Treatment of overdosage: Gastric lavage in the conscious patient together with supportive therapy where necessary. Further treatment is dependent on the individual response to the various constituents of the preparation.

Pharmaceutical precautions Avoid prolonged storage at low temperatures.

Legal category P.

Package quantities Bottles of 500 ml.

Further information *Recommended diluent:* Syru BP.

Robitussin AC contains Ethanol (96%) BP 3.6% v/v.

This product contains 2,500 mg sucrose per 5 ml.

Product licence number 0100/5032.

* *Trade Mark*

Roche Products Limited
PO Box 8
Welwyn Garden City
Hertfordshire AL7 3AY



ALCOBON®

Presentation Round, white tablets with 'ROCHE' printed on one face and a single break bar on the other, containing 500 mg flucytosine.

Infusion bottles containing 2.5 g flucytosine in 250 ml aqueous saline solution. The solution is colourless to slightly yellow. A sterile-packed giving-set is supplied in each bottle.

Properties: Alcobon is a fluorinated pyrimidine effective in the treatment of certain systemic fungal infections. In fungi sensitive to the preparation it acts as competitive inhibitor of uracil metabolism. In man it is excreted largely unchanged almost entirely in the urine. Flucytosine can be removed by haemodialysis.

Indications: Alcobon is indicated for the treatment of systemic infections with *Cryptococcus neoformans*, *Candida albicans* and certain other *Candida* species, *Orulopsis glabrata*, *Hansenula* and fungi which cause chromomycosis; *Phialophora verrucosa*, *Phialophora edrosi* and *Cladosporium carrionii*.

Alcobon for Infusion is indicated only when the patient is unable to accept oral Alcobon.

Dosage and administration For severe infections the total daily oral dose in adults and children is 200 mg/kg body weight divided into 4 doses. In patients harbouring extremely sensitive organisms a total daily dose of 100–150 mg/kg body weight may be sufficient.

Alcobon for Infusion should be administered using the giving-set provided, which contains a special filter. It may be administered directly into a vein, through a central venous catheter, or by intraperitoneal infusion. The recommended dosage is the same as for oral Alcobon, the total daily dose being divided over the 24 hours. Adequate effects can, however, often be obtained with a lower dose of Alcobon when the intravenous route is used.

It is suggested that the duration of the infusion should be of the order of 20 to 40 minutes provided this is balanced with the fluid requirements of the patient. As a rule, treatment with Alcobon for Infusion should rarely be required for periods of more than one week. The patient should be started on oral therapy with Alcobon tablets as soon as this becomes practicable.

Since Alcobon is excreted primarily by the kidneys, patients with renal impairment should be given smaller doses. The following is suggested as a guide for dosage in patients with severe infection associated with renal impairment:

in patients with creatinine clearance

<40 to >20 ml/min: 50 mg/kg every 12 hours.

<20 to >10 ml/min: 50 mg/kg every 24 hours.

<10 ml/min: an initial single dose of 50 mg/kg;

subsequent doses should be calculated according to the results of regular monitoring of the serum concentration of the drug, which should not be allowed to exceed

80 mcg/ml. Blood levels of 25–50 mcg/ml are normally effective.

The duration of treatment should be determined on an individual basis. The outcome of therapy will be affected by variations in the sensitivity of the infecting organism, its accessibility and its susceptibility to Alcobon, as well as by differences in the response of individual patients. In cases of cryptococcal meningitis, treatment should last for at least four months.

Alcobon Tablets are for oral administration.

Alcobon for Infusion is for intravenous or intraperitoneal administration.

Alcobon for Infusion may be given concurrently with other infusions of normal saline, dextrose or dextrose/saline. No other agent should be added to or mixed with Alcobon for Infusion.

Contra-indications, warnings, etc Precautions: Blood levels should be closely monitored in patients with renal insufficiency. If, for any reason, repeated measurements of the blood levels cannot be performed in cases of severe renal failure, Alcobon should not be given.

Because the levels of the drug in blood samples taken during or immediately after administration of Alcobon for Infusion are not a reliable guide to subsequent levels, it is advisable to remove blood for monitoring of blood levels of Alcobon shortly before starting the next infusion.

Special care should be taken in patients with blood dyscrasias and those in whom the bone marrow may be depressed because of disease or treatment. Regular blood counts and tests of liver function should be performed in all patients.

In calculating the fluid and electrolyte intake of patients with impaired renal function, cardiac failure or electrolyte imbalance, due allowance should be made for the volume and chloride content (138 millimole/litre) of Alcobon for Infusion.

Teratogenic effects have been seen in rats, in which species flucytosine is metabolised to fluorouracil. The metabolism may differ in man; nevertheless, the use of Alcobon in pregnancy and in women of childbearing age requires that the potential benefits of therapy be weighed against its possible hazards.

Side-effects: At the recommended doses, Alcobon is well tolerated. Nausea, vomiting, diarrhoea and skin rashes have occurred but are usually of a transient nature. Thrombocytopenia and leucopenia have been reported, mostly in those with serious underlying disease and receiving other medicaments. Changes in tests of liver function have been reported in about 10% of patients. Local irritation or phlebitis does not appear to be a problem with Alcobon for Infusion.

Treatment of overdosage: In the event of overdosage with Alcobon, it is recommended that gastric lavage should be performed and measures taken to encourage diuresis. Haemodialysis produces a rapid fall in the serum concentration of Alcobon.

Pharmaceutical precautions *Storage:* Alcobon Tablets should be stored in a well-closed container, protected against moisture.

Alcobon for Infusion should be stored between 15 and 20°C. If stored below 15°C, precipitation of Alcobon substance may occur, which should be redissolved by heating to 80°C for not more than 30 minutes. Prolonged storage above 20°C could lead to the decomposition of Alcobon resulting in the formation of 5-fluorouracil.

Additives: Alcobon for Infusion may be given concurrently with other infusions of normal saline, dextrose or dextrose/saline. No other agent should be added to or mixed with Alcobon for Infusion.

Legal category POM.

Package quantities Alcobon Tablets are available in packings of 100.

Alcobon for Infusion 2.5 g in 250 ml in packings of 5.

Further information *Availability:* Alcobon Tablets and Alcobon for Infusion are available to hospitals only.

Sensitivity testing: It is recommended that cultures for sensitivity testing be taken before treatment and repeated at regular intervals during therapy. However, it is not necessary to delay treatment until results of these tests are known. To determine sensitivities, the methods of Shadomy (*Appl. Microbiol.* 1969, **17**, 871) and Scholer (*Mykosen*, 1970, **13**, 179) are recommended.

For sensitivity testing it is essential that culture media are free of antagonists to flucytosine.

Product licence numbers

Tablets 0031/0069

Infusion 0031/0094

ALLOFERIN®

Presentation Ampoules containing 10 mg alcuronium chloride in 2 ml. The ampoule solution is almost colourless to pale yellow.

Uses *Properties:* Alloferin is a medium-acting neuromuscular blocking agent. It is a derivative of toxiferine, an alkaloid of calabash curare producing muscle relaxation of the non-depolarizing type.

Indications: Muscle relaxation: Alloferin is used for surgical and anaesthetic procedures in which a muscle relaxant is required.

Dosage and administration Response to Alloferin, as to other non-depolarizing relaxants, is subject to individual variation; underlying disease conditions or concurrently administered agents may significantly alter dosage requirements (see Precautions). The following doses are intended as a guide.

Adults: An initial dose of 0.20 to 0.25 mg/kg body-weight intravenously is usually adequate to achieve 95 per cent neuromuscular block. If endotracheal intubation is to be performed after administration of Alloferin, adequate laryngeal relaxation may be expected after a pause of 90–120 seconds. Profound muscle relaxation will continue for approximately 20–30 minutes when non-potentiating anaesthetic agents are employed. With an initial dose of 0.3 mg/kg body-weight, which may be used when intubating before longer procedures, muscle relaxation is obtained for approximately 40 minutes.

Incremental doses of one-sixth to one-quarter of the initial dose should provide relaxation for additional periods of similar duration to the first.

The following table is given as a more detailed guide to doses for a 70 kg patient

Anaesthetic	Intubation with Alloferin (mg)	Intubation with suxamethonium		
		Abdominal (mg)	Pelvic floor (mg)	Upper abd- men and thorax (mg)
N ₂ /O ₂	14–17.5	9	7	11
Halothane 1.5 to 2 vol. %	8.5–11	6	4.5	6.5

Children: There is insufficient information to recommend a dosage for Alloferin in neonates (up to 28 days of age). Older infants and children should be given 0.125–0.20 mg/kg body-weight.

Alloferin ampoules are for intravenous injection.

Alloferin ampoule solution may be diluted with Water for Injection immediately before use.

Maintenance of stability cannot be guaranteed when Alloferin ampoule solution is diluted.

Contra-indications, warnings, etc

Contra-indications: Alloferin is contra-indicated in patients with a history of hypersensitivity to the agent. Use of muscle relaxants is preferably avoided in patients with myasthenia gravis or myasthenic (Eaton-Lambert) syndrome.

Precautions: Like other neuromuscular blocking agents, Alloferin should only be administered in the presence of an experienced anaesthetist. The patient's ventilation should be controlled.

Alloferin is mainly excreted in the urine and may therefore accumulate in patients with renal impairment when repeated doses are given. Dosage should be reduced accordingly.

Alloferin is partly bound to serum albumin. Dosage requirements may therefore be altered in patients with hepatic or other disease in which serum protein levels are disturbed.

Increased sensitivity to non-depolarizing drugs may be seen in most neuromuscular diseases, especially amyotrophic lateral sclerosis, poliomyelitis, Duchenne muscular dystrophy and multiple neurofibromatosis.

Sensitivity to non-depolarizing relaxants may be increased by the following drugs: Antibiotics of the polymyxin and aminoglycoside groups (streptomycin, neomycin, kanamycin, gentamicin, amikacin, tobramycin), lincomycin; volatile anaesthetics (ether, halothane, methoxyflurane, cyclopropane, isoflurane, enflurane); drugs with local anaesthetic properties (including quinine, beta-blocking drugs, phenytoin, penicillamine); ganglion-blocking agents (e.g. trimetaphan).

In high concentrations, Mg may increase, whilst K, Na and Ca decrease non-depolarizing neuromuscular block. The action of Alloferin is reportedly not significantly altered by changes in blood pH within the physiological range. Where marked electrolyte or acid-base disturbances are present these should be corrected, if possible, before Alloferin is administered. Care should be taken with dosage especially in acidosis.

During hypothermia non-depolarizing neuromuscular blockade may be decreased. However, care is required during subsequent re-warming to ensure that increased effect does not lead to recurrence of paralysis.

No information is available on the effects of Alloferin on the developing foetus and its use in pregnancy should

arefore be avoided. Studies indicate that Alloferin does not cross the placenta in amounts that would affect the fetus at or near term.

de-effects: At doses producing adequate neuromuscular block Alloferin does not have marked ganglion-blocking, histamine-releasing or vagolytic actions. Nevertheless, its administration is usually followed by a transient (2–5 minute) lowering of blood pressure due to a fall in peripheral vascular resistance. Less regularly, there may be a moderate increase in heart rate; cardiac output is not significantly altered. Intraocular pressure remains stable.

A few cases of anaphylactoid reaction have been recorded following administration of Alloferin, in most instances in patients who have had previous anaesthesia or history of allergy.

Effects of overdosage and their treatment: Prolonged respiratory and muscular paralysis are symptoms of overdosage. Artificial ventilation must be continued, and the patient kept under observation until neuromuscular function is restored and there is no risk of recurrence of paralysis.

Prostigmin (neostigmine methylsulphate), given in a dose of 1 to 5 mg (0.08 mg/kg in children) with atropine 4 to 1.25 mg (0.02 mg/kg in children) by intravenous injection, is routinely used to speed reversal of the neuromuscular block.

Pharmaceutical precautions *Storage:* The recommended maximum storage temperature for Alloferin ampoules is 25°C; the Ampoules should be protected from light.

Alloferin should not be administered in the same syringe as thiopentone.

Legal category POM.

Package quantities Alloferin ampoules in packings of 10.

Further information Nil.

Product licence number 0031/5000.

ARFONAD*

Presentation Ampoules containing 250 mg trimethoprim camsylate in 5 ml. The ampoule solution is colourless.

Uses *Properties:* Arfonad is a ganglion-blocking agent which also has a direct dilator effect on peripheral vessels. It has a rapid, short and readily reversible action, which permits minute-to-minute control of the blood pressure.

Indications: Arfonad is used for surgical procedures if a hypotensive technique is clearly indicated. These may include: neurosurgery; vascular surgery; prostatectomy; chest surgery; thyroidectomy; bone and joint surgery.

Dosage and administration *Adults and children:*

1. Dilution to 250 ml with normal saline or glucose saline gives a 0.1% solution (1 mg per ml) which is the strength usually used for an intravenous drip. The Arfonad drip is started at an average of 60 drops approximately 3–4 mg) per minute and, having ascertained the patient's response, the rate of administration is then adjusted to maintain the desired level of

hypotension. Since there is marked variation in individual response, frequent blood pressure determinations are essential to maintain proper control.

2. If a weaker solution is preferred, a 0.05% solution can be prepared by diluting the 5% ampoule solution to 500 ml.

3. It is sometimes advisable to use a more concentrated solution in operations in which intravenous fluid should be restricted. For such patients a solution containing 0.25% Arfonad should be prepared by diluting the original 5% solution to 100 ml with normal saline or dextrose saline. The rate at which the drip is given should be correspondingly reduced.

4. The undiluted solution has also been used by intermittent intravenous injection.

As with other hypotensive drugs, Arfonad should be stopped before wound closure to allow the blood pressure to rise.

Arfonad Ampoules are for administration by intravenous drip and intermittent intravenous injection. Arfonad Ampoule solution may be diluted with Water for Injection, normal saline or dextrose saline immediately before use.

Contra-indications, warnings, etc

Contra-indications: Arfonad should not be used for hypotensive surgery in patients with severe arteriosclerosis or severe cardiac disease.

Effects of overdosage and their treatment: The major effect will be a marked fall in blood pressure below the desired level of hypotension. Tachycardia and respiratory depression may result, particularly if Arfonad is used concomitantly with a muscle relaxant. Vasopressor agents such as phenylephrine, ephedrine or noradrenaline are antidotes and may be used to effect a rapid return to normotensive level.

Pharmaceutical precautions *Storage:* Recommended maximum storage temperature 6°C; avoid freezing.

Additives: It is inadvisable to use the Arfonad drip as a vehicle for administering other drugs. Arfonad is known to be incompatible with thiopentone, gallamine triethiodide, strongly alkaline solutions, iodides and bromides.

Legal category POM.

Package quantities Arfonad Ampoules in packings of 10.

Further information Since the effect of Arfonad is neutralised by vasopressor drugs such as adrenaline, noradrenaline and ephedrine, local adrenaline infiltration at the site of incision is contra-indicated.

Product licence number 0031/5001.

BACTRIM* ROCHE

Approved name: Co-trimoxazole.

Presentation Bactrim tablets: round, pale yellow tablets with 'ROCHE' in a hexagon imprinted on one face, a single break bar on the other, containing 80 mg trimethoprim and 400 mg sulphamethoxazole.

Bactrim Drapsules*: capsuliform, orange, film-coated tablets with 'ROCHE' imprinted on one side, containing 80 mg trimethoprim and 400 mg sulphamethoxazole.

Bactrim Double Strength Tablets: oval, biconvex, white tablets with 'ROCHE' imprinted on one face, a 800 + 160

single break bar on the other, containing 160 mg trimethoprim and 800 mg sulphamethoxazole.

Bactrim Paediatric Tablets; round, white tablets with 'ROCHE' imprinted on one face, containing 20 mg trimethoprim and 100 mg sulphamethoxazole.

Bactrim Suspension (adult); pale yellow, aniseed-flavoured suspension containing 80 mg trimethoprim and 400 mg sulphamethoxazole in 5 ml.

Bactrim Paediatric Syrup; pink, aniseed-flavoured suspension containing 40 mg trimethoprim and 200 mg sulphamethoxazole in 5 ml.

Uses Properties: Bactrim is bactericidal *in vitro* to a wide range of Gram-positive and Gram-negative organisms, including *Streptococcus*, *Staphylococcus*, *Pneumococcus*, *Neisseria*, *Escherichia coli*, *Klebsiella*, *Proteus* spp., *Haemophilus*, *Salmonella*, *Shigella*, *Vibrio cholerae*, *Brucella*, *Pneumocystis carinii*, *Nocardia* and *Bordetella*. A particularly high degree of activity is exhibited against *Haemophilus influenzae*, *E. coli* and *Proteus* spp., making Bactrim particularly suitable for the treatment of chronic bronchitis and urinary tract infections.

Bactrim exerts its bactericidal action by the sequential blockade of two bacterial enzyme systems in the same metabolic pathway. The synergy thus produced accounts for the high degree of bactericidal activity.

Indications: Respiratory infections, including acute and chronic bronchitis (treatment and prophylaxis), also bronchiectasis, lung abscess, lobar and broncho-pneumonia, *Pneumocystis carinii* pneumonitis, sinusitis and otitis media. Urinary tract infections, including urethritis, cystitis, pyelitis, pyelonephritis and prostatitis. Gastro-intestinal tract infections caused by *Salmonella typhi* and *paratyphi*, including the chronic carrier state; bacillary dysentery and cholera (as an adjuvant to fluid and electrolyte replacement). Skin infections, including pyoderma, abscesses and wound infections. Septicaemias. Gonorrhoea. Other infections caused by a wide range of pathogenic bacteria, including acute and chronic osteomyelitis, acute brucellosis, nocardiosis and actinomycetoma, and in South American blastomycosis.

Dosage and administration Adults and children over 12 years: *Bactrim Tablets (adult) and Double Strength Tablets.* Usual dosage 2 Tablets (adult) or 1 Double Strength Tablet twice daily. Minimum dosage and dosage for long-term treatment (more than 14 days), 1 Tablet (adult) or $\frac{1}{2}$ Double Strength Tablet twice daily. For severe infections and septicaemias, 3 Tablets (adult) or $\frac{1}{2}$ Double Strength Tablets twice daily. For uncomplicated gonorrhoea, 4 doses of 4 Tablets (adult) or 2 Double Strength Tablets at 12-hourly intervals over two days may be given. Alternatively 2 doses of 5 Tablets (adult) or $2\frac{1}{2}$ Double Strength Tablets at an interval of up to 12 hours but not less than eight hours. (The same number of Drapsules* instead of Tablets (adult) may be given.) Bactrim Adult Suspension 5 ml = 1 Tablet (adult) or Drapsule.*

Bactrim Tablets (adult) may be dispersed in water or swallowed whole.

Children under 12 years: *Bactrim Tablets (adult).*

6–12 years: 1 tablet twice daily.

Bactrim Paediatric Tablets:

2–5 years: 2 paediatric tablets twice daily.

6–12 years: 4 paediatric tablets twice daily.

Bactrim Paediatric Syrup

6 weeks to 5 months: 2.5 ml twice daily.

6 months to 5 years: 5 ml twice daily.

6–12 years: 10 ml twice daily.

In children, this corresponds to an approximate dose 6 mg trimethoprim/kg body weight/day plus 30 n sulphamethoxazole/kg body weight/day, divided into equal doses.

The dosage required for the treatment of *Pneumocystis carinii* pneumonitis is generally higher than that recommended for other conditions. In children a dosage 20 mg trimethoprim/kg body weight/day, plus 100 n sulphamethoxazole/kg body weight/day, given equally divided doses every six hours for 14 days suggested. For this reason, treatment should be undertaken only if facilities for regular monitoring of blood levels of the sulphamethoxazole component are available.

Duration of therapy: In acute infections Bactrim should be given for at least five days or until the patient has been symptom-free for two days. Treatment for prostatitis and acute brucellosis should be maintained for a period of at least four weeks, whilst nocardiosis, actinomycetoma and South American blastomycosis require long term therapy.

All dosage forms are for oral administration.

Bactrim Adult Suspension and Bactrim Paediatric Syrup may be diluted with Syrup BP. Maintenance of stability cannot be guaranteed when Bactrim preparations are diluted.

Contra-indications, warnings, etc

Contra-indications: Bactrim is contra-indicated in patients showing marked liver parenchymal damage (blood dyscrasias, and in severe renal insufficiency where repeated measurements of the plasma concentration cannot be performed. Bactrim should not be given to patients with a history of sensitivity to sulphonamides (trimethoprim). Treatment must be immediately discontinued on the appearance of a skin rash.

Bactrim should not be given to premature babies nor during the first few weeks of life.

The drug should not be given during pregnancy. The usual caution in prescribing any drug for women of childbearing age should also be exercised with Bactrim.

Precautions: An adequate urinary output should be maintained. In cases with renal impairment a reduced or more widely spaced dosage is indicated to avoid accumulation of the drug. In such patients, measurement of the plasma concentration of the drug is advisable. Regular blood counts are necessary whenever long-term therapy is used. Special caution should be exercised in treating patients with conditions predisposing to folate deficiency.

Care should be taken when giving Bactrim to patients receiving sulphonylurea hypoglycaemic agents or coumarin anticoagulants as the action of these drugs may be increased.

Both trimethoprim and sulphamethoxazole are excreted in breast milk, but this does not contra-indicate the use of Bactrim in lactating mothers.

Side-effects: At the recommended dosage Bactrim is well tolerated. Nausea, vomiting, glossitis and skin rashes, including, rarely, erythema multiforme (Stevens-Johnson syndrome), can occur.

As Bactrim contains a sulphonamide, the possibility of blood dyscrasias like those associated with sulphonamides should be borne in mind. The changes reported with

actrim mainly consist of thrombocytopenia, purpura, leucopenia, neutropenia and, very rarely, agranulocytosis. They have usually proved to be reversible on withdrawal of the drug. Elderly patients are more susceptible to these blood changes. During long-term therapy, isolated cases of megaloblastic changes in the bone marrow have been reported; these are reversible by folic acid therapy.

Effects of overdosage and their treatment: Symptoms of overdosage may include vomiting, mental and visual disturbances, petechiae, purpura and jaundice. Haematuria, crystalluria and anuria may occur in severe cases.

Treatment is symptomatic and may include gastric lavage and forced diuresis. Alkalinisation of the urine may aid the elimination of the sulphamethoxazole component of Bactrim.

Hypersensitivity reactions may require treatment with steroids. Calcium folinate, 3 to 6 mg intramuscularly for 7 to 10 days, may be given to counteract the effects of trimethoprim on haemopoiesis.

Pharmaceutical precautions *Storage:* The recommended maximum storage temperature for Bactrim Adult Suspension and Paediatric Syrup is 30°C. No special precautions are required for other oral presentations of actrim.

Legal category POM.

Package quantities Bactrim Tablets (adult) in packings of 100 and 500.

Bactrim Drapsules in packings of 100 and 500.

Bactrim Double Strength Tablets in packings of 50.

Bactrim Paediatric Tablets in packings of 100.

Bactrim Adult Suspension in bottles of 100 ml.

Bactrim Paediatric Syrup in bottles of 100 ml.

Further information Bactrim IM Injection and, to hospitals only, Bactrim for Infusion are also available for patients in whom parenteral administration is indicated. See separate data sheets.

Product licence numbers

Tablets (adult)	0031/0075
Drapsules	0031/5044
Double Strength Tablets	0031/0110
Paediatric Tablets	0031/5045
Paediatric Syrup	0031/5046
Adult Suspension	0031/5047

IACTRIM® ROCHE IM INJECTION

Improved name: Co-trimoxazole

Presentation Each 3 ml ampoule contains 160 mg trimethoprim and 800 mg sulphamethoxazole in a vehicle containing 52% glycofurol. The pH of the solution, which is faintly yellow, is approximately 9–10.

Uses *Properties:* Bactrim is bactericidal *in vitro* to a wide range of Gram-positive and Gram-negative organisms, including *Streptococcus*, *Staphylococcus*, *Pneumococcus*, *Neisseria*, *Escherichia coli*, *Klebsiella*, *Proteus* spp., *Haemophilus*, *Salmonella*, *Shigella*, *Vibrio cholerae*, *Brucella*, *Pneumocystis carinii*, *Nocardia* and *Tordetella*. A particularly high degree of activity is exhibited against *Haemophilus influenzae*, *E. coli* and *Proteus* spp., making Bactrim particularly suitable for the treatment of chronic bronchitis and urinary tract infections.

Bactrim exerts its bactericidal action by the sequential

blockade of two bacterial enzyme systems in the same metabolic pathway. The synergy thus produced accounts for the high degree of bactericidal activity.

Indications: Clinical experience with oral Bactrim indicates its therapeutic value in the following conditions:

Respiratory tract infections.

Renal and urinary tract infections.

Genital tract infections.

Gastro-intestinal tract infections caused by *Salmonella typhi* and *paratyphi*; bacillary dysentery and cholera (as an adjuvant to fluid and electrolyte replacement).

Skin and wound infections.

Septicaemias, osteomyelitis, acute brucellosis, nocardiosis and other infections caused by sensitive organisms.

Bactrim IM Injection is for use when intramuscular administration is preferable to oral therapy.

Dosage and administration Bactrim IM Injection is suitable only for intramuscular administration as described below. It is *not* suitable for any other route or method of administration.

Adults and children over 12 years: One 3 ml ampoule twice daily.

Maximum dosage (for severe infections): One and a half ampoules (4.5 ml) twice daily or one 3 ml ampoule three times daily.

Children 6–12 years: The recommended dosage is approximately 6 mg trimethoprim/kg body weight/day plus 30 mg sulphamethoxazole/kg body weight/day divided into two equal doses. As a guide, half an ampoule (1.5 ml) twice daily may be used. The dosage required for the treatment of *Pneumocystis carinii* pneumonitis is generally higher than that recommended for other conditions.

Bactrim IM Injection should not be given to children under the age of six years because of their small muscle mass.

Duration of treatment: it is recommended that Bactrim IM Injection should not be administered in the standard dosage (as indicated above) for more than five successive days, or in the maximum dosage for more than three successive days.

Mode of administration of Bactrim IM: Bactrim IM Injection should be given by deep intramuscular injection into the upper and outer quadrant of the buttock. Successive injections should be given alternately on opposite sides.

Any unused ampoule solution should be discarded.

The ampoule solution of Bactrim IM Injection should not be diluted.

Contra-indications, warnings, etc

Contra-indications: Bactrim is contra-indicated in patients showing marked liver parenchymal damage or blood dyscrasias and in severe renal insufficiency where repeated measurements of the plasma concentration cannot be performed. Bactrim should not be given to patients with a history of sensitivity to sulphonamides or trimethoprim. Treatment must be immediately discontinued on the appearance of a skin rash.

Bactrim should not be given to premature babies nor during the first few weeks of life.

The drug should not be given during pregnancy. The usual caution in prescribing any drug for women of childbearing age should also be exercised with Bactrim.

Precautions: An adequate urinary output should be maintained. In cases with renal impairment a reduced or more widely spaced dosage is indicated to avoid

accumulation of the drug. In such patients, measurement of the plasma concentration of the drug is advisable.

Regular blood counts are necessary whenever long-term therapy is used.

Special caution should be exercised in treating patients with conditions predisposing to folate deficiency.

Care should be taken when giving Bactrim to patients receiving sulphonylurea hypoglycaemic agents or coumarin anticoagulants as the action of these drugs may be increased.

Both trimethoprim and sulphamethoxazole are excreted in breast milk, but this does not contraindicate the use of Bactrim in lactating mothers.

Side-effects: At the recommended dosage, Bactrim is well tolerated. Nausea, vomiting, glossitis and skin rashes, including, rarely, erythema multiforme (Stevens-Johnson syndrome), can occur.

As Bactrim contains a sulphonamide, the possibility of blood dyscrasias like those associated with sulphonamides should be borne in mind. The changes reported with Bactrim mainly consist of thrombocytopenia, purpura, leucopenia, neutropenia and, very rarely, agranulocytosis. They have usually proved to be reversible on withdrawal of the drug. Elderly patients are more susceptible to these blood changes. During long-term therapy, isolated cases of megaloblastic changes in the bone marrow have been reported: these are reversible by folic acid therapy.

Local reactions to Bactrim IM Injection do not appear to be a clinical problem and mainly consist of mild to moderate pain at the injection site; induration is uncommon.

Effects of overdosage and their treatment: Symptoms of overdosage may include vomiting, mental and visual disturbances, petechiae, purpura and jaundice. Haematuria, crystalluria and anuria may occur in severe cases.

Treatment is symptomatic and may include gastric lavage and forced diuresis. Alkalinisation of the urine may aid the elimination of the sulphamethoxazole component of Bactrim.

Hypersensitivity reactions may require treatment with steroids. Calcium folinate, 3–6 mg intramuscularly for five to seven days, may be given to counteract the effects of trimethoprim on haemopoiesis.

Pharmaceutical precautions *Storage:* Bactrim IM Injection should be protected from light. The recommended maximum storage temperature is 30°C.

Additives: The ampoule solution of Bactrim IM Injection should not be diluted.

Legal category POM.

Package quantities Bactrim IM Injection, ampoules containing 160 mg trimethoprim and 800 mg sulphamethoxazole, in packings of 10.

Further information *Availability:* Bactrim is also available in tablets, Drapsules®, Double Strength tablets, paediatric tablets, adult suspension, paediatric syrup and, to hospitals only, as Bactrim for Infusion. See separate data sheets.

Product licence number 0031/0118.

BACTRIM® ROCHE FOR INFUSION

Approved name: Co-trimoxazole

Presentation Each 5 ml ampoule contains 80 mg trimethoprim and 400 mg sulphamethoxazole in a vehicle

containing 40% propylene glycol. The solution, which is almost colourless to very pale yellow, has a pH approximately 10.5.

Uses *Properties:* Bactrim is bactericidal *in vitro* to a wide range of Gram-positive and Gram-negative organisms, including *Streptococcus*, *Staphylococcus*, *Pneumococcus*, *Neisseria*, *Escherichia coli*, *Klebsiella*, *Proteus* spp., *Haemophilus*, *Salmonella*, *Shigella*, *Vibrio*, *Brucella*, *Pneumocystis carinii*, *Nocardia* and *Bordetella*. A particularly high degree of activity is exhibited against *Haemophilus influenzae*, *E. coli* and *Proteus* spp. making Bactrim particularly suitable for the treatment of chronic bronchitis and urinary tract infections.

Bactrim exerts its bactericidal action by the sequential blockade of two bacterial enzyme systems in the same metabolic pathway. The synergy thus produced accounts for the high degree of bactericidal activity.

Indications: Clinical experience with oral Bactrim indicates its therapeutic value in the following conditions: Respiratory tract infections. Renal and urinary tract infections. Genital tract infections. Gastro-intestinal tract infections caused by *Salmonella typhi* and *paratyphi* bacillary dysentery and cholera (as an adjuvant to fluid and electrolyte replacement). Skin and wound infection: Septicaemia and other infections caused by sensitive organisms including osteomyelitis, brucellosis and nocardiosis.

Parenteral administration of Bactrim for Infusion is indicated where oral dosage is not possible, for example Pre- and post-operative infections and severe trauma. Other clinical situations where the patient is unable to take or tolerate oral therapy.

Dosage and administration (ONLY to be given when DILUTED in an intravenous infusion – see below).

Adults and children over 12 years: 10 ml twice daily

Maximum dosage (for severe cases): 15 ml twice daily

Children up to 12 years: The recommended dosage is approximately 6 mg trimethoprim/kg body weight/day plus 30 mg sulphamethoxazole/kg body weight/day divided into 2 equal doses. As a guide, the following dosage regimes may be used:

6 weeks to 5 months: 1.25 ml twice daily.

6 months to 5 years: 2.5 ml twice daily.

6–12 years: 5 ml twice daily.

The dosage required for the treatment of *Pneumocystis carinii* pneumonitis is generally higher than that recommended for other conditions. In children a dosage of 20 mg trimethoprim/kg body weight/day plus 100 mg sulphamethoxazole/kg body weight/day, given in equally divided doses every six hours is suggested. For this reason, treatment should be undertaken only in facilities for monitoring of blood levels of the sulphamethoxazole component are available.

Duration of treatment: It is intended that Bactrim for Infusion should be used only during such a period as the patient is unable to accept oral therapy with Bactrim. In general, administration is unlikely to be required for more than a few days. It is recommended that the maximum dose (as indicated above) should not be administered for more than three successive days.

Mode of administration of Bactrim for Infusion: Bactrim for Infusion is suitable only for use as described below after addition to intravenous infusions. It is NOT suitable for any other route or method of administration.

Bactrim for Infusion must ONLY be given by the intravenous route and MUST BE DILUTED according to the schedule given below.

Bactrim for Infusion should only be mixed with one of the following infusion solutions: Dextrose Injection BP % and 10%. Laevulose Injection BP 5%. Compound sodium Lactate Injection BP (Hartmann's Solution). Compound Sodium Chloride Injection BPC 1959 Ringer's Solution). Sodium Chloride Injection BP. Sodium Chloride and Dextrose Injection BP (0.45% sodium chloride and 2.5% dextrose). Dextran 40 Injection BP. Dextran 70 Injection BP. No other agent should be added to or mixed with the infusion.

Dilution should be carried out as follows: One ampoule Bactrim for Infusion (5 ml) to 125 ml infusion solution.

Two ampoules Bactrim for Infusion (10 ml) to 250 ml infusion solution.

Three ampoules Bactrim for Infusion (15 ml) to 500 ml infusion solution.

Dilution should be carried out immediately before use. After addition of Bactrim for Infusion to the infusion solution, the mixture should be well shaken in order to ensure thorough mixing. Should visible turbidity or crystallisation appear in the solution at any time before or during the infusion, the mixture should be discarded.

It is suggested that the duration of the infusion should be of the order of 1½ hours, but this should be balanced against the fluid requirements of the patient.

Contra-indications, warnings, etc

Contra-indications: Bactrim is contra-indicated in patients showing marked liver parenchymal damage or blood dyscrasias and in severe renal insufficiency where repeated measurements of the plasma concentration cannot be performed. Bactrim should not be given to patients with history of sensitivity to sulphonamides or trimethoprim. Treatment must be immediately discontinued on the appearance of a skin rash.

Bactrim should not be given to premature babies nor during the first few weeks of life.

The drug should not be given during pregnancy. The usual caution in prescribing any drug for women of childbearing age should also be exercised with Bactrim.

Precautions: An adequate urinary output should be maintained. In cases with renal impairment a reduced or more widely spaced dosage is indicated to avoid accumulation of the drug. In such patients, measurement of the plasma concentration of the drug is advisable. Special caution should be exercised in treating patients with conditions predisposing to folate deficiency.

Care should be taken when giving Bactrim to patients receiving sulphonylurea hypoglycaemic agents or coumarin anticoagulants as the action of these drugs may be increased.

Side-effects: At the recommended dosage, Bactrim is well tolerated. Nausea, vomiting, glossitis and skin rashes, including, rarely, erythema multiforme (Stevens-Johnson syndrome), can occur.

As Bactrim contains a sulphonamide, the possibility of blood dyscrasias like those associated with sulphonamides should be borne in mind. The changes reported with Bactrim mainly consist of thrombocytopenia, purpura, leucopenia, neutropenia and, very rarely, agranulocytosis. They have usually proved to be reversible on withdrawal of the drug. Elderly patients are more susceptible to these blood changes. During long-term therapy, isolated cases of megaloblastic changes in the

bone marrow have been reported, these are reversible by folic acid therapy.

Bactrim for Infusion has occasionally given rise to local side-effects in the form of pain and phlebitis.

Effects of overdosage and their treatment: Symptoms of overdosage may include vomiting, mental and visual disturbances, petechiae, purpura and jaundice. Haematuria, crystalluria and anuria may occur in severe cases.

Treatment is symptomatic and may include forced diuresis. Alkalinisation of the urine may aid the elimination of the sulphamethoxazole component of Bactrim for Infusion.

Hypersensitivity reactions may require treatment with steroids. Calcium folinate. 3-6 mg intramuscularly for five to seven days, may be given to counteract the effects of trimethoprim on haemopoiesis.

Pharmaceutical precautions *Storage:* Bactrim for Infusion should be protected from light.

Legal category POM.

Package quantities Bactrim for Infusion, ampoules containing 80 mg trimethoprim and 400 mg sulphamethoxazole in 5 ml, in packings of 10.

Further information *Availability:* Bactrim for Infusion is available to hospitals only.

Bactrim is also available as Tablets (adult), Drapsules*, Double Strength Tablets, paediatric tablets, adult suspension and paediatric syrup and as Bactrim Roche IM Injection. See separate data sheets.

Product licence number 0031/0070.

BECOSYM*

Presentation Becosym Tablets: round, dark brown, film-coated tablets with BECOSYM imprinted on one face. They are known as Vitamin B Tablets, Compound, Strong.

Becosym Forte Tablets: round, dark brown, film-coated tablets with BECOSYM FORTE imprinted on one face.

Becosym Syrup: dark red-orange, fruit-flavoured syrup.

The vitamin content of these preparations is shown below.

	<i>Each tablet (mg)</i>	<i>Each Forte tablet (mg)</i>	<i>Syrup 5 ml (mg)</i>
Thiamine			
hydrochloride	5	15	5
Riboflavin	2	15	2
Nicotinamide	20	50	20
Pyridoxine			
hydrochloride	2	10	2

Uses *Properties:* The vitamin B-complex comprises a group of water-soluble factors more or less closely associated in their natural occurrence. It is known that nearly every vitamin of the B-complex forms part of a co-enzyme essential for the metabolism of protein, carbohydrate or fatty acid.

Manifestations of deficiency of the B-vitamins include glossitis, stomatitis, cheilosis, the heart manifestations of

beriberi, the skin manifestations of pellagra, corneal vascularisation and polyneuritis.

Indications: Becosym has been found of value in: clinical and subclinical vitamin deficiency states; supplementation of diet in old age and as an aid to recovery from illness and surgery; adjunct to treatment with broad-spectrum antibiotics.

Dosage and administration

Becosym and Becosym Forte Tablets and Becosym Syrup are for oral administration.

Becosym Syrup may be diluted with Syrup BP. Maintenance of stability cannot be guaranteed when Becosym Syrup is diluted.

	<i>Prophylactic</i>	<i>Therapeutic</i>
Adults	1–3 tablets or 5–15 ml syrup daily	2 or 3 Forte tablets daily
Children	5 to 15 ml syrup daily	1–3 tablets daily
Infants	5 ml syrup daily	

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions *Storage:* The recommended maximum storage temperature for Becosym, Becosym Forte Tablets and Becosym Syrup is 25°C. Becosym Syrup should be protected from light.

Legal category Tablets GSL
Forte Tablets GSL
Syrup GSL

Package quantities Becosym Tablets in packings of 100 and 500.

Becosym Forte Tablets in packings of 25, 100 and 250.

Becosym Syrup in packings of 100 ml.

Further information Nil.

Product licence numbers

Tablets 0031/5005
Forte tablets 0031/5006
Syrup 0031/5007

BENADON*

Presentation Round, white tablets with 'B6 ROCHE' imprinted on one face, containing 20 mg pyridoxine hydrochloride.

Round, white tablets with 'BENADON' imprinted on one face and a single break bar on the other, containing 50 mg pyridoxine hydrochloride.

Uses *Properties:* Vitamin B₆ occurs naturally in three forms, namely pyridoxine, pyridoxal and pyridoxamine, which can be readily interconverted by animal tissues. As co-decarboxylases for several enzymes concerned with decarboxylation and transamination, the phosphates of pyridoxal and pyridoxamine are the functional forms of the vitamin. Thus the vitamin plays an important role in protein metabolism; it is also involved in fat metabolism.

Deficiency of the vitamin may manifest itself as anaemia, peripheral neuritis, convulsions, or lesions of the skin and mucous membranes.

Indications: Benadon is indicated in the treatment of: peripheral neuritis due to isoniazid therapy, or associated with pellagra; pregnancy sickness; radiation sickness;

pyridoxine-responsive anaemia; convulsions in infant which may be due to abnormally large requirements for pyridoxine.

Dosage and administration *Adults:* Usual therapeutic dose, 20–50 mg two or three times daily.

Acute deficiency, treatment of severe radiation or pregnancy sickness, blood disorders, 50–200 mg repeated as necessary.

Treatment of convulsions in children: 20–100 mg daily

Benadon Tablets are for oral administration.

Pharmaceutical precautions *Storage:* Recommended maximum storage temperature 30°C. Benadon Tablets should be protected from light.

Legal category GSL.

Package quantities Benadon Tablets 20 mg in packings of 100.

Benadon Tablets 50 mg in packings of 100.

Further information Nil.

Product licence numbers

Tablets 20 mg 0031/5010
Tablets 50 mg 0031/5011

BENERVA*

Presentation Round, white tablets with 'BENERVA' imprinted on one face, '3' in the centre of the other containing 3 mg thiamine hydrochloride.

Round, white tablets with 'BENERVA 10' imprinted on one face, containing 10 mg thiamine hydrochloride.

Round, white tablets with 'BENERVA 25' imprinted on one face, containing 25 mg thiamine hydrochloride.

Round, white tablets with 'BENERVA 50' imprinted on one face, containing 50 mg thiamine hydrochloride.

Round, white tablets with 'BENERVA 100' imprinted on one face, containing 100 mg thiamine hydrochloride.

Round, white tablets with 'ROCHE' imprinted on one face, containing 300 mg thiamine hydrochloride.

Ampoules containing 25 mg thiamine hydrochloride in 1 ml. The ampoule solution is almost colourless to faintly yellow.

Ampoules containing 100 mg thiamine hydrochloride in 1 ml. The ampoule solution is almost colourless to faintly yellow.

Uses *Properties:* Vitamin B₁ is particularly concerned with carbohydrate metabolism. When phosphorylated on the hydroxyl group it yields the pyrophosphate, co-carboxylase, which is concerned in pyruvate and lactate metabolism. The vitamin is essential for the nutrition of nerve cells, probably by promoting the oxidation of glucose within the central nervous system. Vitamin B₁ deficiency, or beriberi, is characterised by degeneration of the peripheral nerves with peripheral neuritis and by enlargement of the right heart, often accompanied by oedema.

Indications: Vitamin B₁ is specific in the treatment of beriberi.

It has been proved useful in the treatment of painful conditions such as: neuritis accompanying alcoholism and pregnancy; lumbago; sciatica; trigeminal neuralgia; optic neuritis; delirium tremens (large doses of Benerva combined with other vitamins should be given by injection).

Dosage and administration *Adults:* Prophylaxis, 3–10 mg daily.

Mild chronic deficiency, 10–25 mg daily.
Usual therapeutic dose, 10–50 mg daily.
Acute deficiency or treatment of such conditions as
mabgo and sciatica, 100–600 mg daily.

Children: If, on the recommendation of a physician, a
children's dosage is required, then it is suggested that 5–
10 mg daily may be given.

Benerva Tablets are for oral administration. Benerva
Ampoules are for intramuscular or intravenous injection.
Benerva Ampoule solution may be diluted with Water
for Injection. Maintenance of stability cannot be guar-
anteed when Benerva Ampoule solution is diluted.

Contra-indications, warnings, etc Although Be-
nerva is very well tolerated, it is now recognised that an
anaphylactic reaction may sometimes occur after an
injection of vitamin B₁, probably due to sensitisation to
the vitamin. A patient may tolerate one or more courses
of injections without trouble but then experience a
reaction to a later injection. Mild allergic phenomena,
such as sneezing or mild asthma, are warning signs that
further injection may give rise to anaphylactic shock. To
avoid this possibility it is advisable to start a second
course of injections with a dose considerably lower than
that previously used. Because of the above, injections of
B₁ should not be given intravenously, except in the case
of comatose patients who are often given large doses of
vitamins by intravenous drip.

Pharmaceutical precautions *Storage:* Recom-
mended maximum storage temperature 30°C. Benerva
tablets and Ampoules should be protected from light.

Legal category Tablets GSL.
Ampoules POM.

Package quantities Benerva Tablets 3 mg in packings
of 100.

Benerva Tablets 10 mg in packings of 100.

Benerva Tablets 25 mg in packings of 100.

Benerva Tablets 50 mg in packings of 100.

Benerva Tablets 100 mg in packings of 100.

Benerva Tablets 300 mg in packings of 100.

Benerva Ampoules 25 mg in 1 ml in packings of 10.

Benerva Ampoules 100 mg in 1 ml in packings of 10.

Further information Nil.

Product licence numbers

Tablets 3 mg 0031/5050

Tablets 10 mg 0031/5051

Tablets 25 mg 0031/5052

Tablets 50 mg 0031/5053

Tablets 100 mg 0031/5054

Tablets 300 mg 0031/5055

Ampoules 25 mg 0031/5056

Ampoules 100 mg 0031/5057

BENERVA* COMPOUND

Presentation Round, yellow tablets with 'ROCHE'
imprinted on one face, containing 1 mg thiamine
hydrochloride, 1 mg riboflavin and 15 mg nicotinamide.

Uses *Properties:* Benerva Compound Tablets contain
the three principal members of the vitamin B-complex.

The vitamin B-complex comprises a group of water-
soluble factors more or less closely associated in their
natural occurrence. It is known that nearly every vitamin
of the B-complex forms part of a co-enzyme essential for
the metabolism of protein, carbohydrate or fatty acid.

Indications: Treatment of minor degrees of vitamin B-
complex deficiency.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions *Storage:* Recom-
mended maximum storage temperature 25°C. Benerva
Compound Tablets should be protected from light.

Legal category GSL.

Dosage and administration

	<i>Prophylactic</i>	<i>Therapeutic</i>
Adults	1–2 tablets daily	1–3 tablets three times daily
Children:		
Over 12 years	1½–2 tablets daily	1½–2 tablets three times daily
Under 12 years	½–1 tablet daily	½–1 tablet three times daily

Benerva Compound Tablets are for oral administration.

Package quantities Benerva Compound Tablets in
packings of 200.

Further information Nil.

Product licence number 0031/5009.

DALMANE*

Presentation Capsules with opaque grey cap and
opaque yellow body with 'ROCHE 15' printed in red on
both cap and body, containing 16.4 mg flurazepam
monohydrochloride (equivalent to 15 mg flurazepam).
Capsules with black cap and opaque grey body with
'ROCHE 30' printed in red on both cap and body,
containing 32.8 mg flurazepam monohydrochloride
(equivalent to 30 mg flurazepam).

Uses *Properties:* Sleep laboratory studies have shown
that flurazepam significantly increases total sleep time
by reducing sleep induction time and maintaining sleep
with a reduced number of nocturnal awakenings. All-
night studies on healthy subjects have shown that a 30
mg dose produces only minimal changes in the pattern
of rapid eye movement (REM) sleep and that there is no
REM-rebound on withdrawal of the drug. Depression of
stage IV sleep has occasionally been noted.

Indications: Insomnia – difficulty in falling asleep,
frequent nocturnal awakenings and/or early morning
awakening. Sleep disturbances due to organic conditions
in conjunction with specific therapy.

Dosage and administration *Adults:* The dosage
required may vary according to the severity of the
insomnia and the patient's response. As a guide, we
would recommend that the following doses are taken
before retiring.

Severe insomnia: 30 mg.

Moderate to severe insomnia: 15 or 30 mg.

Mild insomnia: 15 mg.

Elderly patients: 15 mg.

Children: No dosage recommendations are made for the
administration of Dalmane to children.

Dalmane Capsules are for oral administration.

Contra-indications, warnings, etc *Precautions:*
With Dalmane, as with all other drugs acting on the
central nervous system, patients should avoid taking

alcohol while under treatment, since the individual response cannot be foreseen. Like all medicaments of this type, Dalmane may modify patients' reactions (driving ability, operation of machinery, etc) to a varying extent, depending on dosage and individual susceptibility.

The use of high doses of benzodiazepines, especially over prolonged periods, may sometimes lead to dependence, particularly in patients with a history of alcoholism or drug abuse. Treatment in these cases should be withdrawn gradually.

Results obtained in trials with several generations of rats and rabbits indicate that no danger of teratogenic effects need be expected from therapeutic doses of Dalmane. Nevertheless, the established medical principle of prescribing medicaments in early pregnancy only when absolutely indicated should be observed.

Treatment in elderly patients should be initiated with 15 mg Dalmane until the response can be judged.

Side-effects: Dalmane is well tolerated. However, morning drowsiness, dizziness and ataxia may occur. Occasionally patients treated with Dalmane experience a bitter after-taste. Extensive clinical and laboratory investigations have revealed no significant changes in the blood picture or liver function.

Effects of overdosage and their treatment: As with other benzodiazepine drugs, overdosage should not present undue problems of management or threat to life. Drowsiness, ataxia and slurred speech are symptoms of overdosage. Treatment is symptomatic, but gastric lavage may be useful if performed soon after ingestion.

Pharmaceutical precautions *Storage:* No special precautions are required for Dalmane capsules stored in amber-glass or plastic bottles.

Legal category POM.

Package quantities Dalmane Capsules 15 mg in packings of 100 and 500.

Dalmane Capsules 30 mg in packings of 100 and 500.

Further information Nil.

Product licence numbers

Capsules 15 mg 0031/0065.

Capsules 30 mg 0031/0066.

DECLINAX®

Presentation Round, white tablets with 'ROCHE 10' imprinted on one face and a single break bar on the other, containing 12.8 mg debrisoquine sulphate (equivalent to 10 mg base).

Round, pale blue tablets with 'ROCHE 20' imprinted on one face and two break bars on the other, containing 25.6 mg debrisoquine sulphate (equivalent to 20 mg base).

Uses *Properties:* Declinax lowers blood pressure markedly and promptly in the hypertensive patient. It does this by blocking the transmission of sympathetic nerve impulses at the nerve terminals, thereby decreasing peripheral vascular resistance. Reduction in post-ganglionic sympathetic transmission is achieved by interfering with the physiological release of noradrenaline, without depleting major catecholamine stores in cardiovascular tissues and without impairing the cardiac contractile mechanism. The action, as with other potent antihypertensive agents, is most marked in the standing position. Declinax normally acts within 4–10 hours and

its effects usually last for 9–24 hours, although an occasional patient may show a longer response. There is no accumulation on maintenance dosage.

Indications: Declinax is indicated for the treatment of all grades of hypertension. It can be given either alone or together with other antihypertensive drugs or diuretics.

Dosage and administration *Adults: Mild to moderate hypertension:* 10 mg once or twice daily. This dose can be increased by 10 mg at three-day intervals. The total dose usually falls within the range 20–60 mg daily. *Severe hypertension:* 20 mg once or twice daily. The dose can be increased, depending on response, by 10–20 mg every three or four days provided a close check is kept on the blood pressure. The total dose usually falls within the range 40–120 mg, but in cases of very severe hypertension 300 mg or more daily may be given.

Should postural hypotension occur with a dosage that controls the blood pressure, the total daily dose should be adjusted to give a small dose in the morning, a relatively large dose at midday and a moderate evening dose.

Children: No dosage recommendations are made for the administration of Declinax to children.

Declinax Tablets are for oral administration.

Contra-indications, warnings, etc *Precautions:* Declinax should be used with caution in those patients with renal insufficiency and should not be given to patients with a pheochromocytoma. Patients on antihypertensive drugs often have a lower blood pressure in warm weather, therefore in hot climates their dose of Declinax may need to be reduced. Evidence from both animal experiments and clinical observation suggests that the hypotensive action of adrenergic neurone blocking drugs such as Declinax may be inhibited by simultaneous treatment with tricyclic antidepressants. Extra care should be taken when prescribing antihypertensive drugs in patients being treated with levodopa. Patients taking Declinax are sensitive to sympathomimetic drugs.

Side-effects: Declinax is well tolerated. Overdosage causes postural hypotension, most noticeable in the early morning or with long standing and associated with weakness, giddiness and fatigue. The patient should be warned of the possibility of these symptoms occurring. This can be minimised by reducing the dose. Other side effects include malaise, nausea, headache, sweating, failure of ejaculation in the male, and sometime frequency of micturition and nocturia. Diarrhoea, common with some other antihypertensive agents, is seen only very rarely.

Effects of overdosage and their treatment: Excessive fall in blood pressure will be shown by orthostatic collapse. This will usually respond rapidly to placing the patient in a recumbent position.

Pharmaceutical precautions *Storage:* Declinax Tablets should be stored in well-closed containers.

Legal category POM.

Package quantities Declinax Tablets 10 mg in packings of 100 and 500.

Declinax Tablets 20 mg in packings of 100 and 500.

Further information Nil.

Product licence numbers

Tablets 10 mg 0031/5059

Tablets 20 mg 0031/5060

'ROMORAN' ROCHE

resentation Round, white tablets with 'ROCHE' printed on one face, two concentric circles on the other, containing 1.5 mg levorphanol tartrate. Ampoules containing 2 mg levorphanol tartrate in 1 ml. The ampoule solution is colourless to pale yellow.

Uses Properties: Dromoran Roche is a more potent and longer-acting analgesic than morphine. The analgesic effect begins within 10–30 minutes after administration and may continue for as long as 8 hours. Dromoran Roche is effective by mouth. Only in acute pain, when it is desirable to obtain rapid relief, is it necessary to give the drug by injection.

indications: Relief of severe pain; pre-operative medication; supplement to nitrous oxide/oxygen anaesthesia.

Dosage and administration Adults: *Oral:* Single dose of 1.5–4.5 mg once or twice daily.

Subcutaneous or intramuscular injection: The usual single dose is 2–4 mg.

Intravenous injection: 1–2 mg.

Supplement to nitrous oxide/oxygen anaesthesia: Total dose usually 1.5–2 mg given in divided doses of 0.25–0.5 mg.

Children: Paediatric dose not established.

Dromoran Roche Tablets are for oral administration.

Dromoran Roche Ampoules are for intramuscular, intravenous or subcutaneous injection.

Dromoran Roche Ampoule solution may be diluted with Water for Injection.

Maintenance of stability cannot be guaranteed when Dromoran Roche Ampoule solution is diluted.

Contra-indications, warnings, etc

Contra-indications: Dromoran Roche should not be given to comatose patients or to patients with respiratory depression or obstructive airways disease. It should not be administered to patients who are receiving monoamine oxidase inhibitors or within two weeks of their withdrawal.

Precautions: Dromoran Roche should only be given with caution, and in reduced dosage, to neonates and premature infants, elderly and debilitated patients, and in patients with head injuries, severe hepatic or renal impairment, biliary tract disorders, hypothyroidism, adrenocortical insufficiency, shock, prostatic hypertrophy, and supraventricular tachycardia.

Caution is also required in patients exhibiting acute alcoholism, raised intracranial pressure or convulsive disorders. Dromoran Roche depresses respiratory function and should be administered with particular care in patients with respiratory insufficiency.

The effects of Dromoran Roche may be potentiated by concurrent administration of other central nervous system depressants, including anaesthetic agents. Concurrent administration of Dromoran Roche with phenothiazines may induce severe hypotension. Patients should be instructed to avoid alcohol while under treatment, since the individual response cannot be foreseen.

Dromoran Roche may modify patients' reactions (driving ability, operation of machinery, etc.) to a varying extent, depending on dosage, administration and individual susceptibility.

There is little reported human usage of Dromoran in pregnancy. Although no adverse effects have been found in animals, the established medical principle of

prescribing medicaments in early pregnancy only when absolutely indicated should be observed.

Dromoran Roche crosses the placenta and may also be secreted in breast milk. This should be borne in mind when considering its use in patients during pregnancy or breast feeding. Administration in labour may cause respiratory depression in the newborn infant.

Repeated administration of Dromoran Roche may induce tolerance to the drug, with a tendency to increasing dosage requirements to obtain the desired effect, or to physical and psychological dependence of the morphine type, with the development of withdrawal symptoms after abrupt cessation of therapy. Cross-tolerance between narcotic analgesics can occur.

Side-effects: Dromoran Roche is usually well tolerated. Neither circulatory disturbances nor effects on the blood-pictures are likely. Appetite, gastro-intestinal and renal functions are less likely to be affected by Dromoran Roche than by morphine; however, nausea, vomiting, constipation and confusion may be troublesome. The drug has a less pronounced hypnotic effect than morphine, and is, therefore, useful for the relief of pain during the day.

Effects of overdosage and their treatment: In overdosage pin-point pupils, depressed respiration and impaired level of consciousness or coma may occur. In severe poisoning there may be dilatation of pupils, shock, severe respiratory depression and pulmonary oedema.

Gastric aspiration and lavage should be performed soon after ingestion and intensive supportive therapy carried out. Lorfan* 1–2 mg i.v., naloxone and nalorphine are antidotes.

Pharmaceutical precautions *Storage:* The recommended maximum storage temperature for Dromoran Roche Ampoules is 25°C; the Ampoules should be protected from light.

Dromoran Roche Tablets in blister packs should be stored in a dry place.

Legal category POM: MDA.

Package quantities Dromoran Roche Tablets in cartons of 500, each carton containing 10 packs of 50 tablets in blister strips of 5 tablets.

Dromoran Roche Ampoules in packings of 10.

Further information Nil.

Product licence numbers

Tablets 0031/5061R

Ampoules 0031/5062R

EFUDIX* ▼

Presentation White, opaque cream containing 5% w/w fluorouracil.

Uses Properties: Efudix is a topical cytostatic preparation which exerts a beneficial therapeutic effect on neoplastic and pre-neoplastic skin lesions without damaging normal skin. The pattern of response follows this sequence: erythema, vesiculation, erosion, ulceration, necrosis and epithelialisation.

Indications: Efudix is used for the topical treatment of superficial pre-malignant and malignant skin lesions; keratoses, including senile, actinic and arsenical forms; keratoacanthoma; Bowen's disease; superficial basal-cell carcinoma.

Deep, penetrating or nodular basal cell and squamous

cell carcinomas do not usually respond to Efudix therapy. It should be used only as a palliative therapy in such cases where no other form of treatment is possible.

Dosage and administration *Pre-malignant conditions:* The cream should be applied thinly to the affected area once or twice daily; an occlusive dressing is not essential.

Malignant conditions: The cream should be applied once or twice daily under an occlusive dressing where this is practicable.

The cream should not harm healthy skin. Treatment should be continued until there is a marked inflammatory response from the treated area, preferably with some erosion in the case of pre-malignant conditions. Severe discomfort may be alleviated by the use of topical steroid cream. The usual duration of treatment for an initial course of therapy is three to four weeks, but this may be prolonged. Lesions on the face usually respond more quickly than those on the trunk or lower limbs whilst lesions on the hands and forearms respond more slowly. Healing may not be complete until one or two months after therapy is stopped.

Efudix Cream is for topical application.

Efudix Cream should not be diluted.

Contra-indications, warnings, etc

Contra-indications: Efudix is contra-indicated during pregnancy and in patients with known hypersensitivity to Efudix or parabens.

Precautions: Efudix is for topical use only and care should be taken to avoid contact with mucous membranes or the eyes. The hands should be washed carefully after applying the cream.

The total area of skin being treated with Efudix at any one time should not exceed 500 cm² (approx 23 × 23 cm). Larger areas should be treated a section at a time.

Side-effects: Efudix is well tolerated and systemic toxicity is negligible. Transient erythema may occur in healthy skin surrounding the area being treated. Pre-existing subclinical lesions may become apparent. Exposure to sunlight may increase the intensity of the reaction.

Effects of overdosage and their treatment: If Efudix is accidentally ingested, signs of fluorouracil overdosage may include nausea, vomiting and diarrhoea. Stomatitis and blood dyscrasias may occur in severe cases. Appropriate measures should be taken for the prevention of systemic infection and daily white cell counts should be performed.

Pharmaceutical precautions *Storage:* The recommended maximum storage temperature for Efudix Cream is 30°C.

Legal category POM.

Package quantities Efudix Cream in tubes of 20 g.

Further information Efudix should be used only under specialist medical supervision.

Availability: Efudix Cream is available through hospital pharmacies for use in hospitals and hospital clinics and can be supplied to retail pharmacies for dispensing prescriptions for patients whose treatment has been initiated in hospital practice.

Product licence number 0031/0027.

EPHYNAL*

Presentation Round, white tablets with 'EPHYNA' imprinted on one face, the other being plain, containing 3 mg tocopheryl acetate.

Round, white tablets with 'EPHYNAL' imprinted on one face and 'TEN' on the other, containing 10 mg tocopheryl acetate.

Round, white tablets with 'EPHYNAL 50' imprinted on one face with a single break bar on the other containing 50 mg tocopheryl acetate.

Round, white to pale cream tablets with 'EPHYNAL 200' imprinted on one face and a single break bar on the other, containing 200 mg tocopheryl acetate.

Uses *Properties:* Ephyenal is a synthetic vitamin E preparation. The exact role of vitamin E in the animal organism has not yet been established. Vitamin E is known to exert an important physiological function as an anti-oxidant for fats, with a sparing action on vitamins A, carotenoids and on unsaturated fatty acids. Other work has demonstrated that vitamin E is connected with the maintenance of certain factors essential for the normal metabolic cycle.

Vitamin E deficiency produces a wide variety of manifestations in many organs and tissues of the body of most animal species that have been studied.

Indications: Ephyenal is indicated in high dosage for the treatment of intermittent claudication of moderate severity.

There is occasionally evidence of tocopheryl deficiency resulting in clinical signs in the following disorders: malabsorption syndromes, e.g. fibrocystic diseases of the pancreas; sprue; premature infants on unsupplemented artificial feeds.

Dosage and administration *Adults:* The recommended daily intake as a vitamin is from 3 to 15 mg but more may be required when large amounts of unsaturated fats are contained in the diet.

For treatment of intermittent claudication doses of 400–600 mg a day should be administered for three months or more.

Children (infants): 1–10 mg/kg body weight daily.

Ephyenal Tablets are for oral administration.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions *Storage:* Ephyenal Tablets should be stored in well-closed containers.

Legal category GSL.

Package quantities Ephyenal Tablets 3 mg in packings of 100.

Ephyenal Tablets 10 mg in packings of 100.

Ephyenal Tablets 50 mg in packings of 100.

Ephyenal Tablets 200 mg in packings of 50.

Further information Nil.

Product licence numbers

Tablets 3 mg 0031/5012

Tablets 10 mg 0031/5013

Tablets 50 mg 0031/5014

Tablets 200 mg 0031/5015

FANSIDAR* ▼

Presentation Round, white tablets with ROCHE and a hexagon imprinted on one face and two break bars on the other, containing 500 mg sulfadoxine and 25 mg pyrimethamine.



Properties: The mode of action of Fansidar is based on the reciprocal potentiation of its two components. Fansidar blocks the action of two enzymes which catalyse consecutive stages in the biosynthesis of folic acid in malaria parasites. Larger doses of the components of Fansidar are necessary if they are given independently and the effect obtained is inferior to that of the combination.

Fansidar is effective against plasmodial strains which are resistant to chloroquine and/or pyrimethamine and other antifolate preparations.

With Fansidar, the danger of emergence of resistance is reduced. Fansidar affects all developmental stages of the parasites. It has a prolonged action, yet effective plasma concentrations are rapidly attained after a single dose. Trophozoites and schizonts quickly disappear from the blood. Pre-erythrocytic stages are also affected and the gametocytes, although increased in number, are rendered much less infective for the vector. A protective effect persists for up to two to four weeks depending on the dose given and the immune state of the subject.

Indications: Malaria prophylaxis in patients who are unable to tolerate chloroquine or in high-risk patients in areas where resistance to this and other antimalarials is known to occur.

Malarial attacks and symptoms produced by: *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae*, *Plasmodium ovale*.

Dosage and administration *Prophylactic management:* The following dose of Fansidar should be taken every seven days:

Adults: 1 tablet.

Children 9–14 years: $\frac{3}{4}$ tablet.

4–8 years: $\frac{1}{2}$ tablet.

Under 4 years: $\frac{1}{4}$ tablet.

Regular dosage is important for continuous protection to be maintained. Routine measures to protect against mosquito bites should not be omitted.

Fansidar prophylaxis should be started a few days before entering the endemic area; this will enable an alternative drug to be selected in the infrequent case where Fansidar is poorly tolerated. **IMPORTANT:** Fansidar prophylaxis should be continued for four to six weeks after returning to a non-malarious area to ensure elimination of possible *falciparum* infections (malignant malaria). However, as with other prophylactic drugs, infections of benign malaria (*vivax* and *malariae* infections) may give rise to clinical attacks up to several months after return, despite regular prophylaxis. *Travelers should be instructed to report to a doctor any fever that occurs during or after their stay in a malarious area.*

Curative treatment of malaria: The appropriate amount of the drug is given in one single dose. This dose should not be repeated for at least seven days.

Adults (according to body weight): 2 to 3 tablets.

Children 9–14 years: 2 tablets.

4–8 years: 1 tablet.

Under 4 years: $\frac{1}{2}$ tablet.

In very severe cases, quinine may be added, preferably parenterally. An adequate supply of fluids and electrolytes should be maintained. Cerebral malaria may require additional corticosteroid therapy.

Fansidar tablets are for oral administration.

Contra-indications, warnings, etc

Contra-indications: Patients with known sulphonamide hypersensitivity or having severe liver or kidney dys-

function. Treatment must be immediately discontinued on the appearance of a skin rash.

Because of the risk of increased neonatal bilirubin levels, Fansidar should not be given during the week before the expected date of delivery. Like all other preparations containing sulphonamides, Fansidar is contra-indicated in premature babies and during the first few weeks of life. Both pyrimethamine and sulfadoxine are secreted in breast milk, therefore Fansidar should not be prescribed to lactating mothers.

Precautions: There is a theoretical risk of foetal malformations with all folate inhibitors given during pregnancy. If pregnancy cannot be excluded, possible risks should be balanced against the expected therapeutic benefit.

Side-effects: Fansidar is usually well tolerated. Side-effects in the form of skin rashes, gastro-intestinal disturbances or allergic-toxic skin reactions may occasionally occur as with other preparations containing sulphonamides or pyrimethamine.

Blood dyscrasias may rarely occur over long periods of administration, hence regular blood counts are recommended during long-term prophylaxis. In this respect particular care should be taken if treatment with other preparations containing folate inhibitors (e.g. cotrimoxazole, methotrexate, anticonvulsants) is given concomitantly.

Adverse reactions occurring after the administration of the sulfadoxine component of Fansidar are not normally more prolonged than those occurring after shorter-acting sulphonamides despite the continued presence of the drug in the body.

Effects of overdosage and their treatment: Treatment is symptomatic and may include forced diuresis. Vigorous gastric lavage should be carried out as early as possible after ingestion. Alkalinization of the urine may aid elimination of the sulfadoxine component of Fansidar. Possible convulsions due to the pyrimethamine components of Fansidar should be watched for and may require anticonvulsant therapy.

Hypersensitivity reactions may require treatment with steroids. Calcium folinate may be given to counteract the effects of pyrimethamine on haemopoiesis.

Pharmaceutical precautions *Storage:* No special precautions are required.

Legal category POM.

Package quantities Fansidar tablets are available in foil strips in packs of 12 and 150.

Further information Nil.

Product licence number 0031/5097.

FLUORO-URACIL ROCHE

Presentation Ampoules containing 250 mg fluoro-uracil in the form of the sodium salt in 10 ml Water for Injection BP. The ampoule solution is colourless to slightly yellow.

Capsules with powder blue opaque cap and medium orange opaque body with ROCHE printed in black along both cap and body, containing 250 mg fluorouracil.

Uses **Properties:** Fluoro-uracil Roche, a cytostatic agent, is a fluorinated pyrimidine belonging to the category of antimetabolites. It inhibits cell division by

interfering with the synthesis of deoxyribonucleic acid (DNA) and to a lesser extent of ribonucleic acid (RNA).

Indications: The palliative treatment of carcinoma.

Dosage and administration Various techniques are employed when using Fluoro-uracil Roche in the treatment of carcinoma. The following examples are given for guidance.

Adults: By the intravenous route: Fluoro-uracil Roche may be administered by intravenous infusion or by intravenous injection. Dosages are generally based on the patient's body weight. If the patient is obese or there has been a spurious gain due to oedema, ascites or other forms of fluid retention, the patient's ideal weight should be used in calculating the dosage. The initial doses given below should be reduced by one-third to a half if the following conditions are present: poor nutritional state; after major surgery (within the previous 30 days); inadequate bone-marrow function (anaemia, leucopenia with white cell count less than 3,500 per mm³, thrombocytopenia with platelet count less than 100,000 per mm³); impaired hepatic or renal function.

Initial treatment: This may be in the form of an infusion or injection, the former usually being preferred because of lesser toxicity.

Infusion: A daily dose of 15 mg/kg but not more than 1 g per infusion is diluted in 500 ml dextrose 5% solution and given by intravenous infusion at the rate of 40 drops per minute over four hours. This daily dose is given on successive days until toxicity occurs or until 12–15 g have been given. This sequence of injections constitutes a 'course' of therapy. Some patients have received up to 30 g at a maximum rate of 1 g daily. The daily dose should never exceed 1 g. An interval of four to six weeks should be allowed between any two 'courses' of Fluoro-uracil Roche.

Injection: A dose of 12 mg/kg i.v. daily on three consecutive days. If there are no signs of toxicity the patient receives 6 mg/kg i.v. on the fifth, seventh and ninth days. If toxicity occurs the signs should be allowed to regress before further doses are administered.

Maintenance therapy consists of 5–15 mg/kg i.v. once weekly.

A more recent alternative method is to give 15 mg/kg i.v. once a week throughout the course of treatment.

This obviates the need for an initial period of daily administration.

Regional perfusion intra-arterially: Continuous infusion of Fluoro-uracil Roche into an artery supplying a localised growth has been shown to produce a better result in some tumours than would have been expected from systemic administration by the intravenous route, together with a decrease in toxicity. The usual dose is 5–7.5 mg/kg daily.

In combination with radiotherapy: Irradiation combined with Fluoro-uracil Roche has been found to be useful in the treatment of certain types of metastatic lesions in the lungs and for relief of pain caused by recurrent, inoperable growth. The standard dose of Fluoro-uracil Roche is used.

By the oral route: Fluoro-uracil Roche may be administered orally using either the capsule or the ampoule solution.

Oral administration is not recommended when Fluoro-uracil Roche is being used initially as the sole agent in palliative treatment of carcinoma. Oral administration may be useful in: palliative therapy employing a combi-

nation of drugs; long-term maintenance or post-operative prophylactic therapy in weekly doses; and when therapy with Fluoro-uracil Roche is indicated, but it is impracticable to administer the drug parenterally.

The usual dosage for maintenance treatment is 15 mg/kg once weekly. For palliative therapy a more rapid onset of therapeutic effect may be obtained by giving a daily dose of 15 mg/kg on six successive days. This is followed by maintenance therapy of 15 mg/kg once weekly. The daily dose should not exceed 1 g.

The capsules should be taken with water after a meal.

The solution may be mixed with fruit juice or other similar beverages immediately before oral ingestion to mask its rather bitter taste. Multi-dose preparations must not be made up.

Children: No dosage recommendations are made for the administration of Fluoro-uracil Roche to children.

Fluoro-uracil Roche Ampoules are for intra-arterial intravenous or oral administration.

Fluoro-uracil Roche capsules are for oral administration.

Contra-indications, warnings, etc

Contra-indications: Fluoro-uracil Roche should not normally be administered to patients who are pregnant or to mothers who are breast-feeding.

Precautions: Fluoro-uracil Roche should be used with great care in debilitated patients.

The margin between the effective and toxic doses of Fluoro-uracil Roche is narrow and a therapeutic response is unlikely without some evidence of toxicity. Even with meticulous selection of patients and careful adjustment of dosage, there may be severe haematological toxicity and gastro-intestinal haemorrhage. Severe toxicity is more likely in poor-risk patients.

Treatment should be discontinued promptly whenever one of the following signs of toxicity appears: Leucopenia (WBC under 3,500 per mm³). Thrombocytopenia (platelets under 100,000 per mm³). Stomatitis (the first small ulceration at the inner margin of the lips is a sign for stopping treatment). Severe diarrhoea (frequent bowel movements and watery stools). Gastro-intestinal ulceration and bleeding. Haemorrhage at any site.

Isolated cases of angina, ECG abnormalities and rarely myocardial infarction have been reported following Fluoro-uracil administration. Caution should therefore be exercised in treating patients who experience chest pain during courses of therapy, or patients with a history of heart disease.

Side-effects: During treatment, diarrhoea, nausea and vomiting commonly occur, but may be controlled by the use of appropriate drugs.

Leucopenia usually follows an adequate course of treatment with Fluoro-uracil Roche. The lowest white cell count commonly occurs between the seventh and fourteenth days after the first dose, but it may be delayed for as long as the twentieth day. By the thirtieth day, the count has usually returned to the normal range. Because of the importance of leucopenia, the white cell count should be checked frequently throughout the course. If it falls, it is advisable to obtain differential counts. If the total is less than 2,000 per mm³, and especially if there is a granulocytopenia, it is recommended that the patient be placed in protective isolation in the hospital and treated with appropriate measures for the prevention of systemic infection.

Alopecia and dermatitis may occur in a substantial proportion of cases. Female patients particularly should

warned as to the possibility of alopecia. Since the speca seems to be reversible, special measures do not em to be indicated.

fects of overdosage and their treatment: Signs and mptoms are qualitatively similar to the side-effects, id similar measures should be taken to treat them.

harmaceutical precautions *Storage:* Fluoro-uracil oche Ampoule solution should be stored between 10°C and 30°C and should be protected from light.

No special precautions are required for Fluoro-uracil oche capsules stored in amber glass or plastic ontainers.

dditives: Fluoro-uracil Roche Ampoule solution may e diluted with Dextrose Injection or Water for Injection P immediately before parenteral use.

Fluoro-uracil Roche Ampoule solution may be diluted ith fruit juice or other similar beverages immediately efore use to facilitate ingestion by the oral route. Fluoro-racil Roche ampoule solution must not be made up into ultli-dose preparations.

egal category POM.

ackage quantities Fluoro-uracil Roche Ampoules i packings of 10.

Fluoro-uracil Roche capsules in packings of 50.

urther information It is recommended that Fluoro-racil Roche be given only by or under the supervision f a physician who is experienced in cancer chemo-herapy and who is well versed in the use of potent ntimetabolites. Because of the possibiity of severe toxic eactions, all patients should be admitted to hospital for nitial treatment.

Availability: Fluoro-uracil Roche Ampoules are available hrough hospital pharmacies for use in hospitals and ospital clinics and can be supplied to retail chemists for ispensing prescriptions for patients whose treatment as been initiated in hospital practice.

Product licence numbers

Ampoules 0031/5079
Capsules 0031/0139

GANTRISIN®

Presentation Round, white tablets with 'Gantrisin' nprinted on one face, containing 500 mg sulpha-jrazole.

White, fruit-flavoured syrup containing 591.5 mg f'-acetylsulphafurazole (equivalent to 500 mg sulpha-jrazole) in 5 ml.

Uses Properties: Gantrisin is a sulphonamide which is characterised by high therapeutic activity, ready solubil-y and low toxicity. High concentrations are obtained in re blood and urine. Its relatively high solubility, even in lightly acid media, reduces the likelihood of crystalluria nd renal complications to a minimum. It is effective gainst sulphonamide-sensitive organisms.

indications: Infections of the respiratory tract and ear, fections of the urinary tract, bacillary dysentery; skin nd soft tissue infections, prophylactic treatment of econdary infections.

Dosage and administration

	Tablets		Syrup in ml	
	Initial	Mainten- ance 4-6 hourly	Initial	Mainten- ance 4-6 hourly
Adults and older children	4	2	20	10
Children 9- 14 years	3	1½	15	7.5
5-6 years	2	1	10	5
2-4 years	1	½	5	2.5
Infants			2.5	1.25

For severe infections twice these doses are given.

Gantrisin Tablets and Syrup are for oral administration.

Gantrisin Syrup may be diluted with Syrup BP.

Maintenance of stability cannot be guaranteed when Gantrisin Syrup is diluted.

Contra-indications, warnings, etc

Contra-indications: Like all other sulphonamides, Gan-trisin is contra-indicated in premature and newborn infants during the first month of life. Because of immaturity of liver enzyme systems, such infants may have difficulty in conjugating sulphonamides normally.

Gantrisin should not be given to patients with a history of sulphonamide sensitivity.

Side-effects: Clinical experience has shown Gantrisin to be exceptionally free from serious side-effects, although, occasionally, patients may experience the reactions common to sulphonamides, including nausea, vomiting, glossitis and skin rashes. Leucopenia may rarely occur over long periods of treatment, hence regular blood counts are recommended during long-term treatment.

Effects of overdosage and their treatment: Symptoms of overdosage may include vomiting, mental and visual disturbances, petechiae, purpura and jaundice. In acute cases, haematuria, crystalluria and anuria may occur.

Treatment is symptomatic; gastric lavage may be useful. An adequate fluid intake should be maintained and the urine made alkaline. Hypersensitivity reactions may require treatment with steroids.

Pharmaceutical precautions *Storage:* All Gantrisin preparations should be protected from light. Gantrisin Tablets should be stored in well-closed containers. The recommended maximum storage temperature of Gantrisin Syrup is 25°C; the Syrup should be stored in glass containers.

Legal category POM.

Package quantities Gantrisin Tablets in packings of 100.

Gantrisin Syrup in packings of 100 ml.

Further information Nil.

Product licence numbers

Tablets 0031/5019
Syrup 0031/5020

GLUTRIL®

Presentation Round, white tablets with 'ROCHE' imprinted on one face and a single break bar on the other, containing 25 mg glibornuride.

Uses Properties: Glutril is an effective and long-acting hypoglycaemic agent. In common with other substances of the sulphonylurea group, the action of Glutril is attributed to the release of endogenous insulin from the beta cells of the pancreatic islets of Langerhans. There is evidence that Glutril also exhibits extra-pancreatic activity.

Indications: The treatment of maturity-onset diabetes mellitus which is not adequately controlled by dietary measures alone and does not require insulin. Glutril is particularly suitable for the treatment of elderly maturity-onset diabetics.

Dosage and administration Adults: The dosage of Glutril varies from individual to individual and only a guide can be given.

Patients not previously treated with hypoglycaemic agents: Treatment should begin with $\frac{1}{2}$ tablet (12.5 mg) Glutril daily taken with breakfast. This dosage may be increased to 1 tablet (25 mg) or 2 tablets (50 mg) daily if necessary. Some patients may require a higher dose to control hyperglycaemia and they may be given $2\frac{1}{2}$ (62.5 mg) or 3 tablets (75 mg) daily.

Where higher doses are required, the total daily dose should be divided. Two tablets should be administered in the morning and the remainder of the dose in the evening.

It is recommended that the dose of Glutril should not exceed 75 mg daily.

Oral hypoglycaemic agents of the biguanide type may be added to the Glutril regimen in instances where a dose of 75 mg daily is reached without satisfactory control of hyperglycaemia.

Patients previously treated with oral hypoglycaemic agents: Patients may be transferred from other oral hypoglycaemic agents to Glutril, the dosage of the latter being based on the amount of the previous therapy required to control hyperglycaemia. The following equivalents may be used as a basis:

Glutril 25 mg is equivalent to 1,000 mg tolbutamide, 250 mg chlorpropamide or 5 mg glibenclamide.

Patients previously treated with insulin: Some patients previously treated with low doses of insulin (less than 40 units daily) may be suitable for transfer to Glutril therapy.

Children: No dosage recommendations are made for the administration of Glutril to children.

Glutril Tablets are for oral administration.

Contra-indications, warnings, etc

Contra-indications: Glutril is contra-indicated in the presence of ketoacidosis and severe renal, hepatic, adrenal and thyroid dysfunction. It should not be used in patients with known intolerance to sulphonylurea derivatives. Juvenile diabetes should not be treated with Glutril. Glutril is not indicated during pregnancy.

Precautions: The action of oral hypoglycaemic agents including Glutril may be influenced by other therapeutic agents. Sulphonamides, salicylates, phenylbutazone, coumarin derivatives, adrenergic beta-receptor blocking drugs, monoamine oxidase inhibitors, cyclophosphamide, chloramphenicol, and tuberculostatics may enhance the effects of Glutril whilst thiazide diuretics, frusemide, ethacrynic acid, diazoxide, oral contraceptives containing oestrogens and corticosteroids may diminish its effects. Alcohol and tetracycline derivatives may also alter the action of Glutril.

In patients suffering from intercurrent infections or trauma, the dosage of Glutril may need to be adjusted. If

such complications are severe, diabetic control may be lost and this will necessitate the withdrawal of Glutril and the maintenance of diabetic control with insulin. Glutril should be reintroduced when the patient has recovered from the infection or trauma.

If the patient requires an anaesthetic, it is recommended that the last dose the patient would normally receive prior to the procedure be omitted and/or glucose be given as soon as the patient recovers. If major surgery is undertaken, control should be maintained with insulin and/or intravenous glucose.

Side-effects: Glutril is well tolerated and, despite its potency, hypoglycaemic reactions are rare. Skin reactions and gastro-intestinal disturbances, such as nausea and vomiting, have been observed, but these occur in only a small proportion of patients. Transient depression of the platelet count has been observed.

Effects of overdosage and their treatment: If a hypoglycaemic reaction should occur, it may be rapidly controlled by the ingestion of appropriate carbohydrates. In the event of severe hypoglycaemia occurring, intravenous glucose or intramuscular glucagon should be given. Gastric lavage may be useful if performed soon after ingestion.

Pharmaceutical precautions Storage: Glutril Tablets should be stored in their original packing. The recommended maximum storage temperature for Glutril Tablets is 30°C.

Legal category POM.

Package quantities Glutril Tablets in blister packs of 100, each pack containing 10 strips each of 10 tablets.

Further information Glutril is rapidly and almost completely absorbed, with peak blood levels being attained two to four hours after administration. The plasma half-life is in the region of eight hours. Glutril is extensively metabolised following oral administration six metabolites having been identified. The metabolites are either inactive or possess hypoglycaemic properties which are considerably less than those of the parent compound.

Product licence number 0031/0059.

KONAKION®

Presentation White, sugar-coated tablets with 'ROCHE' printed in black across one face, containing 10 mg phytomenadione.

Ampoules containing 1 mg phytomenadione in 0.5 ml. The ampoule solution is clear to opalescent greenish-yellow.

Ampoules containing 10 mg phytomenadione in 1 ml. The ampoule solution is clear to opalescent greenish-yellow.

Uses Properties: Konakion is a synthetic preparation of vitamin K₁. The presence of vitamin K (i.e. vitamin K₁ itself or substances with vitamin K activity) is essential for the formation within the body of prothrombin, factor VII, factor IX and factor X. Lack of vitamin K leads to increased tendency to haemorrhage. When an antidote to an anticoagulant is necessary it is essential to use vitamin K₁ itself, as vitamin K analogues are much less effective.

Indications: Konakion is indicated in the treatment of haemorrhage or threatened haemorrhage associated

with a low blood level of prothrombin or factor VII. The main indications are: An antidote to anticoagulant drugs of the dicoumarol type. Prevention and treatment of neonatal haemorrhage.

Dosage and administration *Adults: As an antidote to anticoagulant drugs*

For severe haemorrhage: The anticoagulant should be withdrawn and an intravenous injection of Konakion given slowly in a dose of 10–20 mg (1 or 2 ampoules). The prothrombin level should be estimated three hours later, and if the response has been inadequate, the dose should be repeated. Not more than 40 mg of Konakion should be given intravenously in 24 hours.

Less severe haemorrhage: Konakion is given orally in doses of 10–20 mg (1–2 tablets). The prothrombin level is estimated 8–12 hours later and if the response has been inadequate, the dose should be repeated. Intramuscular injections of Konakion may also be given in doses of 10–20 mg (1 or 2 ampoules), repeated if necessary.

Lowering of prothrombin to dangerous level but no haemorrhage: A dose of 5–10 mg Konakion orally may be given to bring the prothrombin level back to within safe limits. In such instances it is not usually necessary to discontinue the anticoagulant.

Other indications: Adults: 10–20 mg.

Treatment of newborn infants: Prophylactic: 1 mg by intramuscular injection.

Therapeutic: 1 mg by intramuscular injection, repeated at eight-hourly intervals if necessary.

Children: If, on the recommendation of a physician, a children's dosage is required, then it is suggested that 5–10 mg be given.

Konakion Tablets are for oral administration and should be chewed or allowed to dissolve slowly in the mouth.

Konakion Ampoules are for intramuscular or intravenous injection.

Konakion Ampoule solution should not be diluted.

Contra-indications, warnings, etc *Precautions:* Intravenous injections of Konakion must be administered slowly and should be reserved for potentially fatal haemorrhage due to overdosage of anticoagulants of the coumarin and indanedione series. Not more than 40 mg should be given by intravenous injection during a period of 24 hours.

Side-effects: The too rapid intravenous administration of vitamin K₁ has caused reactions, including flushing of the face, sweating, a sense of chest constriction, cyanosis and peripheral vascular collapse.

It has been reported that repeated intramuscular injection of vitamin K₁ preparations, usually over prolonged periods in patients with hepatic disease, may very occasionally give rise to local cutaneous and subcutaneous changes.

Pharmaceutical precautions *Storage:* Konakion Ampoule solution should be protected from light; it should not be allowed to freeze. The recommended maximum storage temperature for Konakion Ampoules is 30°C.

Konakion Tablets should be stored in well-closed containers, protected from light.

Legal category Tablets P.
Ampoules POM.

Package quantities Konakion Tablets in packings of 25.

Konakion Ampoules 1 mg in 0.5 ml and 10 mg in 1 ml in packings of 10.

Further information Large doses of Konakion should be avoided if it is intended to continue with anticoagulant therapy. If haemorrhage is severe, a transfusion of fresh whole blood may be necessary whilst awaiting the effect of the vitamin K₁. Vitamin K₁ is not an antidote to heparin.

Product licence numbers

Tablets	0031/5022
Ampoules 1 mg	0031/5023
Ampoules 10 mg	0031/5077

LARODOPA*

Presentation Round, white tablets with 'ROCHE' in a hexagon imprinted on one face and two break bars on the other, containing 500 mg levodopa.

Uses *Properties:* Larodopa is an anti-Parkinsonian agent. Levodopa is the metabolic precursor of dopamine. The latter is severely depleted in the striatum, pallidum and substantia nigra of Parkinsonian patients and it is considered that administration of Larodopa raises the level of available dopamine in these centres.

Treatment with Larodopa gives worthwhile sustained relief in about two-thirds of these patients. Akinesia usually responds first, then rigidity and then tremor. Amelioration may be seen in other symptoms, including oculogyric crises. It may take six months or more before maximal improvement is achieved.

Indications: Parkinsonism – idiopathic, post-encephalitic. Previous neurosurgery is not a contra-indication to Larodopa.

Dosage and administration Dosage and administration are variable and no more than a guide can be given.

Adults: Hospitalised patients: Initially 0.25–1 g daily in up to five divided doses immediately after food. Dosage should be increased by 0.5–1 g every three to four days until adequate improvement results or intolerable side-effects appear. If severe side-effects appear, the dosage should be gradually decreased to the maximum tolerated. Patients in whom intolerance prevents the achievement of an effective drug level will usually benefit from a change of treatment to Madopar* (levodopa combined with a peripheral decarboxylase inhibitor).

General practice patients and out-patients: Initially 0.125 g twice daily immediately after food. After one week, the dose may be increased to 0.125 g four or five times daily. Thereafter dosage should be increased at weekly intervals by 0.375 g daily, the total daily dose being given in four or five divided doses. The response of individual patients varies and some patients may tolerate a more rapid rate of increase, e.g. by 0.25–0.5 g daily at intervals of three to four days.

Improvement is usually seen in two to three weeks with the normal dosage range being 2.5–8g daily, but further improvement may occur up to six months or even longer.

When the optimum daily dosage for any particular patient has been reached, it may need to be redistributed throughout the day to meet fluctuations in the individual's requirements. Most patients find a four or five times daily dosage scheme satisfactory; some obtain a smoother effect with two-hourly administration; others, who

develop akinetic crises at particular times of the day, learn by experience the daily dosage scheme most suited to their needs.

After a period at the maximum tolerated dosage level, side-effects may slowly develop, usually in the form of involuntary movements. These generally regress without loss of therapeutic effect if the dosage is slightly reduced.

Anticholinergic drugs should be continued during Larodopa therapy. As treatment with Larodopa proceeds and the therapeutic effect is found, the dosage of the anticholinergic drugs may need to be changed. Bromocriptine may be given with Larodopa.

Children: No dosage recommendations are made for the administration of Larodopa to children.

Larodopa Tablets are for oral administration.

Contra-indications, warnings, etc

Contra-indications: Larodopa is contra-indicated in narrow-angle glaucoma (it may be used in wide-angle glaucoma provided that the intra-ocular pressure remains under control); severe psychoneuroses or psychoses.

It should not be given in conjunction with monoamine oxidase inhibitors or within two weeks of their withdrawal.

Suspicion has arisen that levodopa may activate a malignant melanoma. Therefore Larodopa should not be used in persons who have a history of, or who may be suffering from, a malignant melanoma.

Precautions: Pyridoxine (vitamin B₆) which is often included in multivitamin preparations is known to block the effects of levodopa.

Drugs which interfere with central amine mechanisms, such as rauwolfia alkaloids (reserpine), phenothiazines, thioxanthenes, butyrophenones and amphetamines, should be avoided where possible. If, however, their administration is considered essential, extreme care should be exercised and a close watch kept for any signs of potentiation, antagonism or other interactions and for any unusual side-effects.

In the event of general anaesthesia being required, Larodopa therapy may be continued as long as the patient is able to take fluids and medication by mouth. If therapy is temporarily interrupted, the usual daily dosage may be administered as soon as the patient is able to take oral medication. Whenever therapy has been interrupted for longer periods, dosage should again be adjusted gradually; however, in many cases the patient can rapidly be returned to his previous therapeutic dosage.

When other drugs must be given in conjunction with Larodopa, the patient should be carefully observed for unusual side-effects or potentiating effects.

Care should be taken when using Larodopa in the following circumstances: in endocrine, renal, hepatic, pulmonary or cardiovascular disease; particularly where there is a history of myocardial infarction and in patients with peptic ulcer; where sympathomimetic drugs may be required, e.g. bronchial asthma; where antihypertensive drugs are being used. Periodic evaluation of hepatic, haemopoietic, renal and cardiovascular functions is advised.

Patients who improve on Larodopa therapy should be advised to resume normal activities gradually as rapid mobilisation may increase the risk of injury.

Animal experiments in different species have shown no evidence of deleterious effects of Larodopa on the physiology of reproduction or embryonic development. However, the established medical principle of prescribing medicaments in early pregnancy only when absolutely indicated should be observed.

Side-effects: Tolerance to Larodopa varies widely between patients and is often related to the rate of dosage increase. Post-encephalic Parkinsonian patients tolerate the drug less well. Side-effects, usually dose-related, occur at some time in most patients. During the initiation of therapy nausea and vomiting, anorexia, weakness and hypotension, which is usually postural (but a labile hypertension may rarely be seen), are most frequent. Nausea and vomiting may be minimised by administering Larodopa immediately after food, an anti-emetic, e.g. cyclizine hydrochloride 50 mg three times daily, may also be helpful.

Psychiatric disturbances are common in Parkinsonian patients including those being treated with levodopa. They include mild elation, anxiety, agitation, insomnia, depression and dementia.

Anxiety and insomnia may be treated with a benzodiazepine drug, e.g. Valium and Mogadon respectively. Depression may be treated with tricyclic anti-depressants and ECT may be administered if appropriate. Monoamine oxidase inhibitors must not be used.

Involuntary movements, commonly in the form of oral dyskinesias, often accompanied by 'paddling' foot movements, or of the choreoathetoid type, are common, particularly on long-term administration. They are usually dose-dependent and may disappear or become tolerable after dose reduction. With long-term administration, fluctuations in the therapeutic response may be encountered. They include 'freezing' episodes ('on-off') effect and end-of-dose deterioration. Patients may be helped by dosage reduction or by giving smaller and more frequent doses.

Transient rises in SGOT, SGPT and alkaline phosphatase values have been noted; serum uric acid and blood urea nitrogen levels are occasionally increased. On some occasions the urine passed during Larodopa treatment may be altered in colour; usually red-tinged, this will turn dark on standing. These changes are due to metabolites and are no cause for concern.

Effects of overdosage and their treatment: Symptoms of overdosage are qualitatively similar to the side-effects but may be of greater magnitude.

Treatment should include gastric lavage, general supportive measures, intravenous fluids and the maintenance of an adequate airway. Electrocardiographic monitoring should be instituted and the patient carefully observed for the possible development of arrhythmias. If necessary, anti-arrhythmic therapy should be given and other symptoms treated as they arise.

Pharmaceutical precautions *Storage:* Larodopa Tablets should be stored in well-closed containers, protected from light.

Legal category POM.

Package quantities Larodopa Tablets in packings of 200.

Further information Nil.

Product licence number 0031/5063.

LEXOTAN®

Presentation Pink, hexagonal biconvex tablets having L3 imprinted on one face and a single break bar on the other, containing 3 mg bromazepam.

Uses *Properties:* Lexotan is a pyridylbenzodiazepine compound with anxiolytic properties.

Indications: Lexotan is indicated for the short-term treatment of anxiety and associated symptoms such as tension and agitation.

Dosage and administration Adults: It is important that the dosage of Lexotan be determined on an individual basis. The usual doses are: Mild to moderate anxiety 3–6 mg three times daily; severe anxiety states 6–12 mg three times daily.

Some patients may be more sensitive to the effects of Lexotan and may respond to 1.5 mg three times daily.

In exceptionally severe anxiety states, in hospitalised patients, up to 60 mg daily may be given in divided doses.

Maximum daily dosage 60 mg.

Elderly: Elderly patients are more sensitive to the actions of Lexotan. The safety of Lexotan for use in the elderly has not been established and therefore its use should be avoided.

Children: Lexotan is not for paediatric use.

Lexotan tablets are for oral administration.

Contra-indications, warnings, etc

Contra-indications: Patients with known sensitivity to benzodiazepines; acute pulmonary insufficiency; respiratory depression.

Precautions: In patients with chronic pulmonary insufficiency, and in patients with chronic renal or hepatic disease, dosage may need to be reduced. The use of Lexotan during pregnancy should be avoided.

The administration of high doses or prolonged administration of low doses of benzodiazepines in the last trimester of pregnancy or during labour has been reported to produce irregularities in the foetal heart, and hypotonia, poor sucking and hypothermia in the neonate.

Benzodiazepines have been detected in breast milk. If possible, the use of Lexotan should be avoided during lactation.

If Lexotan is combined with centrally-acting drugs such as neuroleptics, tranquillisers, antidepressants, hypnotics, analgesics and anaesthetics, the sedative effects may be intensified.

Patients should be advised that, like all medicaments of this type, Lexotan may modify patients' performance at skilled tasks (driving, operating machinery, etc.) to a varying degree depending upon dosage and individual susceptibility. Patients should further be advised that alcohol may intensify any impairment, and should therefore be avoided during treatment.

The dependence potential of the benzodiazepines is low but this increases when high doses are used, especially when given over long periods. This is particularly so in patients with a history of alcoholism or drug abuse or in patients with marked personality disorders. Regular monitoring in such patients is essential, routine repeat prescriptions should be avoided and treatment should be withdrawn gradually. Symptoms such as depression, nervousness, rebound insomnia, irritability, sweating and diarrhoea have been reported following abrupt cessation of treatment with normal therapeutic doses. In rare instances, withdrawal following excessive dosages may produce confusional states, psychotic manifestations and convulsions.

Abnormal psychological reactions to benzodiazepines have been reported. Rare behavioural effects include paradoxical aggressive outbursts, excitement, confusion, and the uncovering of depression with suicidal tendencies.

Side-effects: Common adverse effects include drowsiness, sedation, unsteadiness and ataxia; these are dose-related and may persist into the following day, even after a single dose. Drowsiness may be a particular problem when Lexotan is used in higher dosage in some patients, especially if they are unused to this form of therapy. Sensitivity to central depressant drugs usually increases with age, and older subjects, particularly those with organic brain changes, may be more liable to develop confusion; in these patients the dosage of Lexotan should be kept to a minimum.

Other adverse effects are rare and include headache, vertigo, hypotension, gastro-intestinal upsets, skin rashes, visual disturbances, changes in libido, and urinary retention. Isolated cases of blood dyscrasias and jaundice have also been reported.

Treatment of overdosage: When taken alone in overdosage Lexotan presents few problems in management. Signs may include drowsiness, ataxia and dysarthria, with coma in severe cases. Treatment is symptomatic. Gastric lavage is useful only if performed soon after ingestion. There is no specific antidote to Lexotan.

When taken with centrally-acting drugs, especially alcohol, the effects of overdosage are likely to be more severe and, in the absence of supportive measures, may prove fatal.

Pharmaceutical precautions Storage: Lexotan tablets should be stored in well-closed containers.

Legal category POM.

Package quantities Lexotan tablets 3 mg in packings of 100 and 500.

Further information Lexotan is rapidly absorbed from the gastro-intestinal tract. The mean half-life for elimination of Lexotan in man is about 16 hours. Metabolites of Lexotan do not contribute significantly to the effects of the drug.

Clinically, the anxiolytic effect of bromazepam 3 mg is generally equivalent to that of diazepam 5 mg.

Product licence number 0031/0128.

LORFAN®

Presentation Ampoules containing 1 mg levallorphan tartrate in 1 ml. The ampoule solution is colourless.

Uses Properties: Levallorphan is strongly antagonistic to some of the characteristic effects of morphine and of similar compounds such as Dromoran® Roche and pethidine. In small doses levallorphan counteracts the respiratory depression caused by morphine-like drugs without appreciably altering their analgesic effect. In large doses the analgesic effect is also antagonised. Levallorphan itself has little or no analgesic activity, nor does it behave in other respects like morphine. There is evidence that it does not cause addiction.

Indications: Narcotic-induced respiratory depression.

Dosage and administration Adults: Anaesthesia: To restore respiration which has been depressed by the administration of morphine-like drugs, 0.5–1 mg intravenously, repeated if necessary at intervals of three to five minutes until normal respiration is achieved.

To prevent respiratory depression, Lorfan is given either before or with the analgesic. Lorfan 0.3–0.5 mg for each 15 mg morphine. Lorfan 1–1.5 mg for each 100 mg

pethidine. Lofran 0.2–0.3 mg for each 2 mg Dromoran* Roche.

Obstetrics: To prevent respiratory depression in the infant, Lofran can be administered intramuscularly to the mother together with each dose of the analgesic. Clinical experience has been mainly with Lofran and pethidine. Dose, Lofran 1.25 mg with each 100 mg pethidine.

To restore respiration in infants with respiratory depression following the administration of pethidine to the mother, Lofran 0.05–0.25 mg may be injected into the umbilical vein immediately after delivery.

Treatment of overdosage of a narcotic: Lofran 1–2 mg intravenously. If adequate spontaneous respiration is not obtained within 5–10 minutes, one-half the initial dose may be repeated. It may be necessary to repeat the dose again some hours later, if signs of narcotic intoxication recur.

Lofran Ampoules are for intravenous injection.

Lofran Ampoule solution may be diluted with Water for Injection.

Maintenance of stability cannot be guaranteed when Lofran Ampoule solution is diluted.

Contra-indications, warnings, etc Precautions: With Lofran, as with other drugs acting on the central nervous system, patients should be instructed to avoid alcohol while under treatment, since the individual response cannot be foreseen. Like all medicaments of this type, Lofran may modify patients' reactions (driving ability, operation of machinery, etc) to a varying extent, depending on dosage and individual susceptibility.

Side-effects: Lofran used alone may produce some respiratory depression.

Effects of overdosage and their treatment: Symptoms of overdosage may include drowsiness, coma, sweating, restlessness, bradycardia, hypotension and miosis. When given alone Lofran may cause psychotic disturbances and respiratory depression.

The airway should be maintained and artificial respiration and oxygen administered. Use of anaesthetics may be of some aid but should not be depended on to maintain respiration.

Pharmaceutical precautions *Storage:* Lofran Ampoules should be protected from light.

Legal category POM.

Package quantities Lofran Ampoules in packings of 10.

Further information Lofran plus pethidine in the proportions of 1.25 mg Lofran to 100 mg pethidine is available as Pethilofran*. See separate data sheet.

Product licence number 0031/5031.

MADOPAR*

Presentation Madapar 62.5 Capsules with blue cap and grey body with 'ROCHE' printed in black on both cap and body, containing 50 mg levodopa and 14.25 mg benserazide hydrochloride (equivalent to 12.5 mg of the base).

Madapar 125 Capsules with blue cap and pink body with 'ROCHE' printed in black on both cap and body, containing 100 mg levodopa and 28.5 mg benserazide hydrochloride (equivalent to 25 mg of the base).

Madapar 250 Capsules with blue cap and caramel body with 'ROCHE' printed in black on both cap and

body, containing 200 mg levodopa and 57 mg benserazide hydrochloride (equivalent to 50 mg of the base).

Uses Properties: Madapar is an anti-Parkinsonian agent. Levodopa is the metabolic precursor of dopamine. The latter is severely depleted in the striatum, pallidum and substantia nigra of Parkinsonian patients and it is considered that administration of levodopa raises the level of available dopamine in these centres. However, conversion of levodopa into dopamine by the enzyme dopa decarboxylase also takes place in extra-cerebral tissues. As a consequence the full therapeutic effect may not be obtained and side-effects occur.

Administration of a peripheral decarboxylase inhibitor, which blocks the extracerebral decarboxylation of levodopa, in conjunction with levodopa has significant advantages: these include reduced gastro-intestinal side-effects, a more rapid response at the initiation of therapy and a simpler dosage regimen.

Madapar is a combination of levodopa and benserazide in the ratio of 4:1 which in clinical trials has been shown to be the most satisfactory.

Indications: Parkinsonism – idiopathic, post-encephalitic. Previous neurosurgery is not a contra-indication to Madapar.

Dosage and administration Dosage and administration are variable and no more than a guide can be given.

Patients not previously treated with levodopa: The initial recommended dose is 1 capsule of Madapar 125 twice daily. This dose may be increased by 1 capsule per day every third or fourth day until a full therapeutic effect is obtained, or side-effects supervene. Individual patient response varies, and some patients may only tolerate a slower rate of increase, e.g. 1 capsule of Madapar 125 at weekly intervals.

The effective dose usually lies within the range of 4–8 capsules of Madapar 125 (2–4 capsules of Madapar 250) daily in divided doses, most patients requiring no more than 6 capsules of Madapar 125 daily.

Madapar 62.5 capsules may be used to facilitate adjustment of dosage to the needs of the individual patient. In some elderly patients, it may suffice to initiate treatment with one capsule of Madapar 62.5 once or twice daily, increasing by one capsule every third or fourth day. Patients who experience fluctuations in response may also be helped by dividing the dosage into smaller, more frequent doses with the aid of Madapar 62.5 capsules.

Optimal improvement is usually seen in one to three weeks, but the full therapeutic effect of Madapar may not be apparent for some time. It is advisable, therefore, to allow several weeks to elapse before contemplating dosage increments above the average dose range. If satisfactory improvement is still not achieved, the dose of Madapar may be increased, but with caution. It is rarely necessary to give more than 10 capsules of Madapar 125 (5 capsules of Madapar 250) per day.

Treatment should be continued for at least six months before failure is concluded from the absence of a clinical response.

Madapar 250 Capsules are only for maintenance therapy once the optimal dosage has been determined using Madapar 125 Capsules.

Patients previously treated with levodopa: The following procedure is recommended:

Levodopa alone should be discontinued and Madapar started on the following day. The patient should be initiated on a total of one less Madapar 125 Capsule

daily than the total number of 500 mg levodopa tablets or capsules previously taken (for example, if the patient had previously taken 2 g levodopa daily, then he should start on 3 capsules Madopar 125 daily on the following day).

Observe the patient for one week and then, if necessary, increase the dosage in the manner described for new patients.

Patients previously treated with other levodopa/decarboxylase inhibitor combinations: Previous therapy should be withdrawn for 12 hours. Madopar therapy should then be started with one capsule of Madopar 125 twice daily. This dose may then be increased in the manner described for patients not previously treated with levodopa.

Other anti-Parkinsonian drugs, e.g. anticholinergics, should be continued during Madopar therapy. As treatment with Madopar proceeds and the therapeutic effect becomes apparent, the dosage of the other drugs may need to be changed. Bromocriptine may be given with Madopar.

Children: Not to be given to patients under 25 years of age; therefore, no dosage recommendations are made for the administration of Madopar to children.

Madopar Capsules are for oral administration.

Madopar Capsules must always be swallowed whole. They should be taken with, or immediately after, meals.

Contra-indications, warnings, etc

Contra-indications: Madopar is contra-indicated in narrow-angle glaucoma (it may be used in wide angle glaucoma provided that the intra-ocular pressure remains under control); severe psychoneuroses or psychoses.

It should not be given in conjunction with monoamine oxidase inhibitors, or within two weeks of their withdrawal.

It should not be given to patients under 25 years of age.

It should not be given to pregnant women; should a woman become pregnant, she should immediately discontinue therapy.

Suspicion has arisen that levodopa may activate a malignant melanoma. Therefore Madopar should not be used in persons who have a history of, or who may be suffering from, a malignant melanoma.

Precautions: Drugs which interfere with central amine mechanisms, such as rauwolfia alkaloids (reserpine), phenothiazines, thioxanthenes, butyrophenones and amphetamines, should be avoided where possible. If, however, their administration is considered essential, extreme care should be exercised and a close watch kept for any signs of potentiation, antagonism or other interactions and for any unusual side-effects.

In the event of general anaesthesia being required, Madopar therapy may be continued as long as the patient is able to take fluids and medication by mouth. If therapy is temporarily interrupted, the usual daily dosage may be administered as soon as the patient is able to take oral medication. Whenever therapy has been interrupted for longer periods, dosage should again be adjusted gradually; however, in many cases the patient can rapidly be returned to his previous therapeutic dosage.

When other drugs must be given in conjunction with Madopar, the patient should be carefully observed for unusual side-effects or potentiating effects. Pyridoxine (vitamin B₆) may be given with Madopar, but not with levodopa alone.

Care should be taken when using Madopar in the

following circumstances: in endocrine, renal, pulmonary or cardiovascular disease; particularly where there is a history of myocardial infarction or arrhythmia, hepatic disorder, peptic ulcer or osteoporosis; where sympathomimetic drugs may be required, e.g. bronchial asthma; where antihypertensive drugs are being used.

Periodic evaluation of hepatic, haemopoietic, renal and cardiovascular functions is advised.

Patients who improve on Madopar therapy should be advised to resume normal activities gradually as rapid mobilisation may increase the risk of injury.

Side-effects: Tolerance to Madopar varies widely between patients and is often related to the rate of dosage increases. Side-effects such as nausea and vomiting, which are frequently observed during the initial stages of levodopa therapy, are much less common in patients treated with Madopar. Also, cardiovascular disturbances such as arrhythmias and orthostatic hypotension may occur, but are less frequent than in patients treated with levodopa alone.

Psychiatric disturbances are common in Parkinsonian patients including those being treated with levodopa. They include mild elation, anxiety, agitation, insomnia, depression and dementia.

Anxiety and insomnia may be treated with a benzodiazepine drug, e.g. Valium and Mogadon respectively. Depression may be treated with tricyclic anti-depressants and ECT may be administered if appropriate. Monoamine oxidase inhibitors must not be used.

Involuntary movements, commonly in the form of oral dyskinesias, often accompanied by 'paddling' foot movements, or of the choreoathetoid type, are common, particularly on long-term administration. They are usually dose-dependent and may disappear or become tolerable after dose reduction.

With long-term administration, fluctuations in the therapeutic response may be encountered. They include 'freezing' episodes ('on-off' effect) and end-of-dose deterioration. Patients may be helped by dosage reduction or by giving smaller and more frequent doses.

Transient rises in SGOT, SGPT and alkaline phosphatase values have been noted; serum uric acid and blood urea nitrogen levels are occasionally increased.

Effects of overdosage and their treatment: Symptoms of overdosage are qualitatively similar to the side effects but may be of greater magnitude.

Treatment should include gastric lavage, general supportive measures, intravenous fluids and the maintenance of an adequate airway. Electrocardiographic monitoring should be instituted and the patient carefully observed for the possible development of arrhythmias. If necessary, anti-arrhythmic therapy should be given and other symptoms treated as they arise.

Pharmaceutical precautions *Storage:* Madopar capsules should be protected from moisture.

Legal category POM.

Package quantities Madopar 62.5 Capsules containing 50 mg levodopa and 12.5 mg benserazide in bottles of 100.

Madopar 125 Capsules containing 100 mg levodopa and 25 mg benserazide in bottles of 100.

Madopar 250 Capsules containing 200 mg levodopa and 50 mg benserazide in bottles of 100.

Further information Nil.

Product licence numbers

Madopar 62.5 Capsules	0031/0125
Madopar 125 Capsules	0031/0073
Madopar 250 Capsules	0031/0074

MADRIBON*

Presentation Round, white tablets with 'Roche' imprinted on one face with two break bars on the other, containing 500 mg sulphadimethoxine.

Uses Properties: Madribon is a long-acting sulphonamide. Therapeutic blood levels are maintained for at least 24 hours after each dose; consequently, a single daily dose is sufficient.

Madribon differs from most sulphonamides in that only small amounts are conjugated in the form of the acetyl derivative, whereas the greater part is conjugated as glucuronide, and excreted in the urine as such. This glucuronide, unlike the acetyl derivatives of most sulphonamides, is highly soluble and, as a result, the risk of renal complications with Madribon is minimal.

Indications: Madribon is indicated in all infections due to organisms which are sulphonamide-sensitive. Trials have shown Madribon to be very effective in the treatment of: bronchitis; ear, nose and throat infections; pneumonia; infections of the urinary tract; bacillary dysentery; skin and soft tissue infections; prophylactic treatment of secondary infections.

Dosage and administration

	<i>Tablets</i>	
	<i>Initial</i>	<i>Maintenance 24-hourly</i>
Adults and older children	4	2
Children		
9-14 years	3	1½
5-8 years	2	1
2-4 years	1	½

For mild infections half the above doses are given. For long-term prophylaxis half the maintenance dose is given daily.

Madribon Tablets are for oral administration.

Contra-indications, warnings, etc

Contra-indications: Like all other sulphonamides, Madribon is contra-indicated in premature and new-born infants during the first weeks of life and in pregnant women during the week before term.

Madribon should not be given to patients with a history of sulphonamide sensitivity. As with many other compounds, rare, but sometimes serious, allergo-toxic skin conditions have been reported in connection with long-acting sulphonamides. Although no direct evidence exists to associate Madribon as the causative agent of such conditions, if a rash occurs during therapy, treatment should be immediately discontinued.

Side-effects: Clinical experience has shown Madribon to be exceptionally free from serious side-effects although, occasionally, patients may experience the reactions common to sulphonamides, including nausea, vomiting, glossitis and skin rashes. Leucopenia may rarely occur over long periods of treatment, hence regular blood counts are recommended during long-term treatment.

Effects of overdosage and their treatment: Symptoms of overdosage may include vomiting, mental and visual disturbances, petechiae, purpura and jaundice. In severe cases, haematuria, crystalluria and anuria may occur, but this is less likely with Madribon than with other sulphonamides since it is excreted mainly as a soluble glucuronide.

Treatment is symptomatic; gastric lavage may be useful. An adequate fluid intake should be maintained and the urine made alkaline. Hypersensitivity reactions may require treatment with steroids.

Pharmaceutical precautions Storage: Madribon Tablets should be stored in well-closed containers, protected from light.

Legal category POM.

Package quantities Madribon Tablets in packings of 50.

Further information Nil.

Product licence number 0031/5032.

MARPLAN*

Presentation Round, pink tablets with 'ROCHE' imprinted across one face with a single break bar on the other, containing 10 mg isocarboxazid.

Uses Properties: Marplan is a potent antidepressant; it is a monoamine oxidase inhibitor, effective in small doses. Its action is thought to be related to its effect on physiological amines such as serotonin and noradrenaline, and this effect is cumulative and persistent.

Indications: Depressive states.

Dosage and administration Adults: A daily dose of 30 mg should be given until the optimal effect is obtained. The maximal effect is only observed after a period varying from one to four weeks. Once this takes place, the dose should be reduced to the lowest possible amount sufficient to maintain the improvement. Clinical experience has shown this to be 10 to 20 mg daily.

Children: No dosage recommendations are made for the administration of Marplan to children.

Marplan Tablets are for oral administration.

Contra-indications, warnings, etc Precautions: Some monoamine oxidase inhibitors have occasionally caused jaundice in patients, therefore frequent examination of the patient should be carried out. If there is any evidence of a toxic reaction, the drug should be withdrawn immediately. The drug should be used cautiously in patients with impaired renal function, to prevent accumulation taking place.

Monoamine oxidase inhibitors potentiate a number of drugs and foods. These include pethidine and other narcotics and depressants, stimulants (including amphetamines), sympathomimetics and vasopressors, local anaesthetics, ganglion-blocking agents, imipramine and amitriptyline derivatives, levodopa, hypotensive compounds, including reserpine, diuretics, and some tranquillisers. Patients should be warned to avoid foodstuffs and beverages with a high amine content, including: cheese, hydrolysed protein extracts, Chianti wines and other foods which are not fresh and are fermented, 'hung', 'matured' or otherwise subject to protein degradation before consumption. As Marplan is a monoamine oxidase inhibitor due consideration should be given to these observations.

The effects of monoamine oxidase inhibitors may persist for up to two weeks and, therefore, an interval of one to two weeks should be allowed after treatment with Marplan before the administration of antidepressants with a different mode of action. If dentistry, surgery or a change in treatment of a patient becomes necessary during that time, the fact that monoamine oxidase inhibitors have been prescribed previously should be known and taken into account. On the other hand, Marplan may be given immediately following treatment with antidepressants having a different mode of action.

In restless, agitated patients, Marplan may precipitate states of excessive excitement.

With Marplan, as with other drugs acting on the central nervous system, patients should be instructed to avoid alcohol while under treatment, since the individual response cannot be foreseen. Like all medicaments of this type, Marplan may modify patients' reactions (driving ability, operation of machinery, etc) to a varying extent, depending on dosage and individual susceptibility.

The established medical principle of prescribing medicaments in early pregnancy only when absolutely indicated should be observed.

Side-effects: In general, Marplan is well tolerated by the majority of patients. If side-effects occur they are those common to the group of monoamine oxidase inhibitors and include orthostatic hypotension, dizziness, constipation, overactivity, insomnia, dryness of the mouth, and blurred vision. Peripheral oedema and rashes have occasionally been observed.

Effects of overdose and their treatment: The primary symptoms of overdose include dizziness, ataxia and irritability. In acute cases, hypotension or hypertension, tachycardia, pyrexia, psychotic manifestations, convulsions, respiratory depression and coma may occur and continue for 8–14 days before recovery.

Gastric lavage should be performed soon after ingestion and intensive supportive therapy carried out. Sympathomimetic agents should not be given to treat hypotension, but plasma expanders may be used in severe cases. Hypertensive crises may be treated by pentolinium or phentolamine, severe shock with hydrocortisone. Haemodialysis is of value in very severe cases.

Pharmaceutical precautions *Storage:* Marplan Tablets should be stored in well-closed containers.

The recommended maximum storage temperature is 25°C.

Legal category POM.

Package quantities Marplan Tablets in packings of 50.

Further information Nil.

Product licence number 0031/5080.

MARSILID*

Presentation Round, light orange tablets with 'm' imprinted on one face and a single break bar on the other, containing 39.1 mg iproniazid phosphate (equivalent to 25 mg iproniazid).

Round, pale yellow tablets with 'm' imprinted on one face and a double break bar on the other, containing 78.2 mg iproniazid phosphate (equivalent to 50 mg iproniazid).

Uses *Properties:* Mersilid is a potent antidepressant: it is a monoamine oxidase inhibitor. Its action is thought to be related to its effects on physiological amines such as serotonin and noradrenaline, and this effect is cumulative and persistent.

Indications: Treatment of the symptoms of severe depressive illness.

Dosage and administration *Adults:* A single daily dose of 100 to 150 mg should be given, normally in the morning, until improvement is observed. Thereafter the dose may be reduced gradually until the patient is taking a maintenance dose as small as 25 or 50 mg daily.

Children: Mersilid is not indicated for paediatric use. Mersilid tablets are for oral administration.

Contra-indications, warnings, etc

Contra-indications: Mersilid is contra-indicated in patients with any impairment of hepatic function, cerebrovascular disorders or severe cardiovascular disease, and in those with actual or suspected phaeochromocytoma.

Like other monoamine oxidase inhibitors, Mersilid potentiates the action of a number of drugs and foods. Patients being treated with a monoamine oxidase inhibitor should not receive indirectly-acting sympathomimetic agents, such as amphetamines, metaraminol, fenfluramine or similar anorectic agents, ephedrine or phenylpropanolamine (contained in many proprietary 'cold-cure' medications), dopamine or levodopa. Patients should also be warned to avoid foodstuffs and beverages with a high tyramine content: matured cheeses (including processed cheeses), hydrolysed yeast or meat extracts, heavy red wines such as Chianti, and other foods which are not fresh and are fermented, pickled, 'hung', 'matured' or otherwise subject to protein degradation before consumption. Broad bean pods (which contain levodopa) and banana skins may also present a hazard.

In extreme cases interactions may result in severe hypertensive episodes. Mersilid should therefore be discontinued immediately upon the occurrence of palpitations or frequent headaches.

Circulatory collapse, respiratory depression, central excitation and coma have been reported from the combination of monoamine oxidase inhibitors and pethidine. If a narcotic analgesic is required in a patient receiving Mersilid, a drug other than pethidine should be used, initially in a small dose, which should be increased cautiously.

Mersilid should not be administered together with, or immediately following, other monoamine oxidase inhibitors or tricyclic antidepressants. An interval of two weeks should be allowed after treatment with Mersilid before the administration of another antidepressant or any other drug which may interact.

Mersilid should be discontinued for at least two weeks prior to elective surgery requiring general anaesthesia.

Precautions: The use of Mersilid should be restricted to patients who have failed to respond to other forms of treatment and, in the first instance, should be initiated in hospital.

Concurrent administration of Mersilid with other central nervous system depressants (especially barbiturates and phenothiazines), stimulants, local anaesthetics, ganglion-blocking agents and other hypotensives (including methyldopa and reserpine), diuretics, vasopressors, anticholinergic drugs and hypoglycaemic agents lead to potentiation of their effects. This should be borne in mind if dentistry, surgery or a change in treatment of

a patient becomes necessary during treatment with Marsilid.

All patients taking Marsilid should be warned against self-medication with proprietary 'cold-cure' preparations (including nasal decongestants) and advised of the dietary restrictions listed under 'Contra-indications'.

With Marsilid, as with other drugs acting on the central nervous system, patients should be instructed to avoid alcohol while under treatment, since the individual response cannot be foreseen. Like all medicaments of this type, Marsilid may modify patients' reactions (driving ability, operation of machinery, etc) to a varying extent, depending on dosage and individual susceptibility.

Hepatic complications and jaundice are known to have occurred during treatment with Marsilid, therefore regular monitoring of liver function should be carried out in patients who receive the drug. If there is any evidence of a hepatotoxic reaction, Marsilid should be withdrawn immediately.

The drug should be used cautiously in patients with impaired renal function, to prevent accumulation taking place, and also in the elderly or debilitated and those with cardiovascular disease, diabetes or blood dyscrasias.

In restless or agitated patients, Marsilid may precipitate states of excessive excitement. Higher doses of Marsilid may precipitate epileptiform fits, especially in patients with a history of epilepsy.

Marsilid should not be used in pregnancy unless there are compelling reasons to do so. No information on transfer of the drug into breast milk is available.

Side-effects: Side-effects caused by Marsilid are those common to the group of monoamine oxidase inhibitors. The most frequently reported have been orthostatic hypotension, associated in some patients with disturbances in cardiac rhythm, peripheral oedema, complaints of dizziness, dryness of the mouth, nausea and vomiting, constipation, difficulty in micturition, impairment of erection and ejaculation, blurred vision, insomnia, drowsiness, headaches, weakness and fatigue. These side-effects can usually be controlled by dosage reduction. There have been less frequent reports of sweating, paraesthesiae, hyperreflexia, agitation, overactivity, muscle tremor, confusion and other behavioural changes, and skin rashes. Peripheral neuritis has sometimes been observed and can be prevented by giving pyridoxine (vitamin B6) to patients on high doses of Marsilid. Response to Marsilid may be accompanied by increased appetite and weight gain.

Treatment of overdosage: The primary symptoms of overdosage include dizziness, ataxia and irritability. In acute cases, hypotension or hypertension, tachycardia, pyrexia, psychotic manifestations, convulsions, respiratory depression and coma may occur and continue for eight to fourteen days before recovery.

Gastric lavage should be performed soon after ingestion and intensive supportive therapy carried out.

Sympathomimetic agents should not be given to treat hypotension but plasma expanders may be used in severe cases. Hypertensive crises may be treated by pentolinium or phentolamine, severe shock with hydrocortisone. Diazepam may be given to control convulsions or severe excitement. Dialysis is of value in eliminating the drug in severe cases.

Pharmaceutical precautions *Storage:* Marsilid Tablets should be stored in well-closed containers. The recommended maximum storage temperature is 30°C.

Legal category POM.

Package quantities Marsilid Tablets 25 mg in packings of 50.

Marsilid Tablets 50 mg in packings of 100.

Further information Nil.

Product licence numbers

Tablets 25 mg 0031/5068

Tablets 50 mg 0031/5069.

MESTINON*

Presentation Round, white tablets with 'ROCHE' imprinted across one face with two break bars on the other, containing 60 mg pyridostigmine bromide.

Ampoules containing 1 mg pyridostigmine bromide in 1 ml. The ampoule solution is colourless to faintly yellow.

Uses *Properties:* Mestinon is an antagonist to cholinesterase, the enzyme which normally destroys acetylcholine. The action of Mestinon can briefly be described, therefore, as the potentiation of naturally occurring acetylcholine. Mestinon has a more prolonged action than Prostigmin* (neostigmine), although it is somewhat slower to take effect; because it has a weaker 'muscarinic' action than Prostigmin, it is usually much better tolerated by myasthenic patients in whom the longer action is also an advantage.

Indications: Myasthenia gravis; intestinal atony; paralytic ileus; post-operative distension; heartburn of pregnancy.

Dosage and administration

Myasthenia gravis: Adults: A daily dose of 5–20 tablets by mouth or 2–5 mg by injection is commonly given, but doses higher than these may be needed by some patients. The daily doses should be spread over the day and taken at times when they are most required.

Myasthenia gravis: Children: If, on the recommendation of a physician, a children's dosage is required then the following is given as a guide:

Newborn infants: Usually 0.2–0.4 mg by injection or 5–10 mg orally every four hours.

Older children: Trial dose of 10 mg orally, increasing by 5 mg increments until a satisfactory result obtains.

Other indications: The usual adult dose is 1–4 tablets by mouth or 1–5 mg by subcutaneous or intramuscular injection; the frequency of dosage may be varied according to the needs of the patient.

Children: If, on the recommendation of a physician, a children's dosage is required, then 15–60 mg by mouth or 0.25–1 mg by injection may be given.

Mestinon Tablets are for oral administration.

Mestinon Ampoules are for intramuscular, intravenous or subcutaneous injection.

Mestinon Ampoule solution may be diluted with Water for Injection.

Maintenance of stability cannot be guaranteed when Mestinon Ampoule solution is diluted.

Contra-indications, warnings, etc *Precautions:* Care should be taken in administering Mestinon to patients with bronchial asthma.

Side-effects: These may include nausea and vomiting, increased salivation, diarrhoea and abdominal cramps.

Effects of overdosage and their treatment: Signs of overdosage due to muscarinic effects may include abdominal cramps, increased peristalsis, diarrhoea, nausea and vomiting, increased bronchial secretions, salivation, diaphoresis and miosis. Nicotinic effects consist of muscular cramps, fasciculations and general weakness. Bradycardia and hypotension may also occur. Artificial respiration should be instituted if respiratory depression is severe. Atropine sulphate 1–2 mg intravenously is an antidote to the muscarinic effects.

Pharmaceutical precautions *Storage:* Recommended maximum storage temperature for Ampoules and Tablets is 25°C. Mestison Tablets and Ampoules should be protected from light. Mestison Tablets should be protected from moisture.

Legal category POM.

Package quantities Mestison Tablets in packings of 100.

Mestison Ampoules in packings of 10.

Further information Nil.

Product licence numbers

Tablets 0031/5036.

Ampoules 0031/5037.

MOGADON®

Presentation Round, white tablets with 'ROCHE' and two semi-circles imprinted on one face with a single break bar on the other, containing 5 mg nitrazepam.



Capsules with black cap and translucent purple body with 'ROCHE 5' printed in red along both cap and body, containing 5 mg nitrazepam.

Uses Properties: Mogadon rapidly induces sleep lasting six to eight hours, by shielding from sensory and emotional stimuli those centres in the brain responsible for maintaining wakefulness. Unlike non-benzodiazepine hypnotics, Mogadon does not force the onset of sleep by a generalised depression of all the brain structures but induces sleep similar to the normal pattern. The sleeper may be readily aroused and yet will be able to return to sleep again without difficulty.

Indications: Sleep disturbances due to anxiety, worry, tension, stress, depression, irritability, overwork and conflict.

Mogadon is particularly valuable in the treatment of sleep disturbances of the middle-aged patient; insomnia in the elderly patient where the use of barbiturates tends to cause confusion; organic sleep disturbances when administered in conjunction with specific therapy.

Dosage and administration *Adults:* 5 mg before retiring. This average dose may if necessary be increased up to 10 mg for out-patients and up to 20 mg for in-patients.

Elderly patients: 2.5–5 mg.

The tablets can be chewed, swallowed whole or taken in liquid.

Children: If, on the recommendation of a physician, a child's dosage is required, it is suggested that 2.5–5 mg may be given.

Mogadon Tablets and Capsules are for oral administration.

Contra-indications, warnings, etc *Precautions:* Potentiation of alcohol by Mogadon has not been demonstrated, but, as with all other drugs acting on the central nervous system, patients should be instructed to avoid taking alcohol while under treatment with Mogadon, since the individual response cannot be foreseen. Like all medicaments of this type, Mogadon may modify patients' reactions (driving ability, operation of machinery, etc) to a varying extent, depending on dosage and individual susceptibility. The rate of metabolism of Mogadon will normally ensure that such effects do not persist to the morning.

The use of high doses of benzodiazepines, especially over prolonged periods, may sometimes lead to dependence, particularly in patients with a history of alcoholism or drug abuse. Treatment in these cases should be withdrawn gradually.

Results obtained in trials with several generations of mice, rats, rabbits and dogs indicate that no danger of teratogenic effects need be expected from therapeutic doses of Mogadon. Nevertheless, the established medical principle of prescribing medicaments in early pregnancy only when absolutely indicated should be observed.

As with many other medications, a reduced dosage may suffice in the elderly. Therefore, treatment should be initiated with a 2.5 mg dose until the response can be judged. Similar care should be taken in patients with respiratory depression.

Side-effects: Mogadon is well tolerated. Minor side-effects such as fatigue and morning drowsiness may occasionally occur. Prolonged and extensive clinical and laboratory investigations have revealed no significant changes in the blood picture or liver function.

Effects of overdosage and their treatment: Reported experience of inadvertent or deliberate overdosage indicates that this presents virtually no problem. Doses of up to approximately 550 mg (110 times the usual dose) have produced no long-term ill-effects. The primary symptoms of overdosage are drowsiness, dizziness, ataxia and slurred speech.

Treatment is symptomatic, but gastric lavage may be useful if performed soon after ingestion.

Pharmaceutical precautions *Storage:* Recommended maximum storage temperature for Mogadon Tablets and Capsules is 30°C. Mogadon Tablets and Capsules should be protected from light.

Legal category POM.

Package quantities Mogadon Tablets 5 mg in packings of 100 and 500.

Mogadon Capsules 5 mg in packings of 100 and 500.

Further information Nil.

Product licence numbers

Tablets 5 mg 0031/0062.

Capsules 5 mg 0031/0083.

NATULAN®

Presentation Capsules with opaque pale yellow cap and body with 'ROCHE' printed in red-brown along both

cap and body, containing 58.3 mg procarbazine hydrochloride (equivalent to 50 mg of procarbazine).

Uses Properties: Natulan, a methylhydrazine derivative, is a cytostatic agent. It is effective in patients who have become resistant to radiation therapy and other cytostatic agents.

Indications: The main indication is Hodgkin's disease (lymphadenoma).

Natulan may also be useful in other advanced lymphomata and a variety of solid tumours which have proved resistant to other forms of therapy.

Dosage and administration *In combination chemotherapeutic regimens:* Natulan is usually administered concomitantly with other appropriate cytostatic drugs in repeated four- to six-weekly cycles. In most such combination chemotherapy regimens currently in use (e.g. the so-called MOPP schedule with mustine, vincristine and prednisone) Natulan is given daily on the first 10–14 days of each cycle in a dosage of 100 mg per sq. metre of body surface (to nearest 50 mg).

As sole therapeutic agent: Adults: Treatment should begin with small doses which are increased gradually up to a maximum daily dose of 250 or 300 mg divided as evenly as possible throughout the day.

Initial dosage scheme

1st day	50 mg	4th day	200 mg
2nd day	100 mg	5th day	250 mg
3rd day	150 mg	6th day et seq.	250–300 mg

Further procedure: Treatment should be continued with 250 or 300 mg daily until the greatest possible remission has been obtained, after which a maintenance dose is given.

Maintenance dose: 50–150 mg daily. Treatment should be continued until a total dose of at least 6 g has been given. Otherwise, a negative result is not significant.

Children: If, on the recommendation of a physician, a children's dosage is required, 50 mg daily should be given for the first week. Daily dosage should then be maintained at 100 mg per sq metre of body surface (to nearest 50 mg) until leucopenia or thrombocytopenia occurs or maximum response is obtained.

Natulan Capsules are for oral administration.

Contra-indications, warnings, etc

Contra-indications: Pre-existing severe leucopenia or thrombocytopenia from any cause; severe hepatic or renal damage. Natulan should not normally be administered to patients who are pregnant or to mothers who are breast-feeding.

Precautions: Important. The first stage of treatment with Natulan should be given in hospital under strict medical supervision.

Regular blood counts are of great importance and if during the initial treatment the total white cell count falls to 3,000 per mm³ or the platelet count to 80,000 per mm³, treatment should be suspended temporarily until the leucocyte and/or platelet levels recover, when therapy with the maintenance dose may be resumed.

Treatment should be interrupted on the appearance of allergic skin reactions.

Natulan is a weak MAO inhibitor and therefore interactions with certain foodstuffs and drugs, although very rare, must be borne in mind. Thus, owing to possible potentiation of the effect of barbiturates, narcotics, phenothiazine derivatives and preparations of the imi-

pramine type, these substances should be given in low doses. Intolerance to alcohol may occur.

Side-effects: Loss of appetite and nausea occur in most cases, sometimes with vomiting. These symptoms are usually confined to the first few days of treatment and then tend to disappear.

Like other effective cytostatics, Natulan causes leucopenia and thrombocytopenia. These haematologica changes are almost always reversible and seldom require complete cessation of therapy.

Effects of overdosage and their treatment: Signs of overdosage include severe nausea and vomiting, dizziness, hallucinations, depression and convulsions; hypotension or tachycardia may occur.

Gastric lavage and general supportive treatment should be performed, with prophylactic treatment against possible infection, and frequent blood counts.

Pharmaceutical precautions *Storage:* Recommended maximum storage temperature 30°C. Natulan Capsules should be stored in a dry place.

Legal category POM.

Package quantities Natulan Capsules in packings of 50.

Further information Nil.

Product licence number 0031/5038.

NIPRIDE* ▼

Presentation Ampoules containing the equivalent of 50 mg sodium nitroprusside for reconstitution with 5% Dextrose Injection BP.

Uses Properties: Nipride is a potent, rapidly-acting peripheral vasodilator. Vasodilatation is achieved by a direct and balanced action on both arterial and venous blood vessels. The resultant circulatory effects depend on the initial haemodynamic status of the patient. Thus in hypertensive and normotensive patients without heart failure a fall in systemic blood pressure is produced with little or no effect on cardiac output. In patients with heart failure, reduction of resistance to left ventricular outflow ('afterload') and lowering of raised ventricular pressure ('preload') regularly lead to increased cardiac output usually without significant hypotension.

Duration of effect is brief due to rapid conversion to cyanide and then thiocyanate. This permits minute-by-minute control of the haemodynamic effects.

Indications: Nipride is indicated for the immediate reduction of blood pressure of patients in hypertensive crises. Oral antihypertensive therapy should be started whilst the blood pressure is being controlled with Nipride.

Nipride may also be used for surgical procedure: where a hypotensive technique is appropriate.

Nipride may also be used to improve cardiac function in acute myocardial infarction, aortic or mitral valve disease, cardiomyopathy and other associated causes of acute or chronic heart failure. This includes its intra-operative or post-operative administration in patients undergoing surgery. Haemodynamic improvement is generally associated with an improvement in clinical symptoms of cardiac failure.

Dosage and administration (Nipride is to be given as an intravenous infusion only – see below.)

In patients who are not
gs, treatment with Nipride
se of 0.5 to 1.5 mcg/kg/
is obtained, the dosage
ial requirements; this will
0.5 to 8 mcg/kg/minute.
g/minute (range of 20 to
t to maintain the blood
cent lower than the pres-
sure. Patients who are
tensive drugs are more
ide and therefore require

evels of cyanide, an end-
sm, and to lessen the
ll in blood pressure, the
is 800 mcg/minute. If a
ressure is not obtained
imum dosage, adminis-
pped.

should be adjusted to
rtensive effect, as deter-
measurements. Nipride
l the patient can be safely
ive agents alone.

hen Nipride is used for
the reason during anaesthesia,
ould be employed. It is
dose should not exceed
practices and precautions
uld be observed.

uld ideally only be used
nitoring of the patient are

be started at a rate of 10-
e raised in increments of
10 minutes until an initial
fter the dose should be
eptic effect is achieved.
e tolerated by hyperten-
dosage is usually in the

should not exceed 400
improvement is achieved
, Nipride infusion should

l until the patient can be
l therapy. Normally this
n 72 hours. If signs of
occur during administra-
te should be reduced or
yes in mental status, neu-
chest pain or arrhythmias,
cations for such dosage

ven in conjunction with
other measures conven-
nt of cardiac failure.

ndations are made for the
ildren.

ide: Nipride must only be

lministration by any other
olution must be prepared
n below.

oule should be dissolved
1 BP provided. No other

diluent may be used. The resulting solution should be
diluted in 500 to 1,000 ml of 5% Dextrose Injection and
the infusion bottle promptly wrapped in the aluminium
foil provided or other opaque materials to protect it from
light. A self-adhesive label is provided for attaching to
the container of the diluted infusion. Both the initial
solution and the infusion solution should be prepared
immediately before use and any unused portion dis-
carded. The freshly-prepared solution for infusion has a
faint orange-brownish tint. If it is highly coloured, it
should not be used.

Once prepared, the solution should not be stored or
administered for a period longer than four hours. No
preparation other than 5% Dextrose Injection should be
added to the Nipride ampoule or mixed with the Nipride
infusion solution.

Contra-indications, warnings, etc

Contra-indications: Nipride should not be used in the
treatment of compensatory hypertension, e.g. that as-
sociated with conditions such as coarctation of the aorta
or arteriovenous shunt.

Cyanide and thiocyanate may interfere with the metab-
olism of cyanocobalamin (vitamin B₁₂). Nipride is
therefore contra-indicated in patients who are deficient
in this vitamin, have impaired liver function or suffer from
Leber's optic atrophy.

Precautions: Thiocyanate inhibits both the uptake and
binding of iodine. Caution should therefore be exercised
in treating patients with hypothyroidism or severe renal
impairment.

Blood pressure should be monitored frequently during
Nipride administration since the hypotensive effect is
rapid. When the rate of infusion is slowed or administra-
tion is stopped, the blood pressure usually begins to rise
immediately and returns to pre-treatment levels within
one to ten minutes. In view of the rapid onset of action
and potency of the drug, Nipride should preferably be
administered via an infusion pump, microdrip regulator
or any similar device which allows precise control of the
flow rate.

If high infusion rates of Nipride are required to control
the blood pressure, especially during hypotensive pro-
cedures, there is a possibility that a metabolic acidosis
may occur.

Nipride should be used with caution in elderly patients.
Treatment should begin with low doses since they may
be more sensitive to the hypotensive effects of Nipride.

The safety of Nipride in pregnant women has not been
established and it should therefore be used in women of
child-bearing age or during pregnancy only when the
potential benefits are considered to outweigh any
possible disadvantages.

Side-effects: Nausea, retching, diaphoresis, apprehen-
sion, headache, restlessness, muscle-twitching, retro-
sternal discomfort, palpitations, dizziness and abdominal
pain have been noted with a too-rapid reduction in blood
pressure. The symptoms rapidly disappear with slowing
of the rate of infusion of Nipride or temporary withdrawal
of the drug. When administration is continued at a slower
rate of infusion symptoms do not usually recur.

Cyanide inhibits cellular oxidative metabolism. Exces-
sive concentrations of cyanide would be manifested by
tachycardia, sweating, hyperventilation, cardiac arrhyth-
mias and profound metabolic acidosis. Unexplained
cyanosis whilst receiving Nipride may be due to
methaemoglobinaemia.

Effects of overdosage and their treatment: Overdosage

will be manifest by a marked fall in blood pressure below the desired level. The duration of action of Nipride is very short, the hypotensive effects ceasing almost immediately upon discontinuation of the infusion. Pre-treatment blood pressure levels are usually regained within one to ten minutes. Discontinuation of administration or a reduction in the rate of administration are usually sufficient measures for managing overdosage of Nipride.

Cyanide intoxication is best managed by the intravenous injection of sodium nitrite in conjunction with sodium thiosulphate, or alternatively cobalt edetate may be used. Hydroxocobalamin has also been suggested as a cyanide antagonist.

Pharmaceutical precautions Nipride ampoules and infusion solution should be protected from light. When the infusion solution is prepared the container should be wrapped in aluminium foil or other opaque material. Solutions of Nipride should not be stored for more than four hours or administered over a period longer than four hours.

In aqueous solution Nipride yields the nitroprusside ion which reacts with minute quantities of a wide variety of inorganic or organic substances to form reaction products which are frequently highly coloured. If coloration is observed, the solution should be discarded.

No preparation other than 5% Dextrose Injection should be added to the Nipride ampoule or mixed with the Nipride infusion solution.

Storage: Nipride ampoules and infusion should be protected from light.

Legal category POM.

Package quantities Nipride ampoules 50 mg accompanied by ampoules of 2 ml 5% Dextrose Injection BP in packings of 5.

Further information *Availability:* Nipride is available to hospitals only.

Nipride is pharmacologically compatible with other drugs commonly used to treat hypertension. In hypertensive patients who are receiving concomitant therapy smaller doses of Nipride may be required. The hypotensive effect of Nipride is augmented by ganglion-blocking agents.

Product licence number 0031/0102.

NITOMAN*

Presentation Round, pale orange-brown tablets with 'Roche' imprinted across one face and a single break bar on the other, containing 25 mg tetrabenazine.

Uses *Properties:* The central effects of Nitoman closely resemble those of reserpine, but it differs from the latter in having less peripheral activity and being much shorter-acting.

It is known from animal experiments that Nitoman intervenes in the metabolism of biogenic amines, such as serotonin and noradrenaline, and that this activity is mainly limited to the brain. It is thought that the effect of Nitoman on brain amines explains its clinical effects in man.

Indications: Movement disorders associated with organic central nervous system conditions, e.g. Huntington's chorea, hemiballismus and senile chorea.

Dosage and administration *Adults:* Dosage and administration are variable and only a guide is given. An

initial starting dose of 25 mg three times a day is recommended. This can be increased by 25 mg a day every three or four days until 200 mg a day is being given or the limit of tolerance, as dictated by unwanted effects is reached, whichever is the lower dose. If there is no improvement at the maximum dose in seven days, it is unlikely that the compound will be of benefit to the patient, either by increasing the dose or by extending the duration of treatment.

Children: No dosage recommendations are made for the administration of Nitoman to children.

Nitoman Tablets are for oral administration.

Contra-indications, warnings, etc

Contra-indications: Nitoman blocks the action of reserpine.

Precautions: Levodopa should be administered with caution in the presence of Nitoman.

The established medical principle of prescribing medicaments in early pregnancy only when absolutely indicated should be observed.

Side-effects: Side-effects are usually mild with little hypotensive action and few digestive disorders. The main unwanted effect reported to date has been drowsiness, which occurs with higher doses. If depression occurs, it can be controlled by reducing the dose or by giving antidepressant drugs such as the monoamine oxidase inhibitors. However, Nitoman should not be given immediately after a course of any of the monoamine oxidase inhibitors as such treatment may lead to a state of restlessness, disorientation and confusion. In man, a Parkinsonian-like syndrome has been reported on rare occasions, usually in doses above 200 mg per day, but this disappears on reducing the dose.

Effects of overdosage and their treatment: Signs and symptoms of overdosage may include drowsiness, sweating, hypotension and hypothermia. Treatment is symptomatic.

Pharmaceutical precautions *Storage:* Nitoman Tablets should be stored in well-closed containers.

Legal category POM.

Package quantities Nitoman Tablets in packings of 500.

Further information Nil.

Product licence number 0031/5073.

NOBRIUM*

Presentation Capsules with ivory opaque cap and coral opaque body with 'ROCHE 5' printed in red along both cap and body, containing 5 mg medazepam.

Capsules with black cap and coral opaque body with 'ROCHE 10' printed in red along both cap and body, containing 10 mg medazepam.

Uses *Properties:* Nobrium has potent anxiolytic properties. The pharmacological evidence available shows that Nobrium exerts its therapeutic effect by rapidly restoring the disturbed functional balance of the emotional centres in the brain, particularly the limbic system and does not affect the reticular activating system or cortex directly so that its effects are usually obtained without impaired alertness. Nobrium helps in the rationalisation and resolution of emotional conflicts, thus restoring drive and allowing continued normal everyday activities.

indications: Conditions where anxiety is an important component of the patient's overall condition.

Dosage and administration *Adults:* In most cases and in all elderly patients the initial recommended dosage is Nobrium 5 mg twice or three times daily.

This dosage may be increased if necessary until the maximal therapeutic effect is attained or signs of intolerance appear.

The normal dosage lies between 15 and 30 mg a day, but in more severe cases the dosage may be increased to 40 mg a day.

Where insomnia is a feature of the overall condition an additional dose is recommended on retiring.

In the treatment of alcoholism a high dosage is recommended at the onset of treatment. This may then be reduced according to response.

Children: If, on the recommendation of a physician, a child's dosage is required, it is suggested that 1–1.5 mg/kg daily or 5–40 mg daily is given.

Nobrium Capsules are for oral administration.

Contra-indications, warnings, etc *Precautions:* With Nobrium, as with other drugs acting on the central nervous system, patients should be instructed to avoid alcohol while under treatment, since the individual response cannot be foreseen. Like all medicaments of this type, Nobrium may modify patients' reactions (driving ability, operation of machinery, etc) to a varying extent, depending on dosage and individual susceptibility.

The use of high doses of benzodiazepines, especially over prolonged periods, may sometimes lead to dependence, particularly in patients with a history of alcoholism or drug abuse. Treatment in these cases should be withdrawn gradually.

Results obtained in trials with several generations of mice, rats and rabbits indicate that no danger of teratogenic effects need be expected from therapeutic doses of Nobrium. Nevertheless, the established medical principle of prescribing medicaments in early pregnancy only when absolutely indicated should be observed.

Side-effects: Nobrium is well tolerated. Minor side-effects such as fatigue and drowsiness may occasionally occur but usually disappear after the first few days of treatment. Prolonged and extensive clinical and laboratory investigations have revealed no significant changes in the blood picture or liver function.

Effects of overdose and their treatment: As with other benzodiazepine drugs, overdose should not present undue problems of management or threat to life. Symptoms of overdose may include drowsiness, ataxia and dysarthria, with coma in very severe cases.

Treatment is symptomatic, but gastric lavage may be useful if performed soon after ingestion.

Pharmaceutical precautions *Storage:* No special precautions are required.

Legal category POM.

Package quantities Nobrium Capsules 5 mg in packings of 100 and 500.

Nobrium Capsules 10 mg in packings of 100 and 500.

Further information Nil.

Product licence numbers

Capsules 5 mg 0031/5039

Capsules 10 mg 0031/5040

NOLUDAR*

Presentation Round, white tablets with 'Noludar' imprinted across one face with two break bars on the other, containing 200 mg methypyrone.

Uses *Properties:* Noludar is an effective sedative hypnotic of moderately rapid onset of action and of moderate duration. When Noludar is used in hypnotic doses, sleep is usually induced within 15 minutes to an hour and lasts about six hours. For daytime sedation, a small dose given three or four times daily has been found effective.

Indications: Mild or moderate insomnia. Daytime sedation.

Dosage and administration

	<i>Hypnotic</i>	<i>Sedative</i>
Adults	200–400 mg taken 15 minutes before bedtime	50–100 mg three or four times daily
Children:		
6–10 years	100 mg	50 mg one to three times daily
Over 10 years	100–200 mg	50 mg one to three times daily

Noludar Tablets are for oral administration.

Contra-indications, warnings, etc *Precautions:* With Noludar, as with other drugs acting on the central nervous system, patients should be instructed to avoid alcohol while under treatment, since the individual response cannot be foreseen. Like all medicaments of this type, Noludar may modify patients' reactions (driving ability, operation of machinery, etc) to a varying extent depending on dosage and individual susceptibility.

Side-effects: Noludar has a wide safety margin. Extensive studies have shown that in therapeutic doses, Noludar should have no undesirable effects on respiration, on the circulation, on the gastro-intestinal tract or on haemopoiesis; however, headache and drowsiness may occur.

Effects of overdose and their treatment: Signs and symptoms of overdose may include drowsiness, pyrexia, hypotension, respiratory depression and slight bradycardia. Later, hyperactivity, coma and convulsions may occur.

Gastric lavage should be performed, with general supportive therapy, including oxygen and airway maintenance and intravenous fluids. Metaraminol or nor-adrenaline should be given to correct hypotension; dialysis may be of use.

Pharmaceutical precautions *Storage:* Noludar Tablets should be protected from moisture and light.

Legal category POM.

Package quantities Noludar Tablets in packings of 100.

Further information Nil.

Product licence number 0031/5041.

OMNOPON*

Presentation Round, white to buff tablets marked 'ROCHE' on one side, containing 10 mg papaveretum.

Ampoules containing 20 mg papaveretum in 1 ml. The ampoule solution is colourless to pale brown.

Uses Properties: Omnopon, a potent analgesic, contains both the phenanthrene and isoquinoline groups of opium alkaloids. The former includes codeine and morphine which exert a marked narcotic action on the central nervous system. The second group is represented by papaverine, which acts mainly at the periphery as an antispasmodic, and noscapine.

Indications: Pre-operative medication; relief of post-operative pain; relief of severe chronic pain, particularly that of inoperable carcinoma, relief of pain and anxiety in coronary thrombosis; for severe pain associated with spasm as in renal and biliary colic.

Dosage and administration Adults: Single dose of 10 to 20 mg by mouth or by injection, usually not to be repeated more often than 4 hourly.

Children: Usual dosage:

1 to 5 years: 2.5 to 5 mg as a maximum single dose.

6 to 12 years: 5 to 10 mg as a maximum single dose.

Omnopon Tablets are for oral administration. They are not recommended for use in children under 12 years of age.

Omnopon ampoules are for intramuscular, intravenous or subcutaneous injection. They are not recommended for use in infants under 1 year of age.

Omnopon ampoule solution may be diluted with Water for Injection. Such dilution is recommended for accurate titration of children's doses.

Maintenance of stability cannot be guaranteed when Omnopon Ampoule solution is diluted.

Contra-indications, warnings, etc

Contra-indications: Omnopon should not be given to comatose patients or patients with respiratory depression or obstructive airways disease. It should not be administered to patients who are receiving monoamine oxidase inhibitors or within two weeks of their withdrawal.

Precautions: Omnopon should only be given with caution, and in reduced dosage, to neonates and premature infants, elderly and debilitated patients, and in patients with head injuries, severe hepatic or renal impairment, biliary tract disorders, hypothyroidism, adrenocortical insufficiency, shock, prostatic hypertrophy, and supraventricular tachycardia.

Caution is also required in patients exhibiting acute alcoholism, raised intracranial pressure or convulsive disorders. Omnopon depresses respiratory function and should be administered with particular care in patients with respiratory insufficiency.

The effects of Omnopon may be potentiated by concurrent administration of other central nervous system depressants, including anaesthetic agents. Concomitant administration of Omnopon with phenothiazines may induce severe hypotension. Patients should be instructed to avoid alcohol while under treatment, since the individual response cannot be foreseen.

Omnopon may modify patients' reactions (driving ability, operation of machinery, etc.) to a varying extent, depending on dosage, administration and individual susceptibility.

There is inadequate evidence of safety of Omnopon in human pregnancy, but the drug has been widely used for many years without apparent ill-consequence, and animal studies have not shown any hazard. Nevertheless, the established medical principle of prescribing medi-

caments in early pregnancy only when absolutely indicated should be observed.

Omnopon crosses the placenta and is also secreted in breast milk. This should be borne in mind when considering its use in patients during pregnancy or breast feeding. Administration in labour may cause respiratory depression in the newborn infant.

Repeated administration of Omnopon may induce tolerance to the drug, with a tendency to increasing dosage requirements to obtain the desired effect, or to physical and psychological dependence of the morphine type, with the development of withdrawal symptom: after abrupt cessation of therapy. Cross-tolerance between narcotic analgesics can occur.

Side-effects: Nausea and vomiting may be troublesome. Constipation and confusion may occur.

Effects of overdosage and their treatment: Signs of overdosage are similar to those with morphine but occur to a lesser extent; they include pin-point pupils, depressed respiration and coma. In severe poisoning there may be dilatation of the pupils, shock, severe respiratory depression and pulmonary oedema.

Gastric lavage should be performed soon after ingestion and intensive supportive therapy carried out. Lorfan 1-2 mg i.v., naloxone or nalorphine are antidotes.

Pharmaceutical precautions Storage: Omnopon Ampoules should be protected from light. Omnopon Tablets in blister packs should be stored in a dry place and protected from light. The recommended maximum storage temperature for Omnopon Ampoules is 25°C and for Omnopon Tablets is 30°C.

Legal category POM; MDA.

Package quantities Omnopon Tablets in cartons of 500, each carton containing 10 packs of 50 tablets in blister strips of 5 tablets.

Omnopon Ampoules in packings of 10.

Further information Nil.

Product licence numbers

Ampoules 20 mg 0031/5100

Tablets 10 mg 0031/5098

OMNOPON* SCOPOLAMINE

Presentation Ampoules containing 20 mg of papaveretum and 0.4 mg of hyoscine (scopolamine) hydrobromide in 1 ml. The ampoule solution is almost colourless to pale yellow.

Uses Properties: Omnopon-scopolamine combines the properties of the opium alkaloids with those of scopolamine. Thus it is an analgesic and sedative and has a marked inhibitory effect on the secretions.

Indication: Pre-anaesthetic medication.

Dosage and administration Adults: Usually $\frac{1}{2}$ to one ampoule injected $\frac{1}{2}$ -1 hour before anaesthesia.

Children:

Weight	Omnopon	Volume of Omnopon-scopolamine solution
10 kg	6 mg	0.3 ml
20 kg	12 mg	0.6 ml
30 kg	18 mg	0.9 ml
35 kg	20 mg	1.0 ml

ampoules are for intramuscular use. The ampoule solution may be diluted. Such dilution is not recommended for children's doses. It cannot be guaranteed when the ampoule solution is diluted.

Warnings, etc

Omnopon-scopolamine should not be given to patients with active airways disease. It should not be given to patients who are receiving or within two weeks of

scopolamine should only be given at the recommended dosage, to neonates and debilitated patients, patients with severe hepatic or renal impairment, hypothyroidism, adrenalectomy, prostatic hypertrophy, etc.

Patients exhibiting acute hypertension or convulsive activity should be given scopolamine depresses respiratory function with particular care and efficiency.

Omnopon-scopolamine may be potentiated by other central nervous system depressants including anaesthetics. Administration of Omnopon-scopolamine may induce severe hypotension. It is recommended to avoid alcohol and to observe the individual response.

Do not modify patients' reaction to anaesthesia of machinery, etc.) to avoid misadministration and

The safety of Omnopon-scopolamine, but the drug has been found to have no apparent ill-effects. It is not shown any hazard. The medical principle of premedication is pregnancy only when observed.

It crosses the placenta and is excreted in the milk. It should be borne in mind that during pregnancy or labour may cause hypotension in the newborn infant.

Omnopon-scopolamine is a sedative drug, with a tendency to cause drowsiness to obtain the desired analgesic effect. Physiological dependence of withdrawal of therapy. Cross-sensitization can occur.

Itching usually occurs. Unpleasant. Constipation

Adverse treatment: Signs of overdosage are seen with morphine. Pinpoint pupils and impaired level of consciousness. In severe poisoning the pupils, shock, severe respiratory oedema.

Intensive supportive therapy should be carried out. Lofran* 1-2 mg i.v., naloxone or nalorphine are antidotes. If excitement due to scopolamine occurs, Valium* Roche or short-acting barbiturates may be administered.

Pharmaceutical precautions Storage: Omnopon-scopolamine Ampoules should be protected from light. The recommended maximum storage temperature is 25°C.

Legal category POM; MDA.

Package quantities Omnopon-scopolamine Ampoules in packings of 10.

Further information Nil.

Product licence number 0031/5096.

PETHIDINE ROCHE

Presentation Round, white tablets with 'ROCHE' imprinted on one face, containing 25 mg pethidine hydrochloride.

Round white tablets with 'ROCHE' imprinted on one face, containing 50 mg pethidine hydrochloride.

Ampoules containing 50 mg pethidine hydrochloride in 1 ml. The ampoule solution is colourless to pale yellow.

Ampoules containing 100 mg pethidine hydrochloride in 2 ml. The ampoule solution is colourless to pale yellow.

Uses Properties: Pethidine Roche combines analgesic and antispasmodic properties; it is relatively short-acting and has little soporific effect. These properties make Pethidine Roche particularly useful for pain relief in labour and as an adjunct to nitrous oxide-oxygen anaesthesia.

Indications: Obstetric analgesia; moderate to severe pain; premedication and analgesia during anaesthesia.

Dosage and administration Adults: The normal single dose, usually not to be repeated more often than four-hourly, is as follows:

Oral: 50-150 mg.

Intramuscular or subcutaneous injection: 25-100 mg.

Intravenous injection: 25-50 mg.

Children: Single dose of 0.5-2 mg/kg body weight orally or intramuscularly.

Pethidine Roche Tablets are for oral administration. Pethidine Roche Ampoules are for intramuscular, intravenous or subcutaneous injection.

Pethidine Roche Ampoule solution may be diluted with Water for Injection. Such dilution is recommended for accurate titration of children's doses.

Maintenance of stability cannot be guaranteed when Pethidine Roche Ampoule solution is diluted.

Contra-indications, warnings, etc

Contra-indications: Pethidine should not be given to comatose patients or to patients with respiratory depression or obstructive airways disease. It should not be administered to patients who are receiving monoamine oxidase inhibitors or within two weeks of their withdrawal.

Precautions: Pethidine should only be given with caution, and in reduced dosage, to neonates and premature infants, elderly and debilitated patients, and in patients with head injuries, severe hepatic or renal impairment, biliary tract disorders, hypothyroidism, ad-

renocortical insufficiency, shock, prostatic hypertrophy, and supraventricular tachycardia.

Caution is also required in patients exhibiting acute alcoholism, raised intracranial pressure or convulsive disorders. Pethidine depresses respiratory function and should be administered with particular care in patients with respiratory insufficiency.

The effects of pethidine may be potentiated by concurrent administration of other central nervous system depressants, including anaesthetic agents. Concomitant administration of pethidine with phenothiazines may induce severe hypotension. Patients should be instructed to avoid alcohol while under treatment, since the individual response cannot be foreseen.

Pethidine may modify patients' reactions (driving ability, operation of machinery, etc.) to a varying extent, depending on dosage, administration and individual susceptibility. There is inadequate evidence of safety of pethidine in human pregnancy, but the drug has been widely used for many years without apparent ill-consequence, and animal studies have not shown any hazard. Nevertheless, the established medical principle of prescribing medicaments in early pregnancy only when absolutely indicated should be observed.

Pethidine crosses the placenta and is also secreted in breast milk. This should be borne in mind when considering its use in patients during pregnancy or breast feeding. Administration in labour may cause respiratory depression in the newborn infant.

Repeated administration of pethidine may induce tolerance to the drug, with a tendency to increasing dosage requirements to obtain the desired effect, or to physical and psychological dependence of the morphine type, with the development of withdrawal symptoms after abrupt cessation of therapy. Cross-tolerance between narcotic analgesics can occur.

Side-effects: Pethidine may cause mild euphoria, dizziness, nausea and vomiting, hypotension and respiratory depression.

Effects of overdosage and their treatment: In acute overdosage, signs and symptoms may include incoordination, tremors and convulsions followed by respiratory depression and coma.

Gastric lavage should be performed soon after ingestion, and intensive supportive therapy carried out. Lofran* 1-2 mg i.v., naloxone or nalorphine are antidotes. The urinary excretion can be increased by rendering the urine acid by the administration of ammonium chloride.

Pharmaceutical precautions *Storage:* Pethidine Roche Tablets in blister packs should be stored in a dry place.

The recommended maximum storage temperature for Pethidine Roche Ampoules is 30°C.

Legal category POM; MDA.

Package quantities Pethidine Roche Tablets 25 mg in cartons of 500, each carton containing 10 packs of 50 tablets in blister strips of 5 tablets.

Pethidine Roche Tablets 50 mg in cartons of 500, each carton containing 10 packs of 50 tablets in blister strips of 5 tablets.

Pethidine Roche Ampoules containing 50 mg in 1 ml in packings of 10.

Pethidine Roche Ampoules containing 100 mg in 2 ml packings of 10.

Further information Nil.

Product licence numbers

Tablets 25 mg	0031/5102
Tablets 50 mg	0031/5103
Ampoules 50 mg	0031/5105
Ampoules 100 mg	0031/5106

PETHILORFAN*

Presentation Ampoules containing pethidine hydrochloride 50 mg and levallorphan tartrate 0.625 mg in 1 ml. The ampoule solution is colourless to pale yellow.

Ampoules containing pethidine hydrochloride 100 mg and levallorphan tartrate 1.25 mg in 2 ml. The ampoule solution is colourless to pale yellow.

Uses *Properties:* Pethilorfan, an analgesic preparation is a combination of pethidine with the narcotic antagonist Lofran* (levallorphan tartrate). It has been shown that Lofran prevents or reduces respiratory depression caused by pethidine. When pethidine and Lofran are combined in the ratio 100:1.25, the respiratory depressant effect of pethidine is inhibited.

Indications: Analgesia in obstetrics, anaesthesia, pre-anaesthetic medication; minor surgical procedures and post-operative pain.

Dosage and administration Single doses should be used which are not to be repeated more often than four hourly.

Adults: Obstetrics: When labour is firmly established to 3 ml Pethilorfan may be given intramuscularly.

Premedication: Up to 2 ml Pethilorfan intramuscularly may be given 1 hour before operation.

Adjunct to nitrous oxide-oxygen anaesthesia: Pethilorfan is used in the same way as pethidine alone, 0.5 to 1 ml being given when anaesthesia is established.

Minor surgical procedures: Up to 2 ml Pethilorfan intramuscularly, or up to 1 ml Pethilorfan intravenously may be given.

For the treatment of post-operative and other pain Pethilorfan may be used in the same way as pethidine.

Children: Children may be given a single dose containing pethidine 0.5 to 2.0 mg/kg body weight, intramuscularly.

Pethilorfan ampoules are for intramuscular, intravenous or subcutaneous injection.

Pethilorfan Ampoule solution may be diluted with Water for Injection. Such dilution is recommended for accurate titration of children's doses.

Maintenance of stability cannot be guaranteed when Pethilorfan ampoule solution is diluted.

Contra-indications, warnings, etc

Contra-indications: Pethilorfan should not be given to comatose patients or to patients with respiratory depression or obstructive airways disease. It should not be administered to patients who are receiving monoamine oxidase inhibitors or within two weeks of their withdrawal.

Precautions: Pethilorfan should only be given with caution, and in reduced dosage, to neonates and premature infants, elderly and debilitated patients, and in patients with head injuries, severe hepatic or renal impairment, biliary tract disorders, hypothyroidism, adrenocortical insufficiency, shock, prostatic hypertrophy and supraventricular tachycardia.

Caution is also required in patients exhibiting acute alcoholism, raised intracranial pressure or convulsive disorders. Pethilorfan depresses respiratory function and

ould be administered with particular care in patients with respiratory insufficiency.

The effects of Pethilorfan may be potentiated by concurrent administration of other central nervous system depressants, including anaesthetic agents. Concurrent administration of Pethilorfan with phenothiazines may induce severe hypotension. Patients should be instructed to avoid alcohol while under treatment since the individual response cannot be foreseen.

Pethilorfan may modify patients' reactions (driving ability, operation of machinery, etc.) to a varying extent, depending on dosage, administration and individual susceptibility.

There is inadequate evidence of safety of Pethilorfan in human pregnancy, but the drug has been widely used for many years without apparent ill-consequence, and animal studies have not shown any hazard. Nevertheless, the established medical principle of prescribing medications in early pregnancy only when absolutely indicated should be observed.

Pethilorfan crosses the placenta and is also secreted in breast milk. This should be borne in mind when considering its use in patients during pregnancy or breastfeeding. Administration in labour may cause respiratory depression in the newborn infant.

Repeated administration of Pethilorfan may induce tolerance to the drug, with a tendency to increasing dosage requirements to obtain the desired effect, or to physical and psychological dependence of the morphine type, with the development of withdrawal symptoms after abrupt cessation of therapy. Cross-tolerance between narcotic analgesics can occur.

Side-effects: Mild euphoria, dizziness, nausea and vomiting, hypotension and respiratory depression may occur.

Effects of overdosage and their treatment: In acute overdosage signs and symptoms may include incoordination, tremors, convulsions and coma. Pethidine alone may cause respiratory depression; however, in combination with Lofran, this is less likely to occur.

Intensive supportive therapy should be carried out. Pethilorfan* 1–2 mg i.v., naloxone or nalorphine are pethidine antidotes. The urinary excretion of pethidine can be increased by rendering the urine acid by the administration of ammonium chloride.

Pharmaceutical precautions *Storage:* Pethilorfan ampoules should be protected from light.

Legal category POM; MDA.

Package quantities Pethilorfan Ampoules containing 0 mg of pethidine hydrochloride and 0.625 mg of orfan in 1 ml in packings of 10.

Pethilorfan Ampoules containing 100 mg of pethidine hydrochloride and 1.25 mg of Lofran in 2 ml in packings of 10.

Further information Nil.

Product licence numbers

Ampoules 50 mg 0031/5082

Ampoules 100 mg 0031/5083

PROSTIGMIN*

Presentation Round, white tablets with 'PROSTIGMIN' imprinted on one face with a single break bar on the other, containing 15 mg neostigmine bromide.

Ampoules containing 0.5 mg neostigmine methyl-

sulphate in 1 ml. The ampoule solution is almost colourless to pale yellow.

Ampoules containing 2.5 mg neostigmine methylsulphate in 1 ml. The ampoule solution is almost colourless to pale yellow.

Uses Properties: Prostigmin is an antagonist to cholinesterase, the enzyme which normally destroys acetylcholine. The action of Prostigmin can briefly be described, therefore, as the potentiation of naturally occurring acetylcholine.

Indications: Myasthenia gravis; antidote to curariform drugs; paralytic ileus; post-operative distension; chronic constipation; urinary retention; heartburn of pregnancy; paroxysmal tachycardia.

Dosage and administration *Adults – Myasthenia gravis:* A daily dose of 5–20 tablets by mouth or 1–2.5 mg by injection is commonly given, but doses higher than these may be needed by some patients. The daily doses should be spread over the day and taken at times when they are most required. With some of the daily doses it may be necessary to take atropine or some other anticholinergic drug.

Antidote to curariform drugs: Prostigmin 1–5 mg intravenously, atropine 0.4–1.25 mg. The atropine is often given some minutes before the Prostigmin.

Other indications: The usual adult dose is 1–2 tablets by mouth or 0.5–2.5 mg by subcutaneous or intramuscular injection; the frequency of dosage may be varied according to the needs of the patient.

Children: If on the recommendation of a physician a children's dosage is required, then the following is given as a guide:

Myasthenia gravis: Newborn infants: Usually 0.05–0.25 mg by injection or 1–5 mg orally every four hours.

Older children: 0.2–0.5 mg daily by injection or 15–60 mg daily orally.

Other indications: 2.5–15 mg orally 0.125–1 mg by injection.

Prostigmin Tablets are for oral administration. Prostigmin Ampoules are for intramuscular, intravenous or subcutaneous injection.

Prostigmin Ampoule solution may be diluted with Water for Injection.

Maintenance of stability cannot be guaranteed when Prostigmin preparations are diluted.

Contra-indications, warnings, etc *Precautions:* Care should be taken in administering Prostigmin to patients with bronchial asthma.

Side-effects: These may include nausea and vomiting, increased salivation, diarrhoea and abdominal cramps.

Effects of overdosage and their treatment: Signs of overdosage due to muscarinic effects may include abdominal cramps, increased peristalsis, diarrhoea, nausea and vomiting, increased bronchial secretions, salivation, diaphoresis and miosis. Nicotinic effects consist of muscular cramps, fasciculations and general weakness. Bradycardia and hypotension may also occur. Artificial respiration should be instituted if respiratory depression is severe. Atropine sulphate 1–2 mg intravenously is an antidote to the muscarinic effects.

Pharmaceutical precautions *Storage:* The recommended maximum storage temperature for Prostigmin Ampoules 2.5 mg is 25°C. All Prostigmin preparations should be protected from light.

Legal category

Tablets POM

Ampoules POM

Package quantities Prostigmin Tablets in packings of 100.

Prostigmin Ampoules 0.5 mg in 1 ml in packings of 10.

Prostigmin Ampoules 2.5 mg in 1 ml in packings of 10.

Further information Nil.**Product licence numbers**

Ampoules 0.5 mg 0031/5084

Ampoules 2.5 mg 0031/5085

Tablets 0031/5086

RIMIFON***Presentation** Ampoules containing 50 mg isoniazid in 2 ml. The ampoule solution is almost colourless.**Uses Properties:** Rimifon is a highly active tuberculostatic drug. It has a high rate of diffusion so that the tuberculostatic action affects intracellular as well as extracellular bacilli.**Indications:** All forms of pulmonary and extra-pulmonary tuberculosis.**Dosage and administration** Rimifon Ampoules are for intramuscular, intrapleural, intrathecal or intravenous injection.

The usual intramuscular or intravenous dose for adults is 200–300 mg daily, for children 100–300 mg daily, but doses much larger than these are sometimes given, especially in conditions such as tuberculous meningitis.

Intrathecal use: In tuberculous meningitis Rimifon 25–50 mg daily may be given intrathecally as a supplement to oral isoniazid for adults. Children may be given 10–20 mg daily according to age.**Intrapleural use:** 50–250 mg may be instilled intrapleurally after aspiration of pus, the dosage of oral isoniazid on that day being correspondingly reduced. The ampoule solution is also used for the local treatment of tuberculous ulcers, for irrigation of fistulae, etc.

It is usual to give Rimifon in conjunction with streptomycin or PAS, or both, provided that the organisms are sensitive to these drugs. Rimifon can also be given together with other antitubercular drugs, e.g. rifampicin, ethambutol, cycloserine.

Rimifon Ampoule solution may be diluted with Water for Injection.

Maintenance of stability cannot be guaranteed when Rimifon Ampoule solution is diluted.

Contra-indications, warnings, etc Side-effects:These include peripheral neuritis, which occurs mainly in patients receiving high doses, or in those taking prolonged courses of the drug. Concurrent Benadon* (vitamin B₆, pyridoxine) can largely prevent the development of neuritis; suggested dose 50 mg daily.

Hypersensitivity reactions, purpura, agranulocytosis and pellagra are rare complications of isoniazid therapy. Psychotic episodes or epileptiform fits are occasionally encountered, usually in patients with a history of epilepsy or of previous psychotic illness; these manifestations usually subside rapidly on withdrawing the drug.

Effects of overdosage and their treatment: Signs of minor overdosage are similar to the side-effects listed. In severe poisoning metabolic acidosis, elevated blood sugar levels, seizures and coma may occur. Intravenous pyridoxine is an antidote to isoniazid poisoning. Sodium bicarbonate may be used to correct metabolic acidosis and intravenous Valium* Roche to control convulsions.**Pharmaceutical precautions Storage:** The recommended maximum storage temperature for Rimifon Ampoules is 25°C; the Ampoules should be protected from light.**Legal category** POM.**Package quantities** Rimifon Ampoules in packings of 10.**Further information** Nil.**Product licence number** 0031/5109.**RO-A-VIT*****Presentation** Round, cream, sugar-coated tablet with 'ROCHE' printed in red on one face, containing 50,000 i.u. retinol (vitamin A) as the acetate.

Ampoules containing 300,000 i.u. retinol as the palmitate (approx. 165 mg) in 1 ml oily solution.

Uses Properties: Ro-A-Vit is a synthetic vitamin A preparation. Vitamin A may be considered to act chiefly as a regulator of the growth and activity of epithelial tissues. It plays an essential role in the visual cycle through its participation in the synthesis of visual purple by the retina.

The cardinal signs and symptoms of vitamin A deficiency are those affecting the eyes, such as xerosis, swelling and destruction of the cornea and night-blindness. Changes in the skin and changes in the mucous membranes of the respiratory, digestive and urinary tracts have been reported.

Indications: Prevention and treatment of vitamin A deficiencies.

Ro-A-Vit Ampoules are indicated when oral therapy is inappropriate (e.g. in malabsorption syndrome).

Dosage and administration Tablets – Adults: 1–6 tablets daily (50,000–300,000 i.u.).**Children:** If, on the recommendation of a physician, a child's dosage is required, then it is suggested that up to 50,000 i.u. daily be given according to age.**Ampoules: Adults and children:** A maintenance dosage of ½–1 ampoule by deep intramuscular injection once monthly is usually sufficient but in acute deficiency states the same dosage may be given once weekly. When prolonged therapy with high, weekly dosages of vitamin A is required it is suggested that Ro-A-Vit Ampoules be given in courses of no longer than six weeks separated by treatment-free intervals of two weeks so that the patient can be observed for signs of possible hypervitaminosis A.

Ro-A-Vit Tablets are for oral administration.

Ro-A-Vit Ampoule solution is only suitable for deep intramuscular injection.

Contra-indications, warnings, etc Precautions:

During the early months of pregnancy, high doses of vitamin A should be avoided or only be administered where there is a firm indication for their use and under doctor's instructions.

Effects of overdose and their treatment: Massive doses of vitamin A are required to produce toxicity and therefore it is extremely unlikely that even exceptionally large single doses would cause hypervitaminosis A (except possibly in children). Manifestations of acute overdose in children include severe headache, nausea, vomiting, drowsiness, irritability and pruritus. In chronic overdose in children the following have been noted after periods of 2½–15 months: hydrocephaly, osteopenia, painful swellings over the long bones, with bone and joint pains, hyperostosis, and deep, hard, tender swellings in the extremities. Adults are likely to complain of bone and joint pains. The vitamin should be discontinued. Symptoms of acute overdose subside within 72 hours and of chronic overdose over a period of several months, without further treatment.

Pharmaceutical precautions *Storage:* Ro-A-Vit tablets should be stored in well-closed containers. The recommended maximum storage temperature for Ro-A-Vit Tablets is 25°C.

Ro-A-Vit Ampoules should be protected from light. Recommended maximum storage temperature 25°C.

Legal category Tablets P.
Ampoules POM.

Package quantities Ro-A-Vit Tablets in packings of 100.

Ro-A-Vit ampoules in packings of 10.

Further information Nil.

Product licence numbers

Tablets 0031/5111

Ampoules 0031/0124

ROCALTROL* ▼

Presentation Soft gelatine capsules, one length red opaque and the other white opaque, containing 0.25 microgram calcitriol. Soft gelatine capsules, both lengths red opaque, containing 0.5 microgram calcitriol.

Uses *Properties:* Calcitriol has the greatest biological activity of the known vitamin D metabolites and is normally formed in the kidneys from its immediate precursor, 25-hydroxycholecalciferol. In physiological amounts it augments the intestinal absorption of calcium and phosphate and plays a significant part in the regulation of bone mineralisation. The defective production of calcitriol in chronic renal failure contributes to the abnormalities of mineral metabolism found in that disorder.

Rocaltrol is a synthetic preparation of calcitriol. Oral administration of Rocaltrol to patients with chronic renal failure compensates for impaired endogenous production of calcitriol which is decreased when the glomerular filtration rate falls below 30 ml/min. Consequently, intestinal malabsorption of calcium and phosphate and the resulting hypocalcaemia are improved, thereby reversing the signs and symptoms of bone disease.

The onset and reversal of the effects of Rocaltrol are more rapid than those of other compounds with vitamin D activity and adjustment of the dose can be achieved sooner and more precisely. The effects of inadvertent overdose can also be reversed more readily.

Indications: Rocaltrol is indicated for the correction of the abnormalities of calcium and phosphate metabolism in patients with renal osteodystrophy.

Dosage and administration The dose of Rocaltrol should be carefully adjusted for each patient according to the biological response so as to avoid hypercalcaemia. The effectiveness of treatment depends in part on an adequate daily intake of calcium, which should be augmented by dietary changes or supplements if necessary. The capsules should be swallowed with a little water.

Adults: It is suggested that treatment should be started with two to four 0.5 mcg capsules of Rocaltrol daily and serum calcium levels monitored at weekly intervals. The daily dose may be increased by increments of 0.25–0.5 mcg to a total of 2 or 3 mcg daily according to the biological response. When dose requirements are stable serum calcium levels may be monitored at intervals of two to four weeks.

When there is biochemical or radiographic evidence of bone healing the requirements for Rocaltrol generally decrease. The dose should then be adjusted to avoid hypercalcaemia.

Higher doses of Rocaltrol may be required when barbiturates or anticonvulsants are given concurrently but this should rarely exceed 5 mcg daily. Reduction of dose is necessary if such drugs are withdrawn.

Children: Dosage in children has not been established.

Rocaltrol capsules are for oral administration only.

Contra-indications, warnings, etc

Contra-indications: Rocaltrol should not be given to patients with hypercalcaemia or evidence of metastatic calcification.

Precautions: All other vitamin D compounds and their derivatives, including proprietary compounds or food-stuffs which may be 'fortified' with vitamin D, should be withheld during treatment with Rocaltrol.

Treatment does not obviate the need to control plasma phosphate with phosphate binding agents. Since Rocaltrol affects phosphate transport in the gut and bone, the dose of phosphate binding agent may need to be modified.

The safety of Rocaltrol during pregnancy has not been established since to date there has been no experience in pregnancy. The usual caution in prescribing any drug for women of child-bearing age should be observed.

Side-effects: Hypercalcaemia and hypercalciuria are the major side-effects of Rocaltrol and indicate excessive dosage. The clinical features of hypercalcaemia include anorexia, nausea, vomiting, headache, weakness, apathy and somnolence. More severe manifestations may include thirst, dehydration, polyuria, nocturia, abdominal pain, paralytic ileus and cardiac arrhythmias. Rarely, overt psychosis and metastatic calcification may occur. The relatively short biological half-life of Rocaltrol permits rapid elimination of the compound when treatment is stopped and hypercalcaemia will recede within two to seven days. The rate of reversal of biological effects is more rapid than when other vitamin D derivatives are used.

Mild, non-progressive and reversible elevations in levels of liver enzymes (SGOT, SGPT) have been noted in a few patients treated with Rocaltrol, but no pathological changes in the liver have been reported.

Effects of overdose and their treatment: In acute overdose gastric lavage should be considered as soon after ingestion as possible provided that the drug was taken within the previous six to eight hours.

Should hypercalcaemia occur, Rocaltrol should be discontinued until plasma calcium levels have returned

to normal. A low-calcium diet will speed this reversal. Rocaltrol can then be restarted at a lower dose or given in the same dose but at less frequent intervals than previously. Severe hypercalcaemia may be treated by ensuring adequate hydration, inducing a diuresis where practicable and by general supportive measures. Calcitonin may increase the rate of fall of serum calcium when bone resorption is increased.

In patients treated by intermittent haemodialysis, a low concentration of calcium in the dialysate may also be used.

Pharmaceutical precautions *Storage:* Rocaltrol capsules should be protected from heat.

Legal category POM.

Package quantities Capsules 0.25 mcg in packings of 100.

Capsules 0.5 mcg in packings of 100.

Further information Nil.

Product licence numbers

Capsules 0.25 mcg 0031/0122

Capsules 0.5 mcg 0031/0123

RONICOL*

Presentation Round, white tablets with 'RONICOL' imprinted across one face with a single break bar on the other, containing 59.4 mg nicotine alcohol tartrate (equivalent to 25 mg nicotine alcohol).

Uses *Properties:* Ronicol is the alcohol corresponding to nicotine acid and has similar vasodilator properties. Its action is more sustained than that of nicotine acid because, in addition to the vasodilator effect of the alcohol itself, partial metabolism of the alcohol results in the gradual release of nicotine acid. Ronicol exerts a direct vasodilator action on the walls of small arteries and arterioles; there is a slight transient tendency towards a fall in blood pressure and slowing of the pulse.

Indications: Circulatory disorders, including peripheral vascular disease, vascular spasm (e.g. Raynaud's disease and acrocyanosis). Ménière's syndrome, chilblains, eye conditions due to deficient retinal circulation.

Dosage and administration *Adults:* 1–2 tablets four times daily.

Children: No dosage recommendations are made for the administration of Ronicol to children.

Ronicol Tablets are for oral administration.

Contra-indications, warnings, etc *Precautions:* Care should be taken in the long-term administration of high doses of Ronicol in patients with pre-diabetic or diabetic metabolic disorders.

Side-effects: Ronicol is very well tolerated and may be given over long periods without toxic effects. Mild, transient flushing of the face and a feeling of warmth in the region of the head may be experienced when the patient is taking an optimal dose.

Effects of overdose and their treatment: In overdose, gastric irritation, diarrhoea, flushing and general vasodilatation and possibly hypotension may occur.

Gastric lavage should be performed and symptoms treated as they arise.

Pharmaceutical precautions *Storage:* Ronicol should be stored in well-closed containers.

Legal category P.

Package quantities Ronicol Tablets in packings of 100.

Further information Nil.

Product licence number 0031/5113.

RONICOL* TIMESPAN*

Presentation Brown-red, sugar-coated tablets with 'ROCHE' printed in black across one face containing 357 mg nicotine alcohol tartrate (equivalent to 150 mg nicotine alcohol).

Uses *Properties:* Ronicol Timespan Tablets are slow release tablets, the active principle being Ronicol, which is the alcohol corresponding to nicotine acid and has similar vasodilator properties. In addition to the vasodilator effect of the alcohol itself, partial metabolism of the alcohol results in the gradual release of nicotine acid. The compound exerts a direct vasodilator action on the walls of small arteries and arterioles which is maintained for 12 hours. There is a slight transient tendency towards a fall in blood pressure and slowing of the pulse.

Indications: Circulatory disorders, including peripheral vascular disease, vascular spasm (e.g. Raynaud's disease and acrocyanosis). Ménière's syndrome, chilblains, eye conditions due to deficient retinal circulation.

Dosage and administration *Adults:* 1 or 2 tablet night and morning, depending on the severity of the condition. They should be swallowed whole.

Children: No dosage recommendations are made for the administration of Ronicol Timespan to children.

Ronicol Timespan Tablets are for oral administration.

Contra-indications, warnings, etc *Precautions* Care should be taken in the long-term administration of high doses of Ronicol in patients with pre-diabetic or diabetic metabolic disorders.

Side-effects: Ronicol Timespan is very well tolerated and may be given over long periods without toxic effects. Mild, transient flushing of the face and a feeling of warmth in the region of the head may be experienced when the patient is taking an optimal dose.

Effects of overdose and their treatment: In overdose, gastric irritation, diarrhoea, flushing and general vasodilatation and possibly hypotension may occur.

Gastric lavage should be performed and symptoms treated as they arise.

Pharmaceutical precautions *Storage:* Ronicol Timespan should be stored in well-closed containers.

Legal category P.

Package quantities Ronicol Timespan Tablets in packings of 100.

Further information Nil.

Product licence number 0031/5114.

SYNKAVIT*

Alternative name: Menadiol sodium diphosphate.

Presentation Round, white tablets with 'SYNKAVIT' imprinted on one face with a single break bar across the other, containing 12.63 mg of the tetra-sodium salt of 2

ethyl-1,4-naphthahydroquinone diphosphate (equivalent to 10 mg of the free ester).

Ampoules containing 126.3 mg of the tetra-sodium salt of 2-methyl-1,4-naphthahydroquinone diphosphate (equivalent to 10 mg of the free ester) in 1 ml. The ampoule solution is colourless to pale yellow.

Ampoules containing 126.3 mg of the tetra-sodium salt of 2-methyl-1,4-naphthahydroquinone diphosphate (equivalent to 100 mg of the free ester) in 2 ml. The ampoule solution is colourless to pale yellow.

Uses Properties: Synkavit is a water-soluble vitamin K analogue. The presence of vitamin K is essential for the formation within the body of prothrombin, factor VII, factor IX and factor X. Lack of vitamin K leads to increased tendency to haemorrhage.

Indications: Synkavit is indicated in the treatment of haemorrhage or threatened haemorrhage associated with a low blood level of prothrombin or factor VII.

The main indications include: obstructive jaundice (before and after surgery); haemorrhage after dental extractions; prevention of neonatal haemorrhage; menorrhagia.

Synkavit, in large doses, may be used as a 'radio-sensitiser' in the treatment of cancer.

Dosage and administration Adults: Usual therapeutic dose – 10–40 mg daily. Large doses (as a 'radiosensitiser') – 100 mg by injection.

Children: If, on the recommendation of a physician, a child's dosage is required, it is suggested that 5–10 mg daily be given.

For haemorrhagic disease of the newborn: Administered prophylactically to the mother: 10 mg by mouth daily for three to four days before labour, or 5 mg by injection during labour.

Administered to the infant: although Synkavit has been used successfully for many years in newborn infants for the prevention and treatment of haemorrhagic disease, it is now considered that Konakion* (vitamin K₁) is preferable for this purpose.

Synkavit Tablets are for oral administration.

Synkavit Ampoules are for intramuscular, intravenous or subcutaneous injection.

Synkavit Ampoule solution may be diluted with Water or Injection.

Maintenance of stability cannot be guaranteed when Synkavit Ampoule solution is diluted.

Contra-indications, warnings, etc Precautions: Caution should be exercised in administering Synkavit and other vitamin K analogues to premature infants. Doses in excess of 10 mg have been associated with hyperbilirubinaemia in such infants. In full-term infants a single dose of up to 5 mg is adequate and without danger.

Pharmaceutical precautions Storage: Recommended maximum storage temperature for Synkavit Tablets and Ampoules 100 mg is 30°C, for Synkavit Ampoules 10 mg 25°C. All Synkavit preparations should be protected from light.

Legal category Tablets P
Ampoules POM.

Package quantities Synkavit Tablets in packings of 10.

Synkavit Ampoules 10 mg in 1 ml in packings of 10.

Synkavit Ampoules 100 mg in 2 ml in packings of 10.

Further information In almost all circumstances Synkavit is as effective as the natural vitamin (vitamin K₁). It is not fully effective however as an antidote to anticoagulant drugs of the dicoumarol type and for this purpose, vitamin K₁ (Konakion*) should be used.

Product licence numbers

Tablets	0031/5115
Ampoules 10 mg	0031/5116
Ampoules 100 mg	0031/5117

TARACTAN*

Presentation Round, pink, sugar-coated tablets with 'ROCHE' printed in red across one face, containing 15 mg chlorprothixene.

Round, dark red-brown, sugar-coated tablets with 'ROCHE' printed in white across one face, containing 50 mg chlorprothixene.

Uses Properties: Taractan is a major tranquillising drug. Animal experiments have shown that it has sedative and adrenolytic properties similar to those of chlorpromazine, but it has much greater anticholinergic activity. It also has antiserotonin, antihistamine and anti-emetic activity.

Indications: Psychoses and psychoneuroses: for the treatment of agitation, anxiety, insomnia, hallucinations, delusions and associated disturbances, without the risk of exacerbating any underlying depression.

Dosage and administration Adults: For conditions manifested by agitation and anxiety (with or without depression), tension, excitation or irritability, 30–45 mg daily in divided doses.

For the treatment of severe psychosis in adults, up to 400 mg daily.

In elderly psychotics, daily doses of up to 150 mg in divided doses.

Dosage should be adjusted to the severity of the condition, beginning with a small dose and increasing it until the optimum level is reached, depending upon tolerance and effectiveness.

Children: If on the recommendation of a physician, a child's dosage is required the following is suggested as a guide.

Under 6 years: 1–2 mg/kg body weight daily.

Over 6 years: 15 mg three to four times daily.

Taractan Tablets are for oral administration.

Contra-indications, warnings, etc Precautions: With Taractan, as with other drugs acting on the central nervous system, patients should be instructed to avoid alcohol while under treatment, since the individual response cannot be foreseen. Like all medicaments of this type, Taractan may modify patients' reactions (driving ability, operation of machinery, etc) to a varying extent, depending on dosage and individual susceptibility. The established medical principle of prescribing medicaments in early pregnancy only when absolutely indicated should be observed.

Care should be taken in the use of anaesthetics, analgesics and hypnotics as their effects may be potentiated by Taractan.

In patients suspected to be suffering from cardiac insufficiency, with disturbances of heart rhythm or conduction, neuroleptics and tricyclic antidepressants should be administered with caution, especially in the elderly.

Particularly in predisposed subjects, the tricyclic antidepressants and neuroleptics may give rise to changes in the EEG: in rare cases, convulsions have been observed.

Side-effects: Taractan is relatively free from side-effects and toxic effects. It has a sedative action which can be useful in the treatment of many patients. Should sedation be too pronounced, it can be lessened by reducing the dose. Tachycardia and postural hypotension have occasionally been observed, but these have rarely been sufficiently serious to warrant discontinuation of the drug. Other side-effects reported in isolated cases are convulsions, constipation, dryness of the mouth and slight oedema. A very small number of cases of granulocytopenia have been reported in which the white cell count rapidly rose to normal after cessation of treatment.

Effects of overdosage and their treatment: The primary symptoms of overdosage are drowsiness, moderate to severe hypotension with shock, general weakness, cyanosis, pyrexia, contracted pupils, tachycardia, respiratory depression and coma. Convulsions may occur later.

Gastric lavage should be performed if soon after ingestion.

If hypotension occurs, the patient should be placed in a head-down position and oxygen and intravenous fluids administered. If an adequate blood pressure is not obtained, noradrenaline or metaraminol may be given, but not adrenaline. Respiration should be maintained by artificial methods. Intravenous Valium® Roche or short-acting barbiturates may be used to control convulsions.

Pharmaceutical precautions *Storage:* Taractan Tablets should be stored in well-closed containers.

Legal category POM.

Package quantities Taractan Tablets 15 mg in packings of 50.

Taractan Tablets 50 mg in packings of 50.

Further information Nil.

Product licence numbers

Tablets 15 mg 0031/5118

Tablets 50 mg 0031/5129

TEMETEX®

Presentation White cream containing 0.1% w/w diflucortolone valerate in an oil-in-water emulsion.

White to yellowish-white fatty ointment containing 0.1% w/w diflucortolone valerate in an anhydrous base.

White to yellowish-white ointment containing 0.1% w/w diflucortolone valerate in a water-in-oil emulsion.

Uses *Properties:* Diflucortolone valerate, the active ingredient of Temetex preparations, is a highly effective topical corticosteroid with rapid onset of action, marked anti-inflammatory action and good cutaneous tolerance. In addition to inhibiting inflammation in inflammatory and allergic skin diseases, it ameliorates the subjective complaints such as itching, burning and pain.

Three different presentations are available, each designed to suit a particular condition of the patient's skin, thereby aiding the achievement of the optimal clinical response.

Indications: Temetex preparations are indicated for the treatment of non-infected eczemas, dermatitis, psoriasis and other corticosteroid-responsive dermatoses.

Dosage and administration *Adults and children* Initially, the Temetex preparation best suited to the particular skin condition (see below) should be applied as a thin film two or three times daily according to the severity of the condition. Once clinical improvement has been obtained, maintenance treatment with one application daily should be sufficient.

Temetex cream is suitable for weeping skin lesions on moist skin regions (anus, flexures) which require a base with a high water-content. It allows secretions to drain and ensures rapid drying of the skin.

Temetex fatty ointment is designed for use in chronic and very dry or scaly conditions. The anhydrous, greasy base retains moisture thereby softening the thickened horny layer of the skin, and so improving the penetration of the active substance. As the fatty ointment has an occlusive effect, this largely dispenses with the need for occlusive dressings.

Temetex ointment has the broadest range of application: being suitable for conditions which are neither weeping nor very dry. The base, which has a balanced fat and water content, greases the skin lightly without having an occlusive effect.

In refractory cases either Temetex ointment or Temetex fatty ointment may be applied under an occlusive dressing large enough to cover completely the affected area of skin and affixed to healthy skin. The dressing should not be left on for more than two days but it may be replaced intermittently, if necessary. However, if the lesion becomes infected during treatment the use of occlusive dressings should be suspended until the infection has been controlled.

Temetex preparations are for external application only.

Contra-indications, warnings, etc

Contra-indications: Temetex should not be applied in the presence of syphilitic, tuberculous or viral (chicken pox, vaccinia) infections that involve the skin. It is not suitable for the treatment of ophthalmic conditions.

Temetex fatty ointment should not be applied to weeping lesions.

Precautions: With Temetex, as with all topical corticosteroid preparations, long-term continuous therapy in infants should be avoided as adrenal suppression can occur, even without the use of occlusive dressings. Babies and infants up to four years of age should not therefore be treated for a period of more than three weeks, especially in areas covered by napkins, which may act as an occlusive dressing.

Care should be taken to avoid contact with the eyes. The hands should be washed carefully after applying Temetex.

In pregnant animals topical application of corticosteroids can cause abnormalities of foetal development. The relevance of these findings to human beings has not been established. Nevertheless, topical corticosteroids should not be used extensively (i.e. in large amounts or for prolonged periods) during the first trimester of pregnancy.

Infections in the treated area require additional specific antimicrobial therapy. This treatment can often be topical, but for severe bacterial infections systemic therapy may be necessary. If fungal infections are present a topically active antimycotic agent should be applied.

side-effects: Temetex is well tolerated locally. Very occasionally a mild burning, itching or irritation may occur at the site of application.

As with all topical corticosteroids, there is a risk of skin atrophy, telangiectasia, striae and acneiform eruptions following extensive use of Temetex, particularly with the fatty ointment or where occlusive dressings are applied. The face is more susceptible to such atrophic changes than other areas of the body. The application of unusually large amounts of Temetex preparations may result in the absorption of systemically active amounts of corticosteroid.

In the event of any untoward reaction, treatment should be discontinued.

treatment of overdosage: It is anticipated that ingestion of Temetex preparations is unlikely to present any problems of management. No specific recommendations for treatment are made.

pharmaceutical precautions *Storage:* Recommended maximum storage temperature 30°C.

legal category POM.

package quantities Temetex cream, fatty ointment and ointment in tubes of 30 g.

further information Nil.

product licence numbers

cream	0031/0080
fatty ointment	0031/0082
ointment	0031/0081

ENSILON*

Presentation Ampoules containing 10 mg edrophonium chloride in 1 ml. The ampoule solution is almost colourless.

Uses Properties: Tensilon is an antagonist to cholinesterase, the enzyme which normally destroys acetylcholine. The action of Tensilon can briefly be described, therefore, as the potentiation of naturally occurring acetylcholine. It differs from Prostigmin* (neostigmine) and Mestinon* (pyridostigmine) in the rapidity and brevity of its action.

indications: Myasthenia gravis, as a diagnostic test; to distinguish between overdosage and underdosage of cholinergic drugs; diagnosis of suspected 'dual block'; treatment of paroxysmal supraventricular tachycardia; antidote to curariform drugs.

Dosage and administration *Adults - Test for myasthenia gravis:* A syringe is filled with the contents of 1 ampoule Tensilon (10 mg) and 2 mg is given intravenously, the needle and syringe being left *in situ*. If no reaction occurs within 30 seconds, the remaining 8 mg is injected. In adults with unsuitable veins, 10 mg is given by intramuscular injection.

To differentiate between 'myasthenic' and 'cholinergic' crises: In a myasthenic patient who is suffering from marked muscle weakness, in spite of taking large doses of Mestinon or Prostigmin, a test dose of 2 mg Tensilon is given intravenously one hour after the last dose of the cholinergic compound. If therapy has been adequate, there is a rapid, transient increase of muscle strength; if the patient has been overtreated, Tensilon causes a transient increase of muscle weakness.

Diagnosis of suspected 'dual block': Tensilon 10 mg intravenously. If the block is due to depolarisation, it is briefly potentiated, whereas in a 'dual block', it is reversed.

Treatment of paroxysmal tachycardia: Tensilon 10-20 mg intravenously, combined with carotid sinus pressure if necessary.

Antidote to curariform drugs: Tensilon 10 mg intravenously, repeated if necessary.

Children weighing up to 35 kg: 1 mg Tensilon intravenously or 2 mg intramuscularly.

Weighting more than 35 kg: 2 mg Tensilon intravenously or 5 mg intramuscularly.

Tensilon Ampoules are for intramuscular or intravenous injection.

Tensilon Ampoule solution may be diluted with Water for Injection.

Maintenance of stability cannot be guaranteed when Tensilon Ampoule solution is diluted.

Contra-indications, warnings, etc *Precautions:* Care should be taken in administering Tensilon to patients with bronchial asthma.

A syringe containing 1 mg of atropine should be kept at hand to counteract severe cholinergic reactions, should they occur.

Side-effects: These may include nausea and vomiting, increased salivation, diarrhoea and abdominal cramps.

Effects of overdosage and their treatment: Tensilon overdosage may give rise to bradycardia, arrhythmias, hypotension and bronchiolar spasm. Perspiration, gastro-intestinal hypermotility and visual disturbances may also occur.

Atropine sulphate 1-2 mg intravenously is an antidote to the muscarinic effects.

Pharmaceutical precautions *Storage:* Tensilon Ampoule solution should be protected from light.

Legal category POM.

Package quantities Tensilon Ampoules in packings of 10.

Further information Nil.

Product licence number 0031/5095.

TIGASON* ▼

Presentation Capsules with buff-yellow cap and buff-yellow body with ROCHE printed in black on both cap and body, containing 10 mg tretinate.

Capsules with orange-yellow cap and buff-yellow body with ROCHE printed in black on both cap and body, containing 25 mg tretinate.

Uses Properties: Retinol (vitamin A) is known to be essential for normal epithelial growth and differentiation, though the mode of this effect is not yet established.

Both retinol and retinoic acid are capable of reversing hyperkeratotic and metaplastic skin changes. However, these effects are generally only obtained at dosages associated with considerable local or systemic toxicity.

Tigason, a synthetic aromatic derivative of retinoic acid, has a more favourable therapeutic ratio, with a greater and more specific inhibitory effect on psoriasis and disorders of epithelial keratinization. The usual therapeutic response to Tigason consists of desquama-

tion (with or without erythema) followed by more normal re-epithelization.

Indications: Severe extensive psoriasis which is resistant to other forms of therapy.

Palmo-plantar pustular psoriasis.
Congenital ichthyosis.

Dosage and administration There is a wide variation in the absorption and rate of metabolism of Tigason. This necessitates individual adjustment of dosage. For this reason the following dosage recommendations can serve only as a guide.

Adults: Other dermatological therapy, particularly with keratolytics, should normally be stopped before administration of Tigason, though use of topical corticosteroids or bland emollient ointment may be continued if indicated.

Tigason should be started at a dose of 0.75–1 mg/kg body-weight per day (in most cases 50–75 mg daily), taken in divided doses, for two to four weeks. By this time involved areas of skin will usually show a marked response and/or side-effects should be apparent. If no therapeutic effect is seen by four weeks, and in the absence of toxicity, daily dosage may then be increased in increments of 10 mg at weekly intervals until a response is observed or a total daily dose of 1.5 mg/kg body-weight is reached.

Once a response has been observed, the dosage of Tigason should be reduced to 0.5 mg/kg body-weight per day, taken in divided doses, for a further six to eight weeks, when the maximum therapeutic effect should usually have been obtained.

In patients with psoriasis, Tigason is normally discontinued when the lesions have shown maximum clearing. Further exacerbations may be treated in the same way as and when they occur. In other conditions, continued maintenance therapy, at the lowest dose which will prevent recurrences (usually 0.25–0.5 mg/kg body-weight per day), may be appropriate.

Elderly: Dosage is the same as for adults.

Children: Dosage should be carried out as outlined above for adults. Clinical experience indicates that Tigason is generally better tolerated by children.

Tigason capsules are for oral administration.

Contra-indications, warnings, etc *Contra-indications:* Tigason is teratogenic. Therefore, in any woman of childbearing potential, the risk must be weighed against the expected therapeutic benefit under all circumstances, taking into account the precautions specified below.

Tigason is contra-indicated in patients with hepatic or renal impairment.

Precautions: For all women of childbearing potential the following precautions must be strictly observed.

1. Any woman of childbearing potential who is receiving Tigason must practise long-term, effective contraception, not only during the treatment period but also for at least 12 months following its cessation.

2. The same contraceptive measures must also be taken in the case of repeated treatment for recurrences of the disease.

3. Any pregnancy occurring during treatment with Tigason, or in the 12 months following its completion, carries a high risk of foetal malformation. This would raise the question of the termination of pregnancy for medical reasons. Therefore, before instituting Tigason the treating physician must explain clearly and in detail

what precautions must be taken. This should include the risks involved and the possible consequences of a pregnancy occurring during Tigason treatment or in the 12 months following its completion.

In view of the importance of the above precautions Tigason Patient Information Cards are available to doctors and it is strongly recommended that these be given to all patients.

It is recommended that liver function tests be carried out after one month of treatment and at three-monthly intervals thereafter.

Blood lipids should be monitored at similar intervals in patients who may be predisposed to hypertriglyceridaemia, especially those with a history of type IV hyperlipidaemia, alcohol abuse, obesity and diabetes mellitus.

Patients should be warned of the possibility of alopecia occurring (see 'Side-effects').

Patients should also be instructed to avoid taking preparations containing high doses of Vitamin A, i.e. more than the recommended dietary allowance of 4,000–5,000 iu per day.

Side-effects: The toxic dose of Tigason is close to the therapeutic dose and most patients experience some side-effects during the initial period whilst dosage is being adjusted. These side-effects are generally minor and acceptable to patients. They have proved reversible with reduction of dosage or discontinuation of therapy.

They commonly consist of dryness, sometimes with erosion, of mucous membranes, especially the lips, nose and conjunctivae; desquamation, erythema, thinning and pruritus, rarely burning, of non-involved skin areas; exfoliation of palmar and plantar skin; paronychia. A bland emollient or topical corticosteroid may be prescribed to alleviate the cutaneous inflammation.

Excess hair loss is common and frank alopecia may occur. This is manifested later than other side-effects from four to eight weeks after starting therapy. Normal hair growth resumes from two to twelve weeks after completion of therapy.

Elevation of serum levels of liver transaminases and bilirubin outside the normal range has been observed in a small percentage of patients whilst receiving Tigason. If hepatotoxicity is suspected in any patient, therapy should be discontinued immediately.

Elevation of serum triglyceride levels above the normal range has been reported to occur in some patients, especially those with a predisposition to hypertriglyceridaemia. The changes are dose-related and reversible and may be controlled by dietary means alone in some cases.

Nausea, headache, drowsiness, sweating and anorexia have been reported infrequently.

Treatment of overdosage: Manifestations of acute vitamin A toxicity include severe headache, nausea or vomiting, drowsiness, irritability and pruritus. Signs and symptoms of accidental or deliberate overdosage with Tigason would probably be similar. They would be expected to be reversible and to subside without need for treatment.

Because of the variable absorption of the drug, gastric lavage may be worthwhile within the first few hours after ingestion.

Pharmaceutical precautions *Storage:* Tigason capsules should be stored in a well-closed container and protected from light. The recommended maximum storage temperature is 30°C.

Legal category POM.

Package quantities Tigason capsules 10 mg in packings of 100.

Tigason capsules 25 mg in packings of 100.

Further information *Availability:* Tigason capsules are available only through hospital pharmacies for use in hospitals and hospital clinics.

It is recommended that Tigason be given only by, or under supervision of, a dermatological specialist.

Product licence numbers

Capsules 10 mg 0031/0134

Capsules 25 mg 0031/0135.

TRH-ROCHE

Approved name: Protirelin.

Presentation Plain glass ampoules containing 0.2 mg TRH-Roche (thyrotrophin-releasing hormone) in 2 ml. The ampoule solution is almost colourless to faintly yellow.

Round, white tablets with 'ROCHE' imprinted on one face and a single break bar on the other and imprinted 'TRH' containing 40 mg TRH-Roche (thyrotrophin-releasing hormone).

'TRH'

Uses *Properties:* TRH-Roche stimulates the secretion of thyroid-stimulating hormone (TSH). Intravenous injection results in a prompt rise in serum TSH levels in normal subjects, peak levels being observed about 20 minutes after administration. There is a concomitant rise in serum levels of prolactin. TRH-Roche is also active orally, the maximum TSH response being apparent some two to four hours after ingestion. The maximum responses of protein-bound iodine (PBI), tri-iodothyronine (T_3) and thyroxine (T_4) occur up to five hours after the administration of a single oral dose.

Indications: The administration of TRH-Roche provides a means of assessing thyroid function and the reserve of TSH in the pituitary gland and is recommended as a test procedure where such assessment is indicated. It is particularly useful as a diagnostic test for: mild hyperthyroidism; ophthalmic Graves' disease; mild or preclinical hypothyroidism; hypopituitarism; hypothalamic disease. It may also be used in place of the T_3 suppression test.

Dosage and administration *Intravenous injection:* Tests employing intravenous TRH-Roche are based on the serum TSH response to a standard dose. They provide a means of both quantitative and qualitative assessment of thyroid function. It is essential for each laboratory to establish its own normal range of values for serum TSH before attempting quantitative assessment of TRH-Roche responses by this means.

Intravenous TRH-Roche test:

1. Blood sample taken for control TSH assay.
2. TRH-Roche 0.2 mg given as a single bolus injection.
3. Blood sample taken 20 minutes after injection for peak TSH assay.
4. If necessary, a further blood sample may be taken 60 minutes after injection to detect a delayed TSH response.

The ampoule solution should not be diluted.

Oral TRH-Roche test: Responses to oral TRH-Roche have not been defined within precise limits and they therefore provide a means of qualitative rather than quantitative assessment.

1. Blood sample taken either immediately before TRH-Roche administration or, if more convenient, on the previous day for control TSH assay and/or PBI, T_3 or T_4 estimations.

2. TRH-Roche 40 mg (1 tablet) administered with half a glass of water to the patient fasted overnight.

3. Patient to fast for one hour after taking the tablet.

4. Blood sample taken four to five hours after dosing for repeat estimations of TSH and/or PBI, T_3 or T_4 .

TRH-Roche tablets are for oral administration.

The procedures for administering TRH-Roche to children are identical with those outlined above.

Interpretation of results: Interpretation of the responses to TRH-Roche is based on the increase in TSH and/or PBI, T_3 or T_4 levels from the basal values. In normal subjects, there is a prompt rise in serum levels of TSH. The changes observed in various conditions are briefly outlined below:

1. Hyperthyroidism – no rise in serum TSH or thyroid hormone levels.

2. Ophthalmic Graves' disease – often no rise in serum TSH or thyroid hormone levels.

3. Primary hypothyroidism – exaggerated and prolonged rise in serum TSH but no change in thyroid hormone levels.

4. Hypopituitarism – absent or impaired TSH or thyroid hormone response implies diminished TSH reserve.

5. Hypothalamic disease – a rise in serum TSH or thyroid hormone levels can occur in the presence of hypothyroidism; delayed responses are common.

The TRH-Roche test provides, in most instances, information similar to that obtained from a T_3 suppression test in that an absent or impaired response usually correlates with an absent or impaired response to T_3 suppression.

The response to TRH-Roche may be modified in subjects taking T_3 , T_4 , antithyroid drugs, corticosteroids, oestrogens, theophylline or levodopa.

Contra-indications, warnings, etc *Precautions:*

There are no absolute contra-indications to TRH-Roche. In view of the postulated effect of bolus injections of TRH-Roche on smooth muscle, administration orally would seem more appropriate in patients with bronchial asthma or other types of obstructive airways disease. Caution should also be observed in patients with myocardial ischaemia. TRH-Roche administration is not normally associated with a fall in blood sugar, but caution is recommended when giving the drug orally to patients with severe hypopituitary disease in the fasting state because of the possibility of hypoglycaemia.

Teratogenic effects have not been demonstrated in animal experiments. Nevertheless, the established medical principle of not administering drugs during early pregnancy should be observed.

Side-effects: TRH-Roche is well tolerated. No impairment of hepatic, renal or haematological function has been reported and the drug has no effect on pulse rate, blood pressure or respiration. Following rapid intravenous injection, side-effects of a mild and transient nature may be experienced. They comprise nausea, a desire to micturate, a feeling of flushing, slight dizziness and a peculiar taste, and have been attributed to a local action of the bolus of TRH-Roche on the plain muscle of the gastro-intestinal and genito-urinary tracts. Side-effects after oral administration are very rare, nausea

being the only one so far observed. No reactions of an allergic nature have been noted with TRH-Roche.

Effects of overdosage: No symptoms of overdosage have been noted in patients receiving up to 1 mg intravenously.

Pharmaceutical precautions *Storage:* The recommended maximum storage temperature for TRH-Roche Ampoules is 30°C. No special precautions are required for the Tablets.

Legal category POM.

Package quantities TRH-Roche Ampoules containing 0.2 mg TRH-Roche in 2 ml in packings of 10. TRH-Roche 40 mg Tablets in packings of 10.

Further information *Availability:* TRH-Roche is available to hospitals only.

Product licence numbers

Ampoules 0031/0064
Tablets 0031/0063

VALIUM® ROCHE

Presentation Round, white tablets with 'ROCHE 2' imprinted on one face and a single break bar on the other, containing 2 mg diazepam.

Round, pale yellow tablets with 'ROCHE 5' imprinted on one face and a single break bar on the other, containing 5 mg diazepam.

Round, blue tablets with 'ROCHE 10' imprinted on one face and a single break bar on the other, containing 10 mg diazepam.

Capsules with opaque, blue cap and opaque, white body with 'ROCHE 2' printed in red-brown along both cap and body, containing 2 mg diazepam.

Capsules with opaque, blue cap and opaque, yellow body with 'ROCHE 5' printed in red-brown along both cap and body, containing 5 mg diazepam.

Pink, raspberry-flavoured syrup containing 2 mg diazepam in 5 ml.

Ampoules containing 10 mg diazepam in 2 ml. The ampoule solution is almost colourless to greenish-yellow.

Ampoules containing 20 mg diazepam in 4 ml. The ampoule solution is almost colourless to greenish-yellow.

Suppositories containing 5 mg diazepam.

Suppositories containing 10 mg diazepam.

Uses *Properties:* Valium Roche has potent anxiolytic, anticonvulsant and central muscle-relaxant properties. These effects are probably mediated through special areas of the central nervous system, such as the limbic system, the reticular activating system and the polysynaptic pathways.

Valium Roche has little autonomic activity.

Indications: *Tablets, Capsules, Syrup and Suppositories:* Anxiety and tension states; insomnia associated with anxiety; psychosomatic and organic illness with associated anxiety and physical tension; tension headache; psychoses accompanied by anxiety; muscle spasm; control of muscle spasm in tetanus (also i.v.); as premedication for the nervous dental patient; epilepsy.

Ampoules: Severe acute anxiety and agitation including delirium tremens, acute muscle spasm; tetanus; status epilepticus and convulsions due to poisoning. As intravenous sedative cover before and during minor surgical procedures in obstetrics, surgery, dentistry, ophthalmology, endoscopy, radiology, cardiac catheterisation and cardioversion.

Dosage and administration *Tablets, Capsules, Syrup and Suppositories:* Acute and chronic anxiety states:

Adults: Mild anxiety in ambulant patients – 2 mg three times daily.

Severe anxiety states and obsessive-compulsive neurosis – 15–30 mg daily in divided doses. In severe cases being treated in hospital, 10 mg i.m. may be given and can be repeated after an interval of not less than four hours.

Insomnia associated with anxiety – 5–30 mg before retiring.

Children: 1–5 mg daily in divided doses.

Conditions associated with muscle spasm:

Spastic children with minimal brain damage – 2–40 mg daily in divided doses.

Cerebral palsy of adults particularly associated with athetoid movements – 2–60 mg daily in divided doses.

Upper motor neurone spasticity – 5–60 mg daily in divided doses.

Muscle spasm of varied aetiology, fibrositis, cervical spondylosis – 2–15 mg daily in divided doses.

As oral pre-medication in dental patients – 5 mg the night before, 5 mg on waking and a further 5 mg two hours before the appointment.

Elderly and debilitated patients; doses should be half those recommended for other adults.

Valium Roche Tablets. Capsules and Syrup are for oral administration.

Valium Roche Suppositories are for rectal administration.

Valium Roche Syrup may be diluted with Sorbitol solution BPC or Syrup BP.

Ampoules: Acute muscle spasm, acute anxiety or agitation – 10 mg by i.v. or i.m. injection which can be repeated after an interval of not less than four hours.

As intravenous sedative cover before and during dental surgery and other unpleasant surgical and medical procedures – the dose is governed by the response of the patient. As a guide 0.2 mg/kg body weight is suggested. Total dose usually varies between 10 to 20 mg, but more than 20 mg may be necessary on occasions.

Tetanus – Initially an i.v. dose of 0.1–0.3 mg/kg body weight, repeated at intervals of one to four hours. Continuous i.v. infusion of 3–10 mg/kg body weight/24 hours can also be used as well as identical daily doses by nasoduodenal tube. The dose should be adapted according to the severity of the case, and in extremely severe cases higher doses have been used.

Status epilepticus – Convulsions due to poisoning – *Adults:* 10 to 20 mg IV or IM. *Children:* 0.2 to 0.3 mg/kg body-weight IV or IM, or 1 mg per year of life. These doses may be repeated, as necessary, thirty minutes or one hour later. If required this may be followed by intravenous infusions (maximum dose: 3 mg/kg body-weight over 24 hours).

Febrile convulsions – 0.2 to 0.3 mg/kg body-weight IV or IM, or 1 mg per year of life. These doses may be repeated as necessary.

Elderly and debilitated patients: doses should be half those recommended for other adults.

Intravenous injection may be associated with local reactions, including thrombophlebitis. In order to reduce the likelihood of untoward effects, it is strongly recommended that intravenous injections of Valium Roche should be given into a large vein of the antecubital fossa, the patient having been placed in the supine position and kept there throughout the procedure.

The injection should be given **slowly** (0.5 ml of the

solution per half-minute) until the patient becomes drowsy, his eyelids droop and his speech becomes slurred, but he is still able to respond to requests. If these conditions for administration of Valium Roche intravenously are adhered to the rare possibility of hypotension or apnoea occurring will be greatly diminished. It is suggested that a second person should be present during this procedure and that facilities for resuscitation should always be available. It is recommended that the patient should not be allowed to leave the surgery until one hour at least has elapsed from the time of injection and should always be accompanied by a responsible adult, with a warning not to drive or to operate machinery for the rest of the day.

Valium Roche Ampoule solution should **not** be diluted. One exception to this is when given slowly in large intravenous infusions of normal saline or glucose, such as are given in the treatment of tetanus and status epilepticus. Then up to 40 mg – 8 ml Ampoule solution – in 500 ml is permissible. This infusion dilution should be made up freshly and used within six hours.

Valium Roche Ampoule solution should **not** be mixed with other drugs in the same infusion solution or in the same syringe.

Maintenance of stability cannot be guaranteed if these rules are not obeyed.

Contra-indications, warnings, etc *Precautions:* With Valium Roche, as with other drugs acting on the central nervous system, patients should be instructed to avoid alcohol while under treatment, since the individual response cannot be foreseen. Like all medicaments of this type, Valium Roche may modify patients' reactions (driving ability, operation of machinery, etc) to a varying extent, depending on dosage, administration and individual susceptibility. Similarly, as with many drugs, dosage of Valium Roche must be adapted to the widely varying limits of tolerance encountered in patients with organic cerebral changes (particularly arteriosclerosis) or with cardiorespiratory insufficiency. In these patients parenteral administration should not as a rule be employed. However, Valium Roche may be given parenterally to such patients when treated in hospital, or in an emergency; in the case of i.v. administration the dosage should then be reduced and the injection given slowly.

The use of high doses of benzodiazepines, especially over prolonged periods, may sometimes lead to dependence, particularly in patients with a history of alcoholism or drug abuse. Treatment in these cases should be withdrawn gradually.

Results obtained in trials with several generations of mice, rats, rabbits and dogs indicate that no danger of teratogenic effects need be expected from therapeutic doses of Valium Roche. Nevertheless the established medical principle of prescribing medicaments in early pregnancy only when absolutely indicated should be observed.

If Valium Roche is combined with centrally acting drugs such as neuroleptics, tranquillisers, antidepressants, hypnotics, analgesics and anaesthetics, it should be borne in mind that their sedative effect may be intensified by Valium Roche. In particular, the possibility of severe respiratory and cardiovascular depression should be considered if central depressant drugs are given parenterally in conjunction with intravenous Valium Roche.

Side-effects: Valium Roche is well tolerated and the occurrence of ataxia is evidence of excessive dosage.

When high doses are used they may also have a sedative effect and cause some degree of drowsiness. In such cases there is an advantage in administering half the total daily intake at night, the remainder being given in divided doses during the day.

Effects of overdosage and their treatment: Reported experience of inadvertent or deliberate overdosage indicates that this presents virtually no problem. Doses of up to approximately 2 g Valium Roche taken alone during attempted suicide have produced no long-term ill-effects.

Symptoms of overdosage may include drowsiness, ataxia and dysarthria, with coma in very severe cases. Treatment is symptomatic, but gastric lavage may be useful if performed soon after ingestion.

Pharmaceutical precautions *Storage:* The recommended maximum storage temperature for Valium Roche Syrup and Ampoules is 30°C. Valium Roche Suppositories should be protected from heat. The oral and parenteral forms should be protected from light.

Legal category POM.

Package quantities

Valium 2 Roche

Tablets 2 mg in packings of 100 and 500. Capsules 2 mg in packings of 100 and 500. Syrup 2 mg/5 ml in packings of 100 ml.

Valium 5 Roche

Tablets 5 mg in packings of 100 and 500. Capsules 5 mg in packings of 100 and 500.

Valium 10 Roche

Tablets 10 mg in packings of 100 and 500. Ampoules 10 mg in 2 ml in packings of 10.

Valium 20 Roche

Ampoules 20 mg in 4 ml in packings of 10.

Valium Roche Suppositories 5 mg and 10 mg in packings of 5.

Further information As with a number of other medicaments, intramuscular injection of Valium Roche (but not oral or intravenous administration) can lead to a rise in serum creatine phosphokinase activity, with a maximum between 12 and 24 hours after the injection. This fact should be taken into account in the differential diagnosis of myocardial infarction.

Product licence numbers

Ampoules 10 mg	0031/0068
Ampoules 20 mg	0031/5128
Capsules 2 mg	0031/5124
Capsules 5 mg	0031/5125
Syrup	0031/5126
Tablets 2 mg	0031/5121
Tablets 5 mg	0031/5122
Tablets 10 mg	0031/5123
Suppositories 5 mg	0031/0119
Suppositories 10 mg	0031/0120

VALRELEASE* ▼

Presentation Capsules with opaque blue cap and opaque light blue body with ROCHE printed in red along both cap and body, containing 10 mg diazepam in a controlled-release form.

Uses *Properties:* Valrelease has the characteristics of the benzodiazepine tranquillizers. The active ingredient, diazepam, is released in a controlled manner thus

avoiding the peaks and troughs in plasma levels which are encountered with conventional three-times daily administration.

Indications: Treatment of the symptoms of anxiety – this includes both psychic and somatic manifestations.

Dosage and administration *Adults:* One capsule daily to be taken usually early in the evening. No dosage recommendations are made for elderly patients.

Children: No dosage recommendations are made for children.

Valrelease capsules are for oral administration.

Valrelease capsules should be taken with water.

Contra-indications, warnings, etc *Contra-indications:* Patients with known sensitivity to benzodiazepines; acute pulmonary insufficiency; respiratory depression.

Precautions: In patients with chronic pulmonary insufficiency, and in patients with chronic renal or hepatic disease, dosage may need to be modified.

The use of diazepam during pregnancy should be avoided unless there are compelling reasons for administration.

Diazepam crosses the placenta and the administration of high doses or prolonged administration of low doses in the last trimester of pregnancy or labour has been reported to produce irregularities in the foetal heart, and hypotonia, poor sucking and hypothermia in the neonate.

Diazepam has been detected in breast milk. If possible, the use of Valrelease should be avoided during lactation.

If diazepam is combined with centrally-acting drugs such as neuroleptics, tranquillizers, antidepressants, hypnotics, analgesics and anaesthetics, the sedative effects may be intensified.

Patients should be advised that, like all medicaments of this type, diazepam may modify patients' performance at skilled tasks (driving, operating machinery, etc.) to a varying degree depending upon dosage, administration and individual susceptibility. Patients should further be advised that alcohol may intensify any impairment, and should therefore be avoided during treatment.

The dependence potential of the benzodiazepines is low but this increases when high doses are used, especially when given over long periods. This is particularly so in patients with a history of alcoholism or drug abuse or in patients with marked personality disorders. Regular monitoring in such patients is essential and routine repeat prescriptions should be avoided. Treat-

ment should be withdrawn gradually. Symptoms such as depression, nervousness, rebound insomnia, irritability, sweating, and diarrhoea have been reported following abrupt cessation of treatment with normal therapeutic doses.

In rare instances, withdrawal following excessive dosages may produce confusional states, psychotic manifestations and convulsions.

Abnormal psychological reactions to benzodiazepines have been reported. Rare behavioural effects include paradoxical aggressive outbursts, excitement, confusion, and the uncovering of depression with suicidal tendencies.

Side-effects: Common adverse effects include drowsiness, sedation, unsteadiness and ataxia; these are dose-related and may persist into the following day even after a single dose.

Other adverse effects are rare and include headache, vertigo, hypotension, gastro-intestinal upsets, skin rashes, visual disturbances, changes in libido, and urinary retention. Isolated cases of blood dyscrasias and jaundice have also been reported.

Treatment of overdose: When taken in overdose, diazepam presents few problems in management. Signs may include drowsiness, ataxia and dysarthria, with coma in severe cases. Treatment is symptomatic. Gastric lavage is useful only if performed soon after ingestion. There is no specific antidote to diazepam.

When taken with centrally-acting drugs, especially alcohol, the effects of overdose are likely to be more severe and, in the absence of supportive measures, may prove fatal.

Pharmaceutical precautions *Storage:* Valrelease capsules should be protected from light and stored in a dry place. Recommended maximum storage temperature is 30°C.

Legal category POM.

Package quantities Valrelease capsules 10 mg in packings of 50.

Further information Nil.

Product licence number 0031/0140

**Trade Mark*

Rona Laboratories Limited

Cadwell Lane
Hitchin
Herts SG4 0SF



ARGOTONE*

Presentation Brown liquid containing the following active ingredients:

Ephedrine Hydrochloride BP	0.9%
Mild Silver Protein BPC 1968	1.0%

Uses Nasal decongestant.

Dosage and administration *Argotone Nasal Drops:* 4–6 drops in each nostril three to five times daily.

Argotone Ready Spray: 2–3 sprays in each nostril four to five times daily.

Contra-indications, warnings, etc As with all sympathomimetic amines: prolonged use may cause rebound congestion, although we have not received reports of this caused by Argotone; concurrent administration with monoamine oxidase inhibitors is contra-indicated.

Side-effects: Either incorrect or excessive usage could cause skin discolouration.

Overdosage – Signs and Symptoms: Argyria – a bluish-black discolouration of the skin would indicate ingestion. The signs and symptoms of toxicity would be those of ephedrine over-dosage. Features such as anxiety, insomnia, irritability, giddiness, headache, nausea and vomiting, palpitations, tachycardia, hypertension, difficulty in micturition may occur. In very large doses paranoid psychosis and hallucinations may be prominent. Theoretically in excessive use sufficient ephedrine could be absorbed via the nasal mucosa, particularly in infants who could then exhibit some of these symptoms. We have received no such reports.

Overdosage – Treatment: Since severe overdosage is considered to be so unlikely, treatment should consist mainly of careful monitoring of the patient, particularly respiration and circulation. Methods directed at prevention of further absorption of the ingredients such as emesis or gastric lavage generally are considered inappropriate.

Pharmaceutical precautions It should be protected from light.

Legal category P.

Package quantities *Argotone Nasal Drops:* Glass bottle containing 20 ml. Plastic container of 100 ml for dispensing.

Argotone Ready Spray: Plastic atomiser containing 15 ml.

Further information Rapid effect against all organisms commonly infecting the nasopharynx. No inhibitory effect on nasal cilia. Relieves congestion of mucous membranes.

Product licence number 0161/5005.

DILORAN*

Presentation *Suspension:* Each 10 ml of white, peppermint-flavoured suspension contains:

Magnesium Oxide	320 mg
Aluminium hydroxide/Magnesium carbonate co-dried gel	80 mg
Activated dimethicone	25 mg

Tablets: White, flat tablets, 13 mm in diameter, with a bevelled edge, marked 'Diloran' on each face. Each spearmint-flavoured tablet contains:

Magnesium Oxide	340 mg
Aluminium hydroxide/Magnesium carbonate co-dried gel	85 mg
Activated dimethicone	25 mg

Uses For the relief of dyspeptic symptoms in those conditions where an antacid/antiflatulent preparation is indicated, for example dyspepsia of functional or organic origin, hyperacidity, hiatus hernia, indigestion, oesophagitis, gastritis, and the symptomatic treatment of peptic ulcer.

Dosage and administration For oral administration.

Suspension: Adults: Two to four 5 ml spoonful three times a day between meals and at bedtime, or as required.

Children (5–12 years): One or two 5 ml spoonful three times daily between meals and at bedtime.

Infants (under 5 years): Half to one 5 ml spoonful four times a day.

Tablets: Adults: 1–2 tablets chewed or sucked three times daily between meals and at bedtime, or as required.

Children (5–12 years): 1 tablet chewed or sucked three times daily between meals and at bedtime.

Infants (under 5 years): The dosage form of Diloran Suspension is more adaptable for this age group and is therefore more suitable than tablets.

Contra-indications, warnings, etc As with other antacids care is necessary in hypophosphataemia, renal failure, debilitated states and during the first trimester of pregnancy unless compelling reasons for use. Aluminium hydroxide may also form complexes with tetracyclines and reduce absorption when given concomitantly.

Overdosage – Signs and Symptoms: There is little or no absorption of magnesium and aluminium ions (except in patients with renal failure), and therefore, this is not considered a problem. In very large doses the remaining magnesium ions (which have not been formed into the relatively insoluble carbonate in the intestine) may result in diarrhoea. Aluminium ions form an insoluble salt with phosphate in the intestine leading to a loss of phosphate which should be considered in overdosage situations.

Overdosage – Treatment: Symptomatic. Monitor patients particularly in relation to plasma phosphate levels.

Pharmaceutical precautions No special storage requirements.

Legal category P.

Package quantities *Suspension*: Bottles of 300 ml.
Tablets: Packs of 30.

Further information Diloran is a well-balanced preparation combining three well-accepted insoluble antacids with activated dimethicone. Diloran provides prompt and effective control of gastric acidity, together with a demulcent and antifatulent effect.

The combination of magnesium and aluminium salts means that there is little likelihood of either diarrhoea or constipation.

Product licence numbers

Diloran Suspension 0161/0014
Diloran Tablets 0161/0013

GLUCOPHAGE*

Presentation White, film-coated tablets, marked 'GLUCOPHAGE 500', containing 500 mg Metformin Hydrochloride BP.

White, film-coated tablets, marked 'GLUCOPHAGE 850', containing 850 mg Metformin Hydrochloride BP.

Uses Diet-failed non-insulin dependent diabetic patients, especially if overweight: alone as initial therapy; in combination with a sulphonylurea. Occasionally as adjuvant therapy in insulin-dependent diabetic patients who are usually obese and not well controlled with insulin.

Dosage and administration It is important that Glucophage tablets should be taken in divided doses with meals. The dose should be increased gradually. One 850 mg tablet twice a day or one 500 mg tablet three times a day is often enough to give good diabetic control. This may be achieved within a few days, but it is not unusual for the full effect to be delayed for up to two weeks. If control is incomplete a cautious increase in dosage to a maximum of 3 g daily is justified. Once control has been obtained it may be possible to reduce the dosage.

Contra-indications, warnings, etc

Contra-indications: Diabetic coma and ketoacidosis. Impairment of renal function. Chronic liver disease. Cardiac failure. Recent myocardial infarction. Alcoholism (acute or chronic). Conditions associated with hypoxaemia. States associated with lactic acidosis such as shock or pulmonary insufficiency. History of lactic acidosis.

Precautions: Glucophage is excreted by the kidney and care is consequently necessary in patients with decreased renal function. This may be particularly relevant in very elderly patients.

The use of Glucophage is not advised: in pregnancy, unless there are compelling reasons for its use; in conditions which may cause dehydration; in patients suffering from serious infections or trauma, and in those undergoing surgery and certain investigations such as intravenous urography and intravenous angiography. Glucophage therapy should be stopped 2-3 days before these events and be reinstated only after control of renal function.

It is prudent to stop Glucophage therapy temporarily if any of the above conditions exist, particularly if gastro-

intestinal disturbances are noted or acidosis is suspected. After ketoacidosis and lactic acidosis have been excluded Glucophage treatment may be resumed if renal function is not impaired.

Patients receiving continuous metformin therapy should have an annual estimation of B_{12} in view of reports of decreased B_{12} absorption.

Glucophage therapy with a sulphonylurea or insulin should be monitored by blood-sugar readings because combined therapy may cause hypoglycaemia. If it is decided to stabilise diabetic patients with Glucophage and insulin therapy it is recommended that this is carried out in hospital because of the possibility of hypoglycaemia until the correct ratio of the two drugs is determined.

As with a number of drugs interaction between Glucophage and anticoagulants is a possibility. Thus patients receiving the two drugs may need adjustment of the anticoagulant dosage.

Side effects: Glucophage is well tolerated but gastrointestinal upsets which are usually minor and transient are often avoided by taking Glucophage with meals (which is always recommended). Occasionally a temporary lowering of the dose may be needed. Only 3% of patients have to discontinue Glucophage therapy because of this complication. Therefore, it is important that treatment is not abandoned at the first sign of intolerance since this has been found to resolve spontaneously, and it is usual for gastro-intestinal upsets to disappear within the period during which diabetic control is achieved. It is unusual for them to return and if such symptoms occur an alternative reason should be sought.

Adverse reactions: Lactic acidosis is a serious and often fatal metabolic complication which has been reported in a number of diseases including diabetes. It is characterised by acidosis (decreased blood pH); electrolyte disturbances with an increased anion gap and an increased lactate level with altered lactate/pyruvate ratio. Azotaemia may also be present. Lactic acidosis often has an insidious onset and non-specific symptomatology. Marked anorexia or unexplained weight loss may indicate the onset and precede the full clinical manifestations of lactic acidosis presenting with nausea, vomiting, hyperventilation, malaise and/or abdominal pain. In the majority of fatal cases patients with these early symptoms have not been investigated for lactic acidosis. In patients with a metabolic acidosis lacking evidence of ketoacidosis (ketonuria and ketonaemia) lactic acidosis should be suspected. Lactic acidosis is a medical emergency which must be treated in hospital immediately.

Certain cases of lactic acidosis reported with Glucophage therapy have occurred in patients with complications included in the contra-indications. The problem of lactic acidosis with Glucophage is negligible provided that patients are correctly selected and attention paid to the correct diet and dosage.

Glucophage may be secreted into breast milk but amounts are considered to be negligible.

Overdosage - Signs and Symptoms: Hypoglycaemia is not normally a problem encountered with Glucophage when used alone (fifty tablets have been ingested with no untoward effects on blood sugar). In combination therapy with a sulphonylurea or insulin or with alcohol hypoglycaemia can occur.

In excessive dosage and particularly if there is a possibility of accumulation lactic acidosis should be suspected. Some of the signs and symptoms suggestive

f this condition are nausea, diarrhoea, abdominal pain, dyspnoea.

Overdosage – Treatment: Intensive supportive therapy is recommended which should be particularly directed at correcting fluid loss and metabolic disturbance.

Pharmaceutical precautions No special storage requirements.

Legal category POM.

Package quantities *850 mg:* Securitainers containing 10 or 300 tablets.
100 mg: Securitainers containing 100 or 500 tablets.

Further information Glucophage does not lower blood-sugar levels in non-diabetics, and in diabetics does not cause hypoglycaemia when used alone. (In combination with other antidiabetic agents hypoglycaemia may occur – see above). Weight is reduced and elevated levels of plasma cholesterol, triglycerides and pre-beta-lipoproteins are lowered. Glucophage improves peripheral glucose metabolism.

Product licence numbers

500 mg 0161/5006

350 mg 0161/5007

HEPACORT PLUS*

Presentation *Cream:* A white, percutaneous cream containing in each 10 g tube the following active ingredients:

Heparin Sodium	10,000 units
Hydrocortisone Acetate BP	10 mg

Suppositories: White suppositories each containing the following active ingredients:

Heparin Sodium	2,000 units
Hydrocortisone Acetate BP	2 mg

Uses *Cream:* Eczematous conditions, varicose eczema, superficial phlebitis and pruritus vulvae.

Suppositories: Haemorrhoids, proctitis, anal eczema and pruritus.

Dosage and administration *Cream:* Massage gently into the affected area three times daily.

Suppositories: Insert 1 suppository into the rectum two or three times daily.

Contra-indications, warnings, etc Viral diseases of the skin, especially herpes simplex. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however, topical corticosteroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

In infants, long-term continuous topical therapy should be avoided. Adrenal suppression can occur, even without occlusion.

Precautions: Local infective conditions may require additional specific antimicrobial or antifungal therapy either topical or systemic.

Side-effects: Excessive use of suppositories could in theory cause rectal bleeding. Removal of suppositories should be sufficient treatment.

Overdosage: Ingestion of either Hepacort cream or suppositories is considered unlikely to produce any

untoward symptoms. Heparin is orally inactive and the low hydrocortisone content is considered insufficient to cause systemic absorption to a problematic degree with the amounts that are likely to be ingested.

Pharmaceutical precautions For the storage of suppositories high temperatures should be avoided.

Legal category POM.

Package quantities *Cream:* Tube containing 10 g percutaneous cream.

Suppositories: Boxes containing a tray of 6 suppositories.

Further information Effectively combines advantages of local hydrocortisone with local heparin. Side-effects minimised by low hydrocortisone content.

Product licence numbers

Cream 0161/5008

Suppositories 0161/5009

IBU-SLO* ▼

Presentation Size 0, opaque pink capsule with a colourless transparent cap containing off-white almost spherical pellets. Each capsule contains 300 mg ibuprofen in a timed release formulation which provides a prolonged therapeutic effect.

Uses Non-steroidal anti-inflammatory agent with marked analgesic and antipyretic properties. For the treatment of rheumatoid arthritis; osteoarthritis; ankylosing spondylitis; seronegative (non-rheumatoid) arthropathies; acute periarticular disorders such as bursitis, capsulitis of the shoulder, tendinitis, tenosynovitis. For the relief of mild to moderate pain in sprains, strains, low back pain, dysmenorrhoea, dental and post-operative pain.

Dosage and administration *Adults and children over 12 years:* Dosage is variable according to the severity of the condition.

Recommended dose: Two capsules (600 mg) twice daily, taken night and morning. This may be increased to three capsules (900 mg) twice daily until the acute phase is controlled.

Recommended maintenance dose: One or two capsules twice daily.

Patients should be instructed not to chew or suck the capsules as this destroys the sustained release properties. Providing this is ensured the contents of a capsule may be sprinkled onto a spoonful of soft food, yoghurt or other similar substance for patients who experience difficulty in swallowing the capsules.

The evening dose of Ibu-Slo capsules will maintain a prolonged therapeutic effect throughout the night and help to prevent morning stiffness.

Contra-indications, warnings, etc Active peptic ulceration.

Precautions: As with other non-steroidal anti-inflammatory agents caution should be exercised when prescribing Ibu-Slo capsules during pregnancy and to nursing mothers. Traces of ibuprofen have been detected in breast milk but no adverse effects have been reported.

Ibu-Slo may be used, with caution, in patients with gastrointestinal disease and may often be tolerated by patients with peptic ulcer, or intolerance to other anti-rheumatic drugs.

Warnings and Adverse Effects: Generally well tolerated with a low incidence of side effects. Adverse effects may include gastrointestinal upsets, rashes, headache, nervousness, tinnitus and oedema. Gastrointestinal haemorrhage may rarely occur. Blurred vision, toxic amblyopia, thrombocytopenia and reversible oliguric renal failure have been reported during ibuprofen treatment, but were resolved on cessation of treatment.

Bronchospasm may be precipitated in patients suffering from, or with a previous history of, bronchial asthma or allergic disease.

If given to patients receiving anticoagulant therapy prothrombin time should be monitored at least daily for the first few days of combined treatment.

Overdosage – Signs and Symptoms: The following have been reported, headache, vomiting, drowsiness, loss of consciousness and hypotension.

Overdosage – Treatment: Symptomatic treatment is recommended directed at maintaining normal blood pressure, and correcting any electrolyte imbalance particularly potassium.

In children emesis and in adults gastric lavage may need to be considered, but only after careful assessment of the patients condition, in particular the level of consciousness.

Pharmaceutical precautions Keep container well closed. Store in a cool, dry place protected from light. Shelf life 3 years.

Legal category POM.

Package quantities Securitainers containing 120 capsules.

Further information Ibuprofen relieves pain, reduces joint inflammation and swelling and frequently facilitates restoration of mobility.

Product licence number 0161/0025.

KELOCYANOR*

Presentation 20 ml ampoule of a sterile aqueous rose-coloured solution containing the following active ingredient.

Dicobalt edetate 300 mg

Uses Specific antidote for acute cyanide poisoning.

Dosage and administration Treatment must be put into effect as soon as possible.

In the most severe cases of cyanide poisoning speed of administration is essential. It is however recommended that the intravenous injection is given steadily taking approximately one minute. If in the doctor's judgement the condition is less severe but still warrants the use of Kelocyanor it is recommended that the injection is administered slowly over a period of approximately five minutes. The intravenous injection of 1 × 20 ml ampoule of Kelocyanor should be followed immediately, using the same needle, by 1 × 50 ml ampoule of Dextrose Injection Strong BPC. If there is inadequate response a second ampoule of Kelocyanor may be given followed by a further 1 × 50 ml ampoule of Dextrose Injection Strong BPC. If there is still no response after five minutes a third ampoule may be given.

Contra-indications, warnings, etc The initial effect of Kelocyanor injection is a fall in blood pressure, a rise in pulse rate and sometimes retching. Immediately after

this phase lasting about one minute the patient should recover.

Cobalt is normally toxic and it is essential to ensure that the condition is cyanide poisoning. A few reports have been received of adverse reactions to Kelocyanor. These have generally occurred either in the absence of free cyanide ions (misdiagnosis) or when the degree of poisoning is very mild. The decision to use Kelocyanor is therefore a question of clinical judgement for the doctor and must be assessed on the severity of the symptoms at the time. Animal experiments have shown that there is a reciprocal antidote action between cyanide and cobalt and that the toxicity of cobalt is diminished by the administration of cyanide – demonstrated by a substantially increased LD₅₀ of Kelocyanor in the presence of cyanide.

Overdosage – Signs and Symptoms: These may be due to cobalt toxicity or to an anaphylactic type reaction, which may be dramatic. They include acute shock, drop in blood pressure, which may be considerable, cardiac irregularities, pain, collapse, urticaria, laryngeal and facial oedema and breathlessness.

Overdosage – Treatment: Intensive supportive therapy is required directed at maintaining blood pressure, a clear airway, respiration and circulation and correcting fluid loss. Patients should be carefully monitored for at least 48 hours.

This information is based only on those cases of misdiagnosis (that is administration in the absence of free cyanide ions or the presence of only low levels) reported to us, and this therapy resulted in complete recovery.

Pharmaceutical precautions Store in a cool place. Shelf-life 3 years.

Legal category POM.

Package quantities Carton containing 6 × 20 ml ampoules.

Further information Nil.

Product licence number 0161/5011.

MADECASSOL*

Presentation Ointment: White ointment containing 1% titrated extract of *Centella asiatica*.

Powder: White powder containing 2% titrated extract of *Centella asiatica*.

Uses Topical use for minor wounds, e.g. bedsores, urinary rash, burns, chapped hands, sunburn, etc.

Dosage and administration Madecassol Ointment and Powder should be applied to the lesion as often as required, preferably two or three times daily. In addition to the usual aseptic precautions, the wound should be cleaned before each application.

Contra-indications, warnings, etc Normal wound hygiene should accompany the use of Madecassol. It does not possess antibiotic properties. Not suitable for ophthalmic use.

Side effects: Very rarely symptoms such as pruritus, burning sensation and eczematous rash have occurred.

Overdosage – Signs and Symptoms: The ingestion of sufficient Madecassol ointment or powder to produce untoward symptoms is considered unlikely, although we have no experience of this occurring.

Overdosage Treatment: No specific treatment is recommended.

Pharmaceutical precautions No special storage requirements.

Legal category GSL.

Package quantities *Ointment:* Tube containing 10 g Madecassol Ointment 1%.

Powder: Puffer pack containing 2 g Madecassol Powder 1%.

Further information Ointment base does not contain anolin.

Product licence numbers

Ointment 0161/5012

Powder 0161/5013

NYDRANE*

Presentation White, uncoated tablets engraved 'Nydrane' on one side and a break line on the reverse, containing the following active ingredient:

3eclamide 500 mg

Uses Behaviour disorders, in epileptic or non-epileptic patients, particularly where instability is marked and aggressiveness a feature. Grand mal and psychomotor epilepsy.

Dosage and administration

1. Behaviour disorders

Adults: Initially 6 tablets (sometimes up to 8 tablets) of Nydrane daily in divided doses. Maintenance dosage will vary according to patient response. This will usually be from 3 to 6 tablets of Nydrane daily, but occasionally more may be required.

Children 5–10: 3 tablets daily in divided doses.

Children under 5: 1½–2 tablets daily in divided doses.

2. Epilepsy

Caution – do not attempt immediate replacement of existing therapy.

Adults: Initially 6 tablets (sometimes up to 8 tablets) of Nydrane daily in divided doses. It is essential to delay reducing previous therapy until the maximum therapeutic effect of Nydrane has been obtained, which may take up to four weeks. Then existing medication may be reduced slowly and cautiously while maintaining control.

Children 5–10: 3 tablets daily in divided doses.

Children under 5: 1½–2 tablets daily in divided doses.

Contra-indications, warnings, etc

Precautions: In epileptics it is essential to delay reducing previous therapy until the maximum therapeutic effect of Nydrane has been obtained, which may take up to four weeks. Caution is particularly essential in patients with a tendency to develop status epilepticus, or with a history of previous attacks. Although no teratogenic effects have been reported during many years of use, in common with the majority of drugs the use of Nydrane during pregnancy should be avoided if possible. Secretion into breast milk; no information is available.

Side effects: The very few side effects reported have been of a mild and transient nature and include eucopenia, renal disturbance, loss of weight, dizziness, gastro-intestinal symptoms, skin irritation and rash.

Overdosage – Signs and Symptoms: Vertigo and vomit-

ing are thought most likely to occur. Nystagmus has been reported. Theoretically there is a possibility of increased drowsiness leading to coma.

Overdosage – Treatment: Symptomatic treatment is recommended and neurological and biochemical monitoring for at least 48 hours. Patients have recovered from overdoses without special treatment. This information is based on two reported cases only.

Pharmaceutical precautions No special storage requirements.

Legal category POM.

Package quantities Securainers containing 100 or 500 tablets.

Further information Free from side-effects commonly associated with anticonvulsant drugs, including gum hypertrophy and somnolence. Specific action in behaviour disorders, particularly if instability is marked and aggressiveness a feature.

Product licence number 0161/5015.

RONYL*

Presentation White, uncoated tablets with 'Ronyl' engraved on one side and a break line on the reverse, containing the following active ingredient:

Pemoline 20 mg

Uses Psychogenic fatigue and fatigue arising post-operatively, or during convalescence. In geriatrics to avoid 'cat napping'. To combat somnolence in combination with tranquillising drugs, and antihistamines.

Dosage and administration In order to avoid interference with sleep, Ronyl should preferably be given before 2 p.m.

Adults: 1 tablet twice daily (the dosage should be adjusted according to individual response and body weight; normally a maximum of 4 tablets daily is sufficient; however, in special situations up to 6 may be given).

Children over 6 years and elderly patients: ½ tablet twice daily. (The dosage should be adjusted according to individual response and body weight and up to 2 tablets daily can be given).

Contra-indications, warnings, etc

Precautions: Theoretically a combination of Ronyl and a monoamine oxidase inhibitor could result in enhanced CNS stimulation, and this should be considered before administering Ronyl with this group of drugs. Although no teratogenic effects have been reported during many years of use, in common with the majority of drugs the use of Ronyl during pregnancy should be avoided if possible. No determinations of pemoline in breast milk have been carried out due to technical difficulties. If it is considered absolutely essential to administer Ronyl to nursing mothers the infant should be carefully monitored.

Side effects: These are mild and transient. Dizziness, sweating, palpitations and headache have been reported only rarely.

Overdosage – Signs and Symptoms: Headache, palpitations, tachycardia, extreme restlessness, dizziness and sweating. In some cases vomiting and constant choreiform movements.

Overdosage – Treatment: This is essentially the same as for any drug which has a stimulant effect on the central nervous system. Intensive supportive therapy is generally recommended.

Gastric lavage may be required but should only be considered after careful assessment of the patients condition and the time since ingestion which should be no more than four hours.

In two reported cases phenobarbitone and I/V Dextrose 5% were successfully used, a more recent report suggests diazepam may be of value in controlling the hyperactivity. Neurological and biochemical monitoring is recommended for two to three days.

Pharmaceutical precautions No special storage requirements.

Legal category POM.

Package quantities Securitainers containing 50 or 250 tablets.

Further information No reports of addiction. Removed from control under Misuse of Drugs Act 1971.

Product licence number 0161/5017.

SLO-PHYLLIN*

Presentation Capsules containing Theophylline BP (anhydrous) in a timed release formulation which provides a prolonged therapeutic effect over 12 hours.

60 mg: Size 2 opaque white capsule with a clear colourless cap, filled with white pellets. Each capsule contains 60 mg Theophylline BP (anhydrous).

125 mg: Size 1 opaque dark brown capsule with a clear colourless cap, filled with a mixture of brown and white pellets. Each capsule contains 125 mg Theophylline BP (anhydrous).

250 mg: Size 0 opaque blue capsule with a clear colourless cap, filled with a mixture of blue and white pellets. Each capsule contains 250 mg Theophylline BP (anhydrous).

Uses As a bronchodilator in the symptomatic and prophylactic treatment of the asthmatic and for reversible bronchoconstriction associated with chronic bronchitis, bronchial asthma and emphysema.

Dosage and administration *Adults and children over 12 years:* 250–500 mg twice daily.

Children 6–12 years (20–35 kg): 125–250 mg twice daily.

Children 2–6 years (10–20 kg): 60–120 mg twice daily. Initially the lowest dosage suggested for each age group is recommended.

This may be increased gradually if optimal bronchodilator effects are not achieved. Generally the total daily (24 hour) dosage should not exceed 20 mg/kg body weight (ranging from 13 mg/kg body weight for adults to 24 mg/kg body weight for children under 9 years), given in divided doses at intervals of 12 hours. If a higher dosage is required it is strongly recommended that plasma theophylline concentrations should be monitored, since it has been established that significant variations occur among individuals in the rate of drug elimination.

N.B.: Careful monitoring is recommended for patients with congestive heart failure or hepatic dysfunction as

they may have lower total clearance of theophylline which could lead to higher than normal plasma levels.

Patients should be instructed not to chew or suck capsules as this destroys the sustained release properties. Providing that this is ensured the contents of a capsule may be sprinkled onto a spoonful of soft food such as yoghurt or other suitable substance for children who experience difficulty in swallowing.

Contra-indications, warnings, etc

Precautions: Normal for theophylline – safety in human pregnancy has not been established, and theophylline can cross the maternal placenta. Caution should be exercised in patients with peptic ulcers, cardiovascular disease (especially if cardiac arrhythmias are present) or in severe hypertension.

Slo-phyllin should not be used concurrently with other preparations containing xanthine derivatives. It is recommended that nursing mothers take their dose of theophylline after breast feeding, since theophylline is distributed to breast milk.

Caution is particularly advised if it is necessary to administer aminophylline to patients receiving a slow release theophylline preparation. Monitoring of plasma theophylline concentrations is recommended at the earliest opportunity.

Side-effects: Tend to occur only if theophylline blood levels exceed 20 mcg/ml and a reduction of daily dosage usually corrects this problem. Gastric irritation, nausea, vomiting and abdominal discomfort should be anticipated in 10% of patients started on a dose of 16 mg/kg body weight daily. Other side-effects are: palpitation, fall in blood pressure, headache, occasional diarrhoea and insomnia. CNS stimulation and diuresis especially in children.

Whilst children may sometimes require higher than conventional doses, the above side-effects may not always be either apparent or expressed and it is, therefore, important not to exceed the recommended dose unless plasma theophylline concentrations are monitored.

Overdosage – Signs and Symptoms: These are varied both in degree and in order of appearance. They include nausea, vomiting, haematemesis, diuresis, restlessness, irritability possibly leading to tremors, convulsions, drowsiness and coma. It is important to be aware that with xanthine derivatives even small doses may produce serious complications and the first symptom could be a convulsion. There may be a latent period of up to 10 hours before any symptoms appear.

Overdosage – Treatment: Intensive therapy is required most importantly directed at maintaining respiration, circulation and correcting fluid loss and electrolyte imbalance, especially potassium. Gastric lavage should only be considered after careful assessment of the patient's condition in particular the level of consciousness.

Under these circumstances, oral activated charcoal may provide a useful alternative treatment. Recent experience gained from overdosage with other theophylline containing preparations would suggest that treatments directed at increasing drug elimination such as charcoal haemoperfusion are more effective. It is essential to monitor the patient carefully for two or three days.

Drug interactions: Relatively few have been documented; these have involved phenytoin, cimetidine, diazepam, lithium carbonate, propranolol, frusemide,

Blood dyscrasias (agranulocytosis, thrombocytopenia, aplastic anaemia) may occur suddenly after a small dose or insidiously after prolonged therapy, particularly in the elderly. Blood counts should be monitored regularly both before and during therapy. Therapy should be stopped if symptoms suggestive of these complications arise (e.g. bruising, fever, sore throat and rash).

Isolated occurrences of an 'acute pulmonary syndrome' – marked by dyspnoea, fever, shadows in radiographs of the lungs, and sometimes also by eosinophilia – have been reported. Although a causal relationship has not been proven, the drug should be withdrawn at first signs of this potentially serious syndrome, for the treatment of which corticosteroids and supportive cardiotherapy may be necessary.

Adverse effects of phenylbutazone therapy should always be weighed against the severity of the patient's condition and the expected clinical effect.

Accidental overdose: There is no known antidote to Butazolidin Alka and treatment is symptomatic. Immediate treatment consists of forced emesis to recover undigested tablets. This is followed by gastric lavage with sodium bicarbonate solution.

Pharmaceutical precautions *Storage:* Tablets – protect from heat and moisture.

Legal category POM.

Package quantities *Mantle tablets:* Containers of 100 and 250.

Further information When rheumatic patients require supplementary antacids the unique formulation of Butazolidin Alka, a mantle of antacids around a central core of Butazolidin and antacid, allows a high percentage of these patients to continue to receive long-term antirheumatic therapy without distressing gastric upsets or the uncertainties of multiple medications with a consequent increased opportunity for uninterrupted successful long-term antirheumatic therapy.

Product licence number 0001/5003.

EURAX*

Presentation The active ingredient, Crothamiton BP, is presented as: white to cream coloured, non-staining ointment with an odour of perfume, containing 10% crothamiton. Also as a white to yellowish-white non-staining emulsion, with an odour of perfume, containing 10% crothamiton.

Uses *Antipruritic/sarcopticide:* Neurodermatitis; anogenital, senile pruritus. Pruritus associated with dermatoses. Pruritus as a symptom of systemic disease; allergic pruritus in the presence of diabetes mellitus or jaundice; pruritus due to drug hypersensitivity. Scabies.

Dosage and administration Eurax is applied externally in either ointment or lotion form.

Method of use: *Pruritus:* Eurax Ointment or Lotion should be massaged into the affected areas as frequently as required to prevent itching. Treatment can be expected to remain effective for 6 to 10 hours after each application.

Scabies: The patient should take a hot bath, using soap and flannel, and dry himself on a towel. Eurax should then be applied to the body from the chin down, with particular attention to the interdigital spaces, the flexor surfaces of the wrists, the inner and outer aspects of the

elbows, the axillae, the under surface of the breasts, the umbilicus, the buttocks, and the inner aspects of the thighs. To ensure complete eradication, a second application 24 hours later is advisable, but a bath should not be taken until the day after, to wash off the application. The clothes should then be changed and sheets sent to the laundry.

Contra-indications, warnings, etc

Contra-indications: Acute exudative dermatoses.

Eurax should not be used near the eyes since contact with the eyelids may give rise to conjunctival inflammation.

Pharmaceutical precautions *Storage:* Ointment and Lotion – protect from heat.

Dilutions: Diluents or other additives to these formulations are not recommended.

Legal category P.

Package quantities

Ointment: Tubes of 30 g and 100 g.

Lotion: Bottles of 150 ml and 1 litre.

Further information Nil.

Product licence numbers

Ointment 0001/5008

Lotion 0001/5009

EURAX* – HYDROCORTISONE

Presentation The active ingredients, Crothamiton BP and Hydrocortisone BP, are presented as: white to cream coloured soft cream with a faint odour of perfume, containing Crothamiton BP 10% and Hydrocortisone BP 0.25%.

Uses *Antipruritic/anti-inflammatory:* Eurax-Hydrocortisone is useful in the symptomatic treatment of many types of itching dermatoses, since it combines a distinctive antipruritic action with bacteriostatic, anti-inflammatory and anti-allergic properties.

Pruritus ani, pruritus vulvae, pruritus scroti, senile pruritus.

Dermatoses with associated pruritus.

Seborrhoeic dermatitis, eczema, contact dermatitis, lichen simplex, dermatitis herpetiformis, neurodermatitis, pityriasis rosea, varicose eczema, urticaria.

Allergic pruritus; pruritus in the presence of diabetes mellitus or jaundice; pruritus due to drug hypersensitivity.

Dosage and administration Eurax-Hydrocortisone is applied externally.

Method of application: A thin layer of Eurax-Hydrocortisone Cream should be applied to the affected area two to three times a day.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to crothamiton.

Chickenpox, skin eruptions following vaccination, tuberculosis of the skin, and syphilitic skin affections.

Eurax-Hydrocortisone should not be used in the presence of acute exudative dermatoses.

Precautions: It has been shown that corticosteroids can be absorbed by eczematous skin. Long-term administration of Eurax-Hydrocortisone to large areas should, therefore, be avoided if possible, regardless of whether occlusion is used. If such administration is unavoidable, precautions similar to those taken with patients receiving

danger of cardiac decompensation. Butazolidin is also contra-indicated in the presence of renal and hepatic disease, including recent hepatitis. History of gastro-intestinal ulceration, blood dyscrasia, drug rash or known sensitivity to pyrazoles (and also lignocaine in the case of Butazolidin ampoules).

Precautions: History of dyspepsia.

Since Butazolidin may potentiate the action of coumarin-type anticoagulants by displacement from plasma protein binding, frequent estimations of prothrombin levels should be undertaken when these drugs are administered concurrently. Similarly, Butazolidin potentiates certain oral hypoglycaemic agents and sulphonamides, the dosage of which may need reducing.

It is suggested that Butazolidin be used with caution in pregnant women, weighing the potential risks against the possible benefits.

Side-effects: Gastro-intestinal intolerance or bleeding due to Butazolidin may occur.

Drug rash, oedema, haematemesis, salivary gland swelling, goitre and jaundice due to intrahepatic cholestasis or parenchymal hepatitis have also been reported.

Blood dyscrasias (agranulocytosis, thrombocytopenia, aplastic anaemia) may occur suddenly after a small dose or insidiously after prolonged therapy, particularly in the elderly. Blood counts should be monitored regularly both before and during therapy. Therapy should be stopped if symptoms suggestive of these complications arise (e.g. bruising, fever, sore throat and rash).

Isolated occurrences of an 'acute pulmonary syndrome' – marked by dyspnoea, fever, shadows in radiographs of the lungs, and sometimes also by eosinophilia – have been reported. Although a causal relationship has not been proven, the drug should be withdrawn at first signs of this potentially serious syndrome, for the treatment of which corticosteroids and supportive cardiotherapy may be necessary.

Adverse effects of phenylbutazone therapy should always be weighed against the severity of the patient's condition and the expected clinical effect.

Accidental overdosage: There is no known antidote to Butazolidin and treatment is symptomatic. Immediate treatment consists of forced emesis to recover undigested tablets. This is followed by gastric lavage.

Pharmaceutical precautions *Storage:* Tablets 100 mg and 200 mg – protect from moisture. Suppositories 250 mg – protect from heat. Ampoules 600 mg in 3 ml with 1% Xylocaine – store in a cold place (2–7°C).

Legal category POM.

Package quantities *Tablets 100 mg:* Containers of 100 and 1,000.

Tablets 200 mg: Containers of 100 and 500.

Suppositories 250 mg: Boxes of 50.

Ampoules 600 mg in 3 ml with 1% Xylocaine: Boxes of 5.

Further information The therapeutic effectiveness of Butazolidin, a non-hormonal antirheumatic agent is based on its powerful and prolonged analgesic activity together with valuable anti-inflammatory and antipyretic activity. This threefold action provides prompt and sustained relief from pain with improvement in functional capacity in a wide range of rheumatic and allied rheumatic conditions.

Product licence numbers

Tablets 100 mg 0001/5004

Tablets 200 mg	0001/5005
Suppositories 250 mg	0001/5038
Ampoules 600 mg in 3 ml with 1% Xylocaine	0001/5037

BUTAZOLIDIN* ALKA

Presentation The active ingredients, Phenylbutazone BP 100 mg, Dried Aluminium Hydroxide Gel BP 100 mg, and Magnesium Trisilicate BP 150 mg, are presented as: round, bi-convex, white, compression-coated tablets, approximately 11.7 mm diameter, impressed GEIGY on one side.

Uses Rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and acute gout.

Osteoarthritis of the spine and degenerative disc disease presenting as lumbago, sciatica or radiculitis.

Prolapsed intervertebral disc.

Reiter's disease and other seronegative (non-rheumatoid) arthropathies.

Bone pain associated with Paget's disease and secondary neoplasm.

Moderate to extensive superficial thrombophlebitis.

Dosage and administration Butazolidin Alka is given orally in tablet form.

Adult: For the initial 48 hours 400–600 mg daily in divided doses with meals. Maintenance doses should be reduced to the minimum amount that will provide continuous therapeutic control, usually 200–300 mg daily.

Note: In acute gout a maximum dosage of 800 mg daily may be necessary.

Paediatric: Dosage is in the range 5–10 mg per kg, with emphasis on the lower end of the scale. As a guide the small seven year old and younger children should be given 1 × 100 mg tablet per day. In children of average weight between 7–12 years of age, 2 × 100 mg tablets per day in divided doses is sufficient.

Contra-indications, warnings, etc

Contra-indications: Butazolidin Alka is contra-indicated in the presence of oedema or hypertension where there is danger of cardiac decompensation. Butazolidin Alka is also contra-indicated in the presence of renal and hepatic disease, including recent hepatitis, history of gastro-intestinal ulceration, blood dyscrasia, drug rash or known sensitivity to pyrazoles.

Precautions: History of dyspepsia.

Since Butazolidin Alka may potentiate the action of coumarin-type anticoagulants by displacement from plasma protein binding, frequent estimations of prothrombin levels should be undertaken when these drugs are administered concurrently. Similarly, Butazolidin Alka potentiates certain oral hypoglycaemic agents and sulphonamides, the dosage of which may need reducing.

It is suggested that Butazolidin Alka be used with caution in pregnant women, weighing the potential risks against the possible benefits.

Side-effects: Whilst the incidence of gastro-intestinal intolerance or bleeding is significantly reduced with Butazolidin Alka, other side-effects associated with Butazolidin should be anticipated.

Drug rashes, oedema, haematemesis, salivary gland swelling, goitre and jaundice due to intrahepatic cholestasis or parenchymal hepatitis have been reported.

It is suggested that Butacote be used with caution in pregnant women, weighing the potential risks against the possible benefits.

Side-effects: Whilst gastro-intestinal intolerance or bleeding due to Butacote is rarely encountered, the following side-effects generally associated with Butazolidin should be anticipated: drug rash, oedema, haematemesis, salivary gland swelling, goitre and jaundice due to intrahepatic cholestasis or parenchymal hepatitis have also been reported.

Blood dyscrasias (agranulocytosis, thrombocytopenia, aplastic anaemia) may occur suddenly after a small dose or insidiously after prolonged therapy, particularly in the elderly. Blood counts should be monitored regularly both before and during therapy. Therapy should be stopped if symptoms suggestive of these complications arise (e.g. bruising, fever, sore throat and rash).

Isolated occurrences of an 'acute pulmonary syndrome' – marked by dyspnoea, fever, shadows in radiographs of the lungs, and sometimes also by eosinophilia – have been reported. Although a causal relationship has not been proven, the drug should be withdrawn at first signs of this potentially serious syndrome, for the treatment of which corticosteroids and supportive cardiotherapy may be necessary.

Adverse effects of phenylbutazone therapy should always be weighed against the severity of the patient's condition and the expected clinical effect.

Accidental overdosage: There is no known antidote to Butacote and treatment is symptomatic. Immediate treatment consists of forced emesis to recover undigested tablets. This is followed by gastric lavage.

Pharmaceutical precautions *Storage:* Tablets – protect from heat and moisture.

Legal category POM.

Package quantities *Tablets 100 mg:* Containers of 100 and 500.

Tablets 200 mg: Containers of 100.

Further information Pharmacological studies confirm that the special formulation of Butacote is completely reliable and will not crack or disintegrate in the acid pH of the gastric juice, but rapidly disintegrates and dissolves in the alkaline pH of the small bowel. Clinical studies confirm that this mode of action significantly reduces the incidence of gastric upsets generally experienced with potent antirheumatics and that it is an effective therapy in the treatment of a wide range of rheumatic conditions.

Product licence numbers

Tablets 100 mg 0001/0024

Tablets 200 mg 0001/0056

BUTAZOLIDIN*

Presentation The active ingredient, Phenylbutazone BP, is presented as: red, sugar-coated tablets, bi-convex, approximately 7.6 mm diameter and imprinted GEIGY on one side, each containing 100 mg.

White, sugar-coated tablets, bi-convex, approximately 10 mm diameter and imprinted GEIGY on one side, each containing 200 mg.

White, waxy suppositories each containing 250 mg.

Ampoules of clear glass containing 600 mg Butazolidin Sodium in 3 ml with 1% Xylocaine.t

Uses Rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and acute gout.

Osteoarthritis of the spine and degenerative disc disease presenting as lumbago, sciatica or radiculitis.

Prolapsed intervertebral disc.

Reiter's disease and other seronegative (non-rheumatoid) arthropathies.

Bone pain associated with Paget's disease and secondary neoplasm.

Moderate to extensive superficial thrombophlebitis.

Dosage and administration Butazolidin may be administered orally, rectally or by deep intramuscular injections, all routes being suitable for the full range of indications.

Oral dosage (adult): For the initial 48 hours 400–600 mg daily in divided doses with meals. Patients with sensitive stomachs should be given a sodium-free antacid at the same time. Maintenance doses should be reduced to the minimum amount that will provide continuous therapeutic control, usually 200–300 mg daily.

Note: In acute gout a maximum dosage of 800 mg daily may be necessary.

Rectal dosage: Suppositories of Butazolidin (250 mg) have been found to be a therapeutically effective alternative or supplementary dosage form.

One or two Butazolidin suppositories (250–500 mg) daily, as a sole therapy achieves a clinical response similar to that obtained by oral maintenance therapy.

When a suppository is required on retiring to control night pain, the total daily dosage of tablets and suppositories should not exceed 650 mg initially, with subsequent reduction to the maximum combined maintenance dose (350 mg).

Parenteral dosage: 1 × 3 ml ampoule (600 mg Butazolidin sodium) every two or three days. Injections can be given less frequently as the patient improves.

Injections should be given into the gluteal muscles only (and never into the arm), under aseptic conditions. The injection should be made into the upper quadrant of the gluteal region (*m. gluteus medius*) with the needle directed sagittally and perpendicularly to the frontal plane. The needle should not be directed medially or caudally, because of the danger of striking the sciatic nerve. From the upper outer quadrant the general direction of the needle should be towards the iliac crest. The injection must be definitely intramuscular, i.e. deep enough to avoid deposition of the drug in fatty tissue. The injection should be made very slowly, with repeated aspiration, and not against abnormal resistance. If the patient feels pain or great discomfort, either at the site of injection or down the leg, the injection should be stopped at once. Abscess formation has occasionally been reported and severe peripheral nerve damage has been observed following a misplaced injection. These complications should not occur if the above precautions are observed.

The intravenous route is **not** advised.

Oral dosage (paediatric): Dosage is in the range 5–10 mg per kg, with emphasis on the lower end of the scale. As a guide the small seven year old and younger children should be given 1 × 100 mg tablet per day; in children of average weight between 7–12 years of age, 2 × 100 mg tablets per day in divided doses is sufficient.

Contra-indications, warnings, etc

Contra-indications: Butazolidin is contra-indicated in the presence of oedema or hypertension where there is

† Licensed by AB Astra (Sweden).

Indication Prevention of cardiac mortality following recent myocardial infarction.

Dosage and administration

Administration: Anturan is administered orally in tablet form with meals or milk.

Dosage: *Adults:* one 200 mg tablet four times daily, commencing approximately one month after myocardial infarction.

Children: Paediatric usage not established.

Contra-indications, warnings, etc

Contra-indications: Active peptic ulcer. Sensitivity to phenylbutazone or other pyrazole derivatives. Severe hepatic disease.

Precautions: Use with caution in patients with impaired renal function or nephrolithiasis; in these cases, regular assessment of renal function is indicated.

Use with caution in patients with healed peptic ulcer.

Salicylates increase bleeding time and may cause haemorrhage; caution should be exercised when administering Anturan and aspirin together.

Since Anturan may potentiate the action of coumarin-type anticoagulants, frequent estimation of prothrombin time should be undertaken when these drugs are given concurrently, and the dosage of the anticoagulant adjusted accordingly.

Anturan may also potentiate the action of other plasma protein-binding drugs such as hypoglycaemic agents and sulphonamides, which may necessitate a modification in dosage.

Anturan should be used with caution in pregnant women, weighing the potential risks against the possible benefits.

Warnings and side-effects: During the early stages of treatment in patients with hyperuricaemia or gout, acute attacks of gout may be precipitated.

To help prevent episodes of urolithiasis or renal colic, ensure adequate fluid intake and alkalisation of the urine during initial stages of therapy.

Gastro-intestinal bleeding has been reported; transient gastro-intestinal side-effects may occur and are usually of a mild nature.

Rash or blood dyscrasias may occur, and are contra-indications to further treatment; onset may be sudden or gradual, and occur after small doses or after long periods of treatment.

For the early detection of a haematological abnormality, careful clinical supervision and a full blood count should be done before and at regular intervals during treatment.

Invalidation of results of renal function tests involving p-aminohippuric acid (PAH), phenolsulphthalein (PSP), or other organic acids may occur.

Accidental overdosage There is no antidote to Anturan and treatment is symptomatic. Immediate treatment consists of forced emesis to recover undigested tablets. This is followed by gastric lavage, preferably with mild alkaline solutions such as sodium bicarbonate solution, and supportive therapy as indicated.

Pharmaceutical precautions *Storage:* Protect from heat and moisture.

Legal category POM.

Package quantities Cartons of 112 consisting of 4 calendar reminder foils of 28.

Further information Upon exposure to a thrombo-

genic stimulus such as damaged vasculature, platelets adhere to the exposed sub-endothelium and release mediators which cause further platelet adhesion, and thrombus formation. This thrombus, or its embolisation distally, may cause vessel occlusion; emboli released into the coronary microcirculation may lead to fatal arrhythmia. As a modulator of platelet function Anturan inhibits thrombus formation, and reduces the risk of sudden cardiac death. It has also been shown to protect the vascular endothelium in primates.

Product licence number 0001/0080.

BUTACOTE*

Presentation The active ingredient, Phenylbutazone BP, is presented as sugar-coated, enteric tablets, bi-convex, approximately 7.6 mm diameter, pale-violet coloured and imprinted GEIGY on one side, each tablet containing 100 mg.

Butacote is also available as sugar-coated, enteric tablets bi-convex, approximately 10.7 mm in diameter, pale-violet coloured and imprinted GEIGY on one side, each tablet containing 200 mg.

Uses Rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and acute gout.

Osteoarthritis of the spine and degenerative disc disease presenting as lumbago, sciatica or radiculitis.

Prolapsed intervertebral disc.

Reiter's disease and other seronegative (non-rheumatoid) arthropathies.

Bone pain associated with Paget's disease and secondary neoplasms.

Moderate to extensive superficial thrombophlebitis.

Dosage and administration Butacote is given orally in tablet form.

Adults: For the initial 48 hours 400–600 mg daily in divided doses with meals.

Maintenance doses should be reduced to the minimum amount that will provide continuous therapeutic control, usually 200–300 mg daily.

Note: In acute gout a maximum dosage of 800 mg daily may be necessary.

Paediatric: Dosage in the range 5–10 mg per kg, with emphasis on the lower end of the scale. As a guide the small seven-year-old and younger children should be given 1 × 100 mg tablet per day.

In children of average weight between 7–12 years of age, 2 × 100 mg tablets per day in divided doses is sufficient.

Contra-indications, warnings, etc

Contra-indications: Butacote is contra-indicated in the presence of oedema or hypertension where there is danger of cardiac decompensation. Butacote is also contra-indicated in the presence of: renal and hepatic disease, including recent hepatitis, history of gastro-intestinal ulceration, blood dyscrasia, drug rash or known sensitivity to pyrazoles.

Precautions: History of dyspepsia.

Since Butacote may potentiate the action of coumarin-type anticoagulants by displacement from plasma protein binding, frequent estimations of prothrombin levels should be undertaken when these drugs are administered concurrently. Similarly, Butacote potentiates certain oral hypoglycaemic agents and sulphonamides, the dosage of which may need reducing.

Andursil during the first three months of pregnancy is only advised if there are compelling reasons for so doing.

Side-effects: Side-effects are unlikely to occur in the recommended dosage.

Pharmaceutical precautions *Storage:* Protect from heat.

Legal category P.

Package quantities *Suspension:* Bottles of 100 ml and 300 ml.

Tablets: Carton of 100 tablets containing 5 packs of 20 tablets.

Further information *In vitro* tests on Andursil Suspension and Tablets have shown that the optimum buffering pH of between pH 3.0 and pH 5.0 is reached very quickly and is prolonged without producing a systemic alkalosis. Andursil is non-constipating and is not a laxative.

Product licence numbers

Andursil Suspension 0001/0049

Andursil Tablets 0001/0060

ANTURAN*

Presentation The active ingredient, Sulphinpyrazone BP is presented as pale yellow, sugar-coated tablets, bi-convex, approximately 8.5 mm diameter imprinted GEIGY on one side, containing 100 mg in each tablet.

Uses *Mode of action:* Anturan lowers serum urate levels by blocking tubular re-absorption, thereby increasing renal excretion of uric acid. As a result of increased excretion, serum urate deposits are mobilised and tophi are no longer formed.

Indications: Chronic including tophaceous gout, recurrent gouty arthritis. Hyperuricaemia.

Dosage and administration *Administration:* Anturan is administered orally in tablet form, with meals or milk.

Dosage: Adults: Chronic gout, hyperuricaemia: Anturan should be given daily in equally divided doses; in some cases a single dose may suffice. 100–200 mg daily increasing gradually (over the first two or three weeks) to 600 mg (rarely 800 mg) daily and maintained until serum urate level has fallen within the normal range. Subsequent dosage should be reduced to the lowest level which maintains serum urate within the normal range. Maintenance dose may be as low as 200 mg daily, and rarely 100 mg.

Chronic gout with renal impairment: Anturan is effective in all but the most severely affected patients. Low dosage should be used initially and increased only under detailed supervision until the correct maintenance dose is established.

Children: Paediatric usage not established.

Contra-indications, warnings, etc

Contra-indications: Active peptic ulcer. Sensitivity to phenylbutazone or other pyrazole derivatives. Severe hepatic disease.

In the treatment of chronic gout salicylates antagonise the action of Anturan and should not be given concurrently.

Precautions: Use with caution in patients with impaired renal function or nephrolithiasis; in these cases, regular assessment of renal function is indicated.

Use with caution in patients with healed peptic ulcer.

Since Anturan may potentiate the action of coumarin-type anticoagulants, frequent estimation of prothrombin time should be undertaken when these drugs are given concurrently, and the dosage of the anticoagulant adjusted accordingly.

Anturan may potentiate the action of plasma protein-binding drugs such as hypoglycaemic agents and sulphonamides, which may necessitate a modification in dosage.

Anturan should be used with caution in pregnant women, weighing the potential risks against the possible benefits.

Side-effects: During the early stages of the treatment in patients with hyperuricaemia or gout, acute attacks of gout may be precipitated.

To help prevent episodes of urolithiasis or renal colic, ensure adequate fluid intake and alkalinisation of the urine during initial stages of therapy.

Gastro-intestinal bleeding has been reported; transient gastro-intestinal side-effects may occur and are usually of a mild nature.

Rash or blood dyscrasias may occur, and are contra-indications to further treatment; onset may be sudden or gradual, and occur after small doses or after long periods of treatment.

For the early detection of a haematological abnormality, careful clinical supervision and a full blood count should be done before and at regular intervals during treatment.

Invalidation of results of renal function tests involving p-aminohippuric acid (PAH), phenolsulphthalein (PSP) or other organic acids may occur.

Accidental overdose: There is no antidote to Anturan, and treatment is symptomatic. Immediate treatment consists of forced emesis to recover undigested tablets. This is followed by gastric lavage preferably with mild alkaline solution such as sodium bicarbonate solution and supportive therapy as indicated.

Pharmaceutical precautions *Storage:* Tablets – protect from moisture.

Legal category POM.

Package quantities *Tablets 100 mg:* Containers of 100.

Further information Anturan lowers serum uric acid levels by blocking tubular re-absorption of uric acid and increasing renal excretion where glomerular filtration is still adequate and where tubular function is not too severely impaired.

Product licence number 0001/5002.

ANTURAN* 200 MG TABLETS

Presentation Tablets containing 200 mg Sulphinpyrazone BP, light yellow, sugar-coated, round, biconvex approximately 10.6 mm diameter printed GEIGY on one side.

Mode of action Regulation of platelet function.

Anturan has been shown to increase platelet survival time and decrease platelet turnover in thromboembolic conditions. In addition to inhibiting platelet adhesion and aggregation, Anturan has also been shown to inhibit the platelet release reaction and prostaglandin synthesis, processes known to be important in thromboembolism.

pregnancy; there is evidence of harmful effects in pregnancy in animals, when given in exceptionally high doses.

Nursing mothers should be advised to cease breast feeding.

Drug interactions: Anafranil should not be given concurrently, or within 2 weeks of cessation of therapy, with monoamine oxidase inhibitors.

Anafranil may decrease the antihypertensive effect of guanethidine, debrisoquine, bethanidine and possibly clonidine, and methyl dopa. It would be advisable to review all antihypertensive therapy during treatment with tricyclic antidepressants.

Anafranil should not be given with sympathomimetic agents such as adrenaline, ephedrine, isoprenaline, noradrenaline, phenylephrine and phenylpropanolamine.

Barbiturates may decrease and methylphenidate and neuroleptics may increase the plasma level of clomipramine.

Side-effects: The following adverse effects, although not necessarily all reported with Anafranil have occurred with other tri/tetracyclic antidepressants:

Atropine-like side effects including dry mouth, disturbances of accommodation, tachycardia, constipation and hesitancy of micturition may occur early in treatment, but usually lessen.

Other possible adverse effects include nausea, drowsiness, sweating, postural hypotension, hypomania, tremor, paraesthesia, ataxia and, rarely, skin rashes.

Male patients may occasionally experience ejaculation disorders and, more rarely, impotence. Women occasionally experience orgasmic impotence.

Epileptiform convulsions have been experienced in a small number of patients.

Serious adverse effects are rare; these include impaired liver function and jaundice, bone marrow depression, including leucopenia, eosinophilia and thrombocytopenia. Agranulocytosis has occasionally occurred in patients receiving tricyclic antidepressants. It is advisable to perform blood counts during treatment with Anafranil especially if the patient develops fever, sore throat or other signs of infection. Cardiac arrhythmias and severe hypotension are likely to occur with high dosage or in deliberate overdose. They may also occur in patients with pre-existing heart disease taking normal dosage.

Although not indicative of addiction, withdrawal symptoms may occur on abrupt cessation of therapy and include insomnia, irritability and excessive perspiration.

Withdrawal symptoms in neonates whose mothers receive tri/tetracyclic antidepressants during the third trimester have also been reported.

Psychotic manifestations, including mania and paranoid delusions, may be exacerbated during treatment with tricyclic antidepressants.

Accidental overdose: Major symptoms of overdose include coma, convulsions, cardiovascular disturbances. Gastric lavage should be performed immediately and patients removed to an intensive care unit where cardiac monitoring is possible. Although there is no specific antidote, slow intravenous injection of physostigmine has yielded particularly good results in the presence of central nervous disturbances (coma, myoclonia, athetoid movements); physostigmine may possibly also exert a favourable effect on cardiac arrhythmias. The single dosage, which must be adapted to the patient's requirements and can, if necessary, be repeated several times, is 1–4 mg for adults and 0.5 mg for children.

Pharmaceutical precautions *Storage:* Capsules – protect from heat and moisture. Syrup – protect from heat. Keep containers tightly closed. Ampoules – protect from heat and light.

Dilutions: Syrup – dilutions down to 15 mg/5 ml can be prepared with boiled, distilled or de-ionised water. For dilutions below 15 mg/5 ml the recommended diluent is equal parts simple Syrup BP and freshly prepared Mucilage of Tragacanth BP. After dilution the solution should be used within a few days.

Legal category POM.

Package quantities

Capsules 50 mg: Blister packs of 100.

Capsules 25 mg: Blister packs of 100.

Capsules 10 mg: Blister packs of 100.

Syrup 25 mg/5 ml: Bottles of 150 ml.

Ampoules 25 mg/2 ml: Boxes of 10.

Further information Nil.

Product licence numbers

Capsules 50 mg 0001/0068

Capsules 25 mg 0001/5000

Capsules 10 mg 0001/0037

Syrup 25 mg/5 ml 0001/5001

Ampoules 25 mg/2 ml 0001/5036

ANDURSIL*

Presentation *Andursil suspension:* White slightly thixotropic suspension odour and flavour of mint, containing the active ingredients

Aluminium hydroxide gel	≡ Al ₂ O ₃	200 mg
Magnesium hydroxide		200 mg
Aluminium hydroxide/magnesium carbonate co-dried gel		200 mg
Activated polymethylsiloxane		150 mg
		in each 5 ml

Andursil tablets: White, bevelled-edge, five-cornered tablets with the 'GEIGY' signet impressed on to one side, diameter approximately 2.1 cm, containing the active ingredients:

Aluminium hydroxide/magnesium carbonate co-dried gel	750 mg
Activated polymethylsiloxane	250 mg
	in each tablet

Uses *Antacid/antiflatulent:* Symptomatic relief of pain, discomfort, abdominal distension, heartburn (including heartburn of pregnancy), flatulence and vomiting associated with peptic ulceration, hiatus hernia, gastritis, functional gastro-intestinal disorders.

Dosage and administration Andursil is taken orally in either suspension or tablet form.

Andursil Suspension: 5–10 ml three or four times a day and at bedtime or when necessary.

Andursil Tablets: 1 or 2 tablets three or four times a day and at bedtime or when necessary.

Contra-indications, warnings, etc

Contra-indications: With the exception of hypophosphataemia, there are no known contra-indications to Andursil.

Precautions: As with other drugs, the administration of

Geigy Pharmaceuticals

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RH12 4AB

ANAFRANIL*

Presentation The active ingredient, Clomipramine Hydrochloride, is presented as:

Two-tone blue/caramel-coloured capsules, hard gelatin size No. 4, imprinted GEIGY, each containing 50 mg.

Two-tone orange/caramel-coloured capsules, hard gelatin size No. 4, imprinted GEIGY, each containing 25 mg.

Two-tone yellow/caramel-coloured capsules, hard gelatin size No. 4, imprinted GEIGY, each containing 10 mg.

Orange flavoured and coloured syrup containing the equivalent of 25 mg clomipramine hydrochloride in 5 ml.

Ampoules of clear glass containing 25 mg clomipramine hydrochloride in 2 ml.

Uses *Antidepressant:* Endogenous depression, including manic-depressive, periodic and involutional depression. Reactive and neurotic depression. Obsessive and phobic states. Cataplexy associated with narcolepsy.

Dosage and administration *Administration:* Anaftranil is generally given orally in capsule or syrup form, but in severe cases it may be given intramuscularly or by intravenous infusion.

Dosage: Adults: Oral – 10 mg/day initially, increasing gradually to 30–150 mg/day, if required, in divided doses throughout the day or as a single dose at bedtime. Many patients will be adequately maintained on 30–50 mg/day. Higher doses may be needed in some patients, particularly those suffering from obsessional or phobic disorders.

Elderly: (patients over 60 years of age) 10 mg/day initially. The initial dose should be increased with caution under close supervision to a maximum of 75 mg daily.

Children: not established.

Intramuscular administration: In severe cases of depression or in patients who are unco-operative, treatment may be commenced with intramuscular injections of up to 6 × 25 mg ampoules daily, or even more in very severe cases. Once therapy has started to be effective, a change to oral dosage can be made.

Dosage: Intravenous infusion: Any standard giving set may be used but a cannula or fine needle with a flange which can be strapped in position should be chosen. Anaftranil ampoules may be diluted with either physiological saline or 5% Dextrose BP. The required dose of Anaftranil should be introduced into the infusion fluid with a sterile syringe and the contents should be agitated to ensure even distribution of the drug before infusion is commenced, into a forearm vein.

In the first instance a small dose of Anaftranil (25 mg or 50 mg) should be diluted in 200–500 ml of infusion fluid and infused over a period of two hours to assess tolerance. If satisfactory, the dose may be increased by 25 mg daily until an optimum therapeutic dose has been achieved. At the same time the bulk of fluid may be

reduced (to a minimum of 125 ml) and the duration of infusion decreased (to a minimum of 45 minutes).

On average the optimum therapeutic dose will be in the region of 100 mg but higher doses may be required in more severe depressions or in obsessional and phobic states.

Length of treatment: Infusions are usually given for 7–10 days to acutely depressed patients but severely depressed and obsessional and phobic patients may require more prolonged treatment. Regular daily treatment is preferable but when administration is inconvenient on certain days – for instance at weekends, oral therapy using double the intravenous dose may be substituted.

Changeover to oral therapy: Following a satisfactory response to infusion, the quantity of intravenous Anaftranil should be gradually reduced and oral therapy substituted. It is advisable to give double the maximum intravenous dosage orally until the patient's response is assured. Thereafter, a suitable maintenance dose, if considered necessary, can be selected.

Monitoring during treatment: During the course of infusion, patients should be carefully monitored for adverse effects. Particular attention should be paid to blood pressure recording, especially if there are any changes of position after conclusion of the infusion, as hypotension may occur. Patients often feel pleasantly drowsy during treatment and not infrequently fall asleep.

Contra-indications, warnings, etc

Contra-indications: Recent myocardial infarction, cardiac failure, any degree of heart block or other cardiac arrhythmias. Severe liver disease. Concurrent administration with monoamine oxidase inhibitors. Narrow angle glaucoma. Retention of urine.

Precautions: The elderly are particularly liable to experience adverse effects, especially agitation, confusion and postural hypotension. (See dosage).

Avoid if possible in patients with a history of epilepsy or with symptoms of bladder neck obstruction, e.g. prostatic hypertrophy.

Patients posing a high suicide risk require close initial supervision.

Tricyclic antidepressants potentiate the central nervous depressant action of alcohol.

Anaesthetics given during tri/tetracyclic antidepressant therapy may increase the risk of arrhythmias and hypotension. If surgery is necessary, the anaesthetist should be informed that a patient is being so treated.

As improvement may not occur during the first 2–4 weeks of treatment, patients should be closely monitored during this period.

Anaftranil may initially impair alertness. Patients should be warned of the possible hazard when driving or operating machinery.

Do not use during pregnancy, especially during the first and last trimesters, unless there are compelling reasons. There is no evidence as to drug safety in human

RYNACROM*

Presentation *Nasal Spray*: a plastic squeeze bottle containing a clear aqueous solution of Sodium Cromoglycate BP, 2.0% w/v.

Nasal Drops: a plastic dropper bottle containing a clear, aqueous solution of Sodium Cromoglycate BP, 2.0% w/v.

Cartridges: pink, transparent hard gelatin cartridges, each bearing the overprint 'RYNACROM'. Each cartridge contains 10 mg Sodium Cromoglycate BP in powder form for nasal insufflation.

Uses Rynacrom is indicated for the preventive treatment of allergic rhinitis (seasonal and perennial). Sodium cromoglycate inhibits the release from sensitised mast cells of histamine, SRS-A and chemotactic factors which mediate the allergic reaction. In the nose this inhibition of mediator release prevents the symptoms of rhinitis.

Dosage and administration Since therapy with Rynacrom is essentially preventive, it is important that the patient is instructed to maintain regular dosage, as distinct from using the drug intermittently to relieve symptoms.

Adults and children – Rynacrom Nasal Spray: 2 squeezes to each nostril six times daily.

Rynacrom Nasal Drops: Instil 2 drops into each nostril six times daily.

Rynacrom Cartridges: The contents of one cartridge are insufflated into each nostril up to four times daily. The first dose should be insufflated on rising and the last one immediately before retiring.

Contra-indications, warnings, etc There are no specific contra-indications.

Side-effects: Occasional irritation of the nasal mucosa may occur during the first days of use. In rare cases wheezing or tightness of the chest have been reported by patients.

Overdosage: No action other than medical supervision should be necessary.

Pharmaceutical precautions Store below 30°C. Rynacrom Nasal Spray and Nasal Drops should be protected from direct sunlight. Rynacrom Cartridges should be protected from light and kept dry.

Legal category P.

Package quantities Rynacrom Nasal Spray: bottle of 17.5 ml.

Rynacrom Nasal Drops: bottle of 15 ml.

Rynacrom Cartridges: containers of 100 cartridges.

Rynacrom Insufflators are supplied in separate containers. Instructions for use are supplied with each pack.

Further information A reduction in concomitant antihistamine therapy will often be possible.

An alternative presentation for nasal use of a 2% solution of Sodium Cromoglycate is available as Lomusol.

Product licence numbers

Rynacrom Nasal Spray: 0113/0040

Rynacrom Nasal Drops: 0113/0040

Rynacrom Cartridges: 0113/5032

THEO-DUR* ▼

Presentation A slow release tablet containing Theophylline BP (anhydrous), designed to give therapeutic blood levels over 8–12 hours.

200 mg Tablet: Off-white mottled flat elliptical scored tablet.

300 mg Tablet: Off-white mottled bi-convex oblong scored tablet.

Uses As a bronchodilator in the symptomatic or prophylactic relief of bronchospasm associated with asthma and chronic bronchitis.

Dosage and administration

Adults: The initial recommended dose is one 300 mg tablet 12 hourly. This dose can be increased by $\frac{1}{2}$ tablet (150 mg) increments, if sufficient therapeutic effect is not obtained.

Alternatively, treatment can be started with one 200 mg tablet 12 hourly and increased by $\frac{1}{2}$ tablet (100 mg) increments until sufficient therapeutic effect is achieved or side effects occur.

Children: < 35 kg body weight: 100 mg ($\frac{1}{2}$ 200 mg tablet 12 hourly).

> 35 kg body weight: 200 mg 12 hourly.

If sufficient therapeutic effect is not achieved or side effects occur the dose can be adjusted up or down by 100 mg ($\frac{1}{2}$ 200 mg tablet).

Note: The tablet must not be crushed or chewed, but should be swallowed whole or as a half.

Contra-indications, warnings, etc

Contra-indications: None.

Side effects: Side effects of theophylline depend to a great extent on serum concentration and are frequent only at theophylline concentrations exceeding 20 mcg/ml. The Theo-Dur slow release formulation reduces fluctuation in serum levels of theophylline, thereby reducing the incidence of side effects.

Most common side effects are gastro-intestinal disturbances (nausea, vomiting and anorexia) which, in most cases, disappear on reducing the dose.

Severe side effects (cramps, convulsions and supraventricular tachycardia) may appear at very high serum concentration, in which case the medication should be discontinued.

If side effects appear, serum levels of theophylline should be monitored.

Pregnancy and lactation: No influence on the reproduction process is reported. Only small amounts of theophylline pass out to maternal milk. In therapeutic dose there is no risk of influence on the child.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities 100 tablets.

Further information Nil.

Product licence numbers 0113/0081 200 mg
0113/0082 300 mg

* Trade Mark

Overdosage: As Nalcrom is absorbed only to a very limited extent, no action other than medical observation should be necessary.

Pharmaceutical precautions Store in a dry place. Reclose the container tightly after use.

Legal category POM.

Package quantities Containers of 100 capsules.

Further information

1. If oral steroid therapy is to be reduced or withdrawn this should be done cautiously and not more rapidly than 10% per week.

2. Dosages of 2,000 mg daily have been used in some cases of proctocolitis.

3. Sodium cromoglycate has been administered as an enema in addition to oral use in the management of proctitis and ulcerative colitis. The powder contents of the capsules were dissolved in water prior to being given as a retention enema.

Product licence number 0113/0073.

OPTICROM* EYE DROPS

Presentation A clear colourless aqueous solution of Sodium Cromoglycate BP 2% w/v, with benzalkonium chloride 0.01% w/v.

Uses For the relief and treatment of acute allergic conjunctivitis such as hay fever, chronic allergic conjunctivitis and vernal kerato conjunctivitis. Sodium cromoglycate inhibits the release from sensitised mast cells of histamine, SRS-A and chemotactic factors which mediate the allergic reaction.

Dosage and administration One or two drops into each eye four times daily.

Contra-indications, warnings, etc Known hypersensitivity to benzalkonium chloride.

Pharmaceutical precautions Store below 30°C. Protect from direct sunlight.

Legal category POM.

Package quantities 10 ml.

Further information Discard any remaining contents four weeks after opening the bottle. As with other ophthalmic solutions containing benzalkonium chloride, soft contact lenses should not be worn during the treatment period.

Product licence number 0113/0039.

PARACODOL*

Presentation Large, white, soluble, effervescent tablets each containing:

Paracetamol BP 500 mg
Codeine Phosphate BP 8 mg

Uses For the treatment of pain, including muscular and rheumatic pains, headache, migraine, neuralgia, toothache, sore throat, period pains, aches and pains. Discomfort associated with influenza, feverishness and feverish colds.

Dosage and administration The tablets are to be dissolved in water before oral administration.

Adults: 1–2 tablets, which may be repeated every four to six hours with a maximum of 8 in 24 hrs.

Children: Aged 6–12 years: $\frac{1}{2}$ –1 tablet. Not more than 4 doses to be taken in 24 hours.

Under 6 years: To be taken only on the direction of the physician.

Contra-indications, warnings, etc **Precautions:** The tablet base is designed to be equivalent to 1.5 g Sodium Citrate BP equivalent to 352 mg or 15.3 millimole Na⁺. It should therefore be prescribed with caution in long term treatment of patients in whom a restricted salt intake is indicated.

Preparations containing paracetamol should be given with care to patients with impaired liver function.

Overdosage: It is unlikely that a toxic dose of large, effervescent tablets would be ingested. In the event of an overdose, the toxic effects of codeine may be reversed by the administration of naloxone injection. Symptoms of paracetamol overdose are often delayed for at least 24 hours but to prevent hepatic damage, treatment should be given as soon as possible and within 10 hours of ingestion. Treatment is by the administration of oral methionine, oral or intravenous acetylcysteine.

Pharmaceutical precautions Store in a cool dry place.

Legal category P.

Package quantities Boxes of 10 or 100 tablets.

Further information Nil.

Product licence number 0113/5076.

PSOROX* OINTMENT

Presentation A smooth, off-white ointment.

Active ingredients:

Salicylic Acid BP	3.0% w/w
Ammoniated Mercury BP	2.0% w/w
Purified Coal Tar Fractions	2.4% w/w

The coal tar fractions are therapeutically equivalent to 10% crude coal tar and comprise:

Phenol	4.2%	Toluene	8.3%
Pyridine	2.1%	Naphthalene	41.6%
α -Picoline	2.1%	O-Cresol	4.2%
Carbazole	10.4%	Quinoline	2.1%
Xylene	4.2%	Phenanthrene	16.6%
Anthracene	4.2%		

Uses Psoriasis.

Dosage and administration **Adults:** Rub in thoroughly, directly to affected area, twice a day.

Children: Not suitable for use by children.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities Tubes of 25 g and 50 g.

Further information Nil.

Product licence number 0113/5081.

70 have been infused. This prevents over-dilution of clotting factors and maintains oxygen-carrying capacity. Where clotting factors are already reduced (e.g. in hypofibrinogenaemia or thrombocytopenia) correction of this condition must be undertaken prior to or concomitantly with the infusion.

Pharmaceutical precautions Do not store in excess of 25°C or expose to undue fluctuations in temperature. Do not use if cloudy or if a deposit is present. Discard any unused solution.

Legal category POM.

Package quantities Bottles of 500 ml.

Further information Nil.

Product licence numbers

Lomodex 70 in Dextrose 0113/5060

Lomodex 70 in Saline 0113/5061

LOMUSOL* NASAL SPRAY

Presentation A metered-dose presentation of a clear aqueous solution of Sodium Cromoglycate BP 2% w/v. The Lomusol pack contains a bottle of solution, and a pump; the appliance is assembled by the patient from these component parts.

Uses Lomusol is indicated for the preventative treatment of allergic rhinitis (seasonal and perennial).

Sodium cromoglycate inhibits the release from sensitised cells of histamine, SRS-A and chemotactic factors which mediate the allergic reaction. In the nose, this inhibition of mediator release prevents the symptoms of rhinitis.

Dosage and administration Since Lomusol therapy is essentially prophylactic, it is important that the patient is instructed to maintain regular dosage, as distinct from using the drug intermittently to relieve symptoms.

Adults and children: 1 squeeze to each nostril six times daily.

One squeeze delivers approximately 2.6 mg of sodium cromoglycate from the metered-dose device.

Contra-indications, warnings, etc

Contra-indications: There are no specific contra-indications.

Side-effects: Occasional irritation of the nasal mucosa may occur during the first days of use. In rare cases wheezing or tightness in the chest have been reported by patients.

Overdosage: No action other than medical supervision should be necessary.

Pharmaceutical precautions Store in a cool place and protect from direct sunlight.

Legal category P.

Package quantities 26 ml bottle and pump.

Further information Concomitant antihistamine therapy can often be reduced or discontinued when the allergic rhinitis has been brought under control.

Alternative presentations for nasal use of a 2% solution of sodium cromoglycate are available as Rynacrom Nasal Spray and Drops.

Product licence number 0113/0066.

NALCROM*

Presentation Nalcrom is a presentation of sodium cromoglycate for oral use. It is presented in clear/clear hard gelatin capsules printed Fisons 101 in black. Each capsule contains 100 mg sodium cromoglycate as a white powder.

Uses a) *Chronic inflammatory bowel disease:* As an adjuvant in the treatment of ulcerative colitis, proctitis and proctocolitis.

Nalcrom may be used in patients with a history of hypersensitivity to or intolerance of sulphasalazine.

Nalcrom may be used in conjunction with steroid therapy and sulphasalazine in the management of ulcerative colitis, proctitis and proctocolitis.

b) *Food allergy:* Food allergy (where adequate investigations have been performed to determine sensitivity to one or more ingested allergens) in conjunction with restriction of main causative allergens.

Sodium Cromoglycate inhibits the release from mast cells of histamine, SRS-A and chemotactic factors which mediate the allergic reaction. In gastro-intestinal disease the release of mediators causes a local inflammation which can either result in gastrointestinal symptoms or may allow absorption of antigenic material leading to systemic allergic reactions.

Dosage and administration *Dosage:*

a) *Chronic inflammatory bowel disease: Initial dose:*

Adults: 2 capsules four times daily before meals.

Children: From 2-14 years: 1 capsule four times daily before meals.

Maintenance dose: To prevent relapses dosage should be maintained indefinitely at 2 capsules four times daily in adults and 1 capsule four times daily in children.

b) *Food allergy: Initial dose: Adults:* 2 capsules four times daily before meals.

Children: From 2-14 years: 1 capsule four times daily before meals.

For adults and children if satisfactory control is not achieved within two to three weeks the dosage may be doubled but should not exceed 40 mg/kg/day.

Maintenance dose: Once a therapeutic response has been achieved the dose may be reduced to the minimum required to maintain the patient free of symptoms.

Patients who are unable to avoid allergenic foods under certain circumstances (e.g. school meals, restaurants) may be able to protect themselves against the effect of these foods by taking a single dose of Nalcrom 15 minutes before the meal. The optimum dosage will need to be determined for each patient and a suitable starting dose would be 200 mg in adults and 100 mg in children.

Administration: The capsules may be swallowed whole or the powder contents may be dissolved in a small quantity of very hot water and diluted with cold water to drink. Administration as a solution in water is probably the method of choice in food allergy.

Contra-indications, warnings, etc

Contra-indications: There are no specific contra-indications.

Warnings: The safety of Nalcrom in pregnancy and for the treatment of children under two years has not yet been established.

Side-effects: Nausea, skin rashes and joint pains have been reported in a few cases.

Dosage and administration

1. *Crush syndrome, fat embolism, severe burns and mesenteric infarction:* 1st day: 500–1,000 ml Lomodex 40 should be given by i.v. infusion, followed by a further 1,000–2,000 ml given slowly over the next 24 hours. 2nd day: 1,000–2,000 ml by slow infusion. 3rd day: 500–1,000 ml by slow infusion (N.B. larger doses may be required in burns.)

2. *Vascular surgery:* Before surgery: 500 ml by continuous infusion. During surgery: a further 500 ml. After surgery: 500 ml daily for at least three days.

3. *Extra-corporeal circulation procedures:* Lomodex 40 is added to the perfusion fluid (not more than 20 ml Lomodex 40/kg body weight).

4. *Before angiography, e.g. aortography:* 10–15 ml Lomodex 40/kg body weight is administered by intravenous infusion over 30 minutes.

5 and 6. *Plastic surgery and vascular insufficiency:* The rate of infusion and dosage will depend on clinical circumstances, bearing in mind the precautions indicated below.

7. *Peripheral vascular disorders:* 500 ml are given every 12 hours until 2,000 ml have been infused. Repeat infusions are required two to four times a year.

8. *Shock:* A rapid infusion of 500 ml followed by a further 500–1,000 ml over the next three to five hours, depending on the degree of shock.

Contra-indications, warnings, etc *Anaphylactoid reactions* occur rarely. They are more common and may be more severe in patients with a history of asthma.

The most frequently observed signs of such reactions are hypotension and bronchospasm, progressing on very rare occasions to cardiac arrest. In addition, skin manifestations such as erythema and urticaria may be seen.

In view of the above, it is essential to observe patients closely throughout the infusion, particularly during the first few minutes. If there is any suspicion of an anaphylactoid reaction, treatment with Lomodex should be discontinued *immediately* and appropriate resuscitative measures instituted.

Lomodex 40 should not be used in patients with renal failure, with blood urea levels above 10 mmol/litre (60 mg/100 ml) or whose urine output cannot be maintained above 1,500 ml/day.

Renal function should be monitored, especially when treatment is prolonged for more than two to three days consecutively. Lomodex 40 should be withdrawn if the specific gravity of the urine rises above 1.045 or if there is a reduced output of urine. If oliguria occurs, urine output should be stimulated with diuretics and intravenous fluids as appropriate.

Dehydration should preferably be corrected prior to, or at least, concomitantly with, the infusion of Lomodex 40. Until dehydration is corrected, the infusion rate should not exceed 500 ml/hour.

In surgery, dosage for any one infusion should not exceed 20 ml Lomodex 40/kg body weight because of the risk of capillary oozing. When clotting factors are already reduced (e.g. in hypofibrinogenaemia or thrombocytopenia) correction of the condition must be undertaken prior to, or concomitantly with, infusion of Lomodex 40.

With Lomodex 40 there is no necessity to take blood for cross-matching prior to infusion as there is no interference if a sample is subsequently required.

Pharmaceutical precautions Do not store in excess

of 25°C or expose to undue fluctuations in temperature. Do not use if cloudy or if a deposit is present. Discard any unused solution.

Legal category POM.

Package quantities Bottles of 500 ml.

Further information Nil.

Product licence numbers

Lomodex 40 in Dextrose 0113/5062

Lomodex 40 in Saline 0113/5063

LOMODEX* 70 IN DEXTROSE

LOMODEX* 70 IN SALINE

Presentation *Lomodex 70 in Dextrose:* a clear, almost colourless, slightly viscous liquid. Dextran 70 Injection BP in 5% Dextrose. A sterile solution containing 6% w/v dextrans of weight average molecular weight 70,000 in 5% w/v Dextrose Injection BP.

Lomodex 70 in Saline: a clear, almost colourless, slightly viscous liquid. Dextran 70 Injection BP in 0.9% sodium chloride. A sterile solution containing 6% w/v dextran of weight average molecular weight 70,000 in Sodium Chloride Injection BP.

Uses

1. Prevention of post-operative deep vein thrombosis
2. Short-term blood volume expansion.

Dosage and administration

1. *Prevention of post-operative deep vein thrombosis* Continuous infusion before, during and after surgery. A total infusion of 1,000 ml over a period of six hours.

2. *Short-term blood volume expansion: Haemorrhage:* In moderate blood loss 500 ml are infused rapidly taking 15 minutes. A further 500 ml are given more slowly taking 30–45 minutes. In severe haemorrhage 1,000 ml are infused as rapidly as possible. A further 500 ml may be given more slowly, depending on the clinical condition of the patient and the availability of cross-matched blood.

Crush injuries: The loss of plasma proteins into injured tissues and the consequent attraction of water out of the circulation may be combated by the infusion of 500–1,500 ml of Lomodex 70. The rate of infusion is dictated by the degree of shock. Where this is severe, rapid infusion is necessary.

Burns: As a guiding principle, up to 3,000 ml of Lomodex 70 may be given in the first 36–48 hours. Electrolytes, dextrose and possibly blood will also be required according to the clinical situation.

Contra-indications, warnings, etc *Anaphylactoid reactions* occur rarely. They are more common and may be more severe in patients with a history of asthma. The most frequently observed signs of such reactions are hypotension and bronchospasm, progressing on very rare occasions to cardiac arrest. In addition, skin manifestations such as erythema and urticaria may be seen.

In view of the above, it is essential to observe the patients closely throughout the infusion, particularly during the first few minutes. If there is any suspicion of an anaphylactoid reaction, treatment with Lomodex should be discontinued *immediately* and appropriate resuscitative measures instituted.

In continuing haemorrhage, whole blood or packed cells may be indicated after 1,000–1,500 ml of Lomodex

ate and a plastic mouthpiece. Instructions for use are supplied with each pack.

Further information

Concomitant bronchodilator therapy: Where a concomitant aerosol bronchodilator is prescribed, it is recommended that this be administered prior to the Intal inhaler.

Concomitant steroid therapy: In patients currently treated with steroids the addition of Intal Inhaler to the regimen may make it possible to reduce the maintenance dose or to discontinue steroids completely. The patient must be carefully supervised while the steroid dose is reduced; a rate of reduction of 10% weekly is suggested.

If reduction of steroid dosage has been possible Intal inhaler should not be withdrawn until steroid cover has been re-instituted.

Use in pregnancy: As with all medication particular caution must be exercised during the first trimester of pregnancy.

Product licence number 0113/0080.

INTAL* NEBULISER SOLUTION

Presentation Intal Nebuliser Solution is presented in ampoules containing Sodium Cromoglycate BP 20 mg in 2 ml of a clear colourless sterile aqueous solution.

Uses Intal Nebuliser Solution is indicated for the preventive treatment of bronchial asthma which may be due to allergy, exercise, cold air or chemical and occupational irritants. Sodium cromoglycate inhibits the release from sensitised mast cells of histamine, SRS-A and chemotactic factors which mediate the allergic reaction. In the lung this inhibition of mediator release prevents both the immediate and late asthmatic response (i.e. Type I and Type III responses) to immunological stimuli. Sodium cromoglycate also prevents the bronchoconstriction caused by exercise, cold air and chemical irritants.

Dosage and administration Intal Nebuliser Solution should be administered from a power-operated nebuliser at an adequate flow rate, via a face mask or mouthpiece. Information on suitable power operated nebulisers is available on request. Hand operated nebulisers are not suitable for the administration of Intal Nebuliser Solution.

Dosage: Since Intal Nebuliser Solution therapy is essentially preventive, it is important that regular dosage is maintained, as distinct from intermittent use to relieve symptoms.

Adults and children: The contents of one ampoule are administered by nebulisation four times a day, i.e. night and morning and at intervals of 3-6 hours. In severe cases frequency of administration may be increased to 5 or 6 times daily.

Contra-indications, warnings, etc

Contra-indications: There are no specific contra-indications. Intal Nebuliser Solution must not be given by injection.

Side-effects: Occasional irritation of the throat and trachea, and in rare cases severe bronchospasm, have been reported with powder forms of sodium cromoglycate.

Overdosage: No action other than medical observation should be necessary.

Withdrawal of Intal Nebuliser Solution therapy: Since

sodium cromoglycate acts prophylactically, it is important to continue treatment in those patients who benefit. If it is necessary to withdraw Intal Nebuliser Solution this should be done progressively over a period of one week. Symptoms of asthma may recur.

Use in pregnancy: As with all medication, particular caution must be exercised during the first trimester of pregnancy.

Pharmaceutical precautions Store in a cool place protected from sunlight. Should the physician decide to mix Intal Nebuliser Solution with other agents, the mixture should be prepared just prior to use and discarded if any turbidity develops. Any unused solution should be discarded immediately and the chamber of the nebuliser thoroughly cleaned.

Legal category POM.

Package quantities Box containing 48 x 2 ml ampoules.

Further information **Concomitant steroid therapy:** In patients currently treated with steroids, the addition of Intal Nebuliser Solution to the regime may make it possible to reduce the maintenance dose or to discontinue steroids completely. The patient must be carefully supervised while the steroid dose is reduced; a rate of reduction of 10% weekly is suggested. An increase in steroid dosage may be necessary if symptoms increase and at times of infection, severe antigen challenge or stress.

If reduction of steroid dosage has been possible, Intal Nebuliser Solution should not be withdrawn until steroid cover has been re-instituted.

Concomitant bronchodilator therapy: If bronchodilators are used concomitantly, patients may find that the frequency of bronchodilator usage can be reduced as their asthma is stabilised with Intal Nebuliser Solution.

Product licence number 0113/0068.

LOMODEX* 40 IN DEXTROSE LOMODEX* 40 IN SALINE

Presentation *Lomoxed 40 in Dextrose:* a clear, almost colourless, slightly viscous liquid. Dextran 40 Injection BP in 5% dextrose. A sterile solution containing 10% w/v dextrans of weight average molecular weight 40,000 in 5% w/v Dextrose Injection BP.

Lomoxed 40 in Saline: a clear, almost colourless, slightly viscous liquid. Dextran 40 Injection BP in 0.9% sodium chloride. A sterile solution containing 10% w/v dextrans of weight average molecular weight 40,000 in Sodium Chloride Injection BP.

Uses Lomoxed 40 solutions are given by intravenous infusion for the prevention and treatment of intravascular 'sludging':

1. In the management of the crush syndrome, fat embolism, severe burns and mesenteric infarction.
2. In vascular surgery.
3. In extra-corporeal circulation procedures.
4. Before angiography.
5. In plastic surgery e.g. skin grafts.
6. Vascular insufficiency.
7. Peripheral vascular disorders.
8. Short-term plasma expander in shock.

Uses Intal Compound is indicated for the preventive treatment of bronchial asthma which may be due to allergy, exercise, cold air or chemical and occupational irritants. Sodium cromoglycate inhibits the release from sensitised mast cells of histamine, SRS-A and chemotactic factors which mediate the allergic reaction. In the lung this inhibition of mediator release prevents both the immediate and late asthmatic response (i.e. Type I and Type III responses) to immunological stimuli. Sodium cromoglycate also prevents the bronchoconstriction caused by exercise, cold air and chemical irritants. Isoprenaline sulphate is included to offset the transient bronchospasm which occurs in some patients on inhalation of a fine dry powder.

Dosage and administration Intal Compound is presented in a single dose cartridge, the 'Spincap', for use in a specially developed turbo-vibratory inhaler, the 'Spinhaler'. Inhalation of the drug is controlled by the patient's inspiratory effort. Intal Compound is not effective if the 'Spincap' is swallowed because prevention of the asthmatic attack depends upon local application to the lung.

Dosage: Since Intal Compound therapy is essentially preventive, it is important that the patient is instructed to maintain regular dosage, as distinct from inhaling the drug intermittently to relieve symptoms.

Adults and children: The normal dose is one 'Spincap' four times daily, i.e. one night and morning and at intervals of 3-6 hours in between. It may be necessary to increase this to 6-8 times daily in more severe cases or during periods of severe antigen challenge. Additional doses may be taken before exertion to prevent exercise induced asthma or before exposure to other trigger factors.

When the asthmatic condition is stabilised, it may be possible to reduce the dosage provided that adequate control of the asthma is maintained.

Contra-indications, warnings, etc

Contra-indications: There are no specific contra-indications.

Side-effects: Occasional irritation of the throat and trachea may occur. In rare cases severe bronchospasm has been reported, usually at the beginning of treatment, necessitating withdrawal of the drug.

Precautions: The precautions normally applying to isoprenaline should be observed. Where concomitant bronchodilator therapy is prescribed, the possibility of isoprenaline overdose should be remembered.

Overdosage: No action other than medical observation should be necessary.

Withdrawal of Intal Compound therapy: Since Intal Compound acts prophylactically, it is important to continue treatment in those patients who benefit. If it is necessary to withdraw Intal Compound, this should be done progressively over a period of one week. Symptoms of asthma may recur.

Use in pregnancy: As with all medications, particular caution must be exercised during the first trimester of pregnancy.

Pharmaceutical precautions Store in a moisture-proof container in a cool, dry place protected from light.

Legal category POM.

Package quantities Containers of 50 'Spincap' cartridges are available singly or in packs of two. 'Spinhaler'

in insufflators are supplied in individual containers. Instructions for use are supplied with each pack.

Further information *Concomitant steroid therapy:* In patients currently treated with steroids, the addition of Intal Compound to the regime may make it possible to reduce the maintenance dose or to discontinue steroid completely. The patient must be carefully supervised while the steroid dose is reduced; a rate of reduction of 10% weekly is suggested. An increase in steroid dosage may be necessary if symptoms increase and at times of infection, severe antigen challenge or stress.

If reduction of steroid dosage has been possible Intal Compound should not be withdrawn until steroid cover has been re-instituted.

Concomitant bronchodilator therapy: If additional bronchodilators are used concomitantly, patients may find that the frequency of bronchodilator usage can be reduced as their asthma is stabilised with Intal Compound.

Product licence number 0113/5023.

INTAL* INHALER ▼

Presentation Metered dose pressurised aerosol delivering 200 inhalations each containing a total of 1.0 mg Sodium Cromoglycate, BP.

Uses Intal Inhaler is indicated for the treatment of bronchial asthma, including the prevention of exercise induced asthma.

Dosage and administration Since Intal Inhaler therapy is essentially preventative it is important that the patient is instructed to maintain regular dosage, as distinct from inhaling the drug intermittently to relieve symptoms.

Adults and Children: Two inhalations of the inhaler four times daily for routine prevention of asthma. The dose may be increased to two inhalations six or eight times daily in more severe cases or during periods of severe antigen challenge. Additional doses before exercise may also be taken.

Contra-indications, warnings, etc

Contra-indications: There are no specific contra-indications.

Side-effects: No significant side-effects have been reported. Although it has not been reported with Intal Inhaler, where Intal Spincaps have been administered via the Spinhaler, rare cases involving severe bronchospasm have been reported.

Overdosage: No action other than medical observation should be necessary.

Withdrawal of Intal Inhaler Therapy: Since the therapy is essentially prophylactic it is important to continue therapy in those patients who benefit. If it is necessary to withdraw this treatment, it should be done progressively over a period of one week. Symptoms of asthma may recur.

Pharmaceutical precautions Store the inhaler in a cool place. The Intal Inhaler canister is pressurised. The canister should be protected from direct sunlight and must not be punctured or burnt, even when empty.

Legal category POM.

Package quantities Each pack contains a canister delivering 200 metered inhalations of sodium cromogly-

Nevertheless, as iron deficiency anaemia occurring in the first trimester can be adequately treated with oral iron, or by a series of intramuscular injections of Imferon not exceeding 5 ml per day, it is recommended that total dose infusion and large intravenous doses of undiluted Imferon be reserved for use in the second and third trimesters.

Adverse reactions: Rarely, anaphylactoid reactions (sometimes severe, including fatal) have been reported; also occasional transient reactions such as urticaria and other rashes; arthralgia; lymphadenopathy; pyrexia. Local phlebitis at injection site (i.v. injection, Total Dose Infusion). Possible exacerbation of joint pain and swelling in rheumatoid arthritis.

Pharmaceutical precautions Protect from heat. Do not freeze.

Legal category POM.

Package quantities Ampoules of 2 ml (100 mg Fe) in boxes of 10 and 100.

Ampoules of 5 ml (250 mg Fe) in boxes of 5 and 50. TDI ampoules of 20 ml (1,000 mg Fe) in boxes of 5.

Further information The intramuscular and subcutaneous injection of iron-carbohydrate complexes in very large doses under experimental conditions in animals produced sarcomas in rats, mice, rabbits, possibly hamsters but not in guinea-pigs. Cumulative information and independent assessment indicates if there is a risk, it is minimal. Iron-dextran complex (Imferon) contains very little free ionic iron, allowing initially high serum iron levels without completely saturating or exceeding the iron binding capacity. The absence of untoward reactions to high serum levels of iron and low toxicity is due to the very high stability of the iron-dextran complex.

Product licence number 0113/5073.

INTAL*

Presentation Intal is a presentation for inhalation of sodium Cromoglycate BP 20 mg in micronised powder form. It is presented in a yellow/colourless, transparent, hard gelatin cartridge, bearing the overprint 'FISONS INTAL P'.

Uses Intal is indicated for the preventive treatment of bronchial asthma which may be due to allergy, exercise, cold air or chemical and occupational irritants. Sodium cromoglycate inhibits the release from sensitised mast cells of histamine, SRS-A and chemotactic factors which mediate the allergic reaction. In the lung this inhibition of mediator release prevents both the immediate and late asthmatic response (i.e. Type I and Type III responses) to immunological stimuli. Sodium cromoglycate also prevents the bronchoconstriction caused by exercise, cold air and chemical irritants.

Dosage and administration Intal is presented in a single dose cartridge, the 'Spinicap', for use in a specially developed turbo-vibratory inhaler, the 'Spinhaler'. Inhalation of the drug is controlled by the patient's inspiratory effort. Intal is not effective if the 'Spinicap' is swallowed because the prevention of the asthmatic attack depends upon local application to the lung.

Dosage: Since Intal therapy is essentially preventive, it is important that the patient is instructed to maintain regular dosage, as distinct from inhaling the drug intermittently to relieve symptoms.

Adults and children: The normal dose is one 'Spinicap' four times daily, i.e. one night and morning and at intervals of 3-6 hours in between. It may be necessary to increase this to 6-8 times daily in more severe cases or during periods of severe antigen challenge. Additional doses may be taken before exertion to prevent exercise induced asthma or before exposure to other trigger factors.

When the asthmatic condition is stabilised, it may be possible to reduce the dosage provided that adequate control of the asthma is maintained.

Contra-indications, warnings, etc

Contra-indications: There are no specific contra-indications.

Side-effects: Occasional throat irritation or coughing may occur in some patients sensitive to the inhalation of a dry powder. These can usually be overcome by changing to Intal Compound. In rare cases, severe bronchospasm has been reported, usually at the beginning of treatment, necessitating withdrawal of the drug.

Overdosage: No action other than medical observation should be necessary.

Withdrawal of Intal therapy: Since Intal acts prophylactically, it is important to continue treatment in those patients who benefit. If it is necessary to withdraw Intal, this should be done progressively over a period of one week. Symptoms of asthma may recur.

Use in pregnancy: As with all medications, particular caution must be exercised during the first trimester of pregnancy.

Pharmaceutical precautions Store in a moisture-proof container in a cool, dry place protected from light.

Legal category POM.

Package quantities Containers of 50 'Spinicap' cartridges are available singly or in packs of two. 'Spinhaler' insufflators are supplied in individual containers. Instructions for use are supplied with each pack.

Further information *Concomitant steroid therapy:* In patients currently treated with steroids, the addition of Intal to the regime may make it possible to reduce the maintenance dose or to discontinue steroids completely. The patient must be carefully supervised while the steroid dose is reduced; a rate of reduction of 10% weekly is suggested. An increase in steroid dosage may be necessary if symptoms increase and at times of infection, severe antigen challenge or stress.

If reduction of steroid dosage has been possible Intal should not be withdrawn until steroid cover has been re-instituted.

Concomitant bronchodilator therapy: If bronchodilators are used concomitantly, patients may find that the frequency of bronchodilator usage can be reduced as their asthma is stabilised with Intal.

Product licence number 0113/5022.

INTAL* COMPOUND

Presentation Intal Compound is a presentation for inhalation of Sodium Cromoglycate BP 20 mg (micronised) and Isoprenaline Sulphate BP 0.1 mg in powder form. It is presented in an orange/colourless, transparent, hard gelatin cartridge bearing the overprint 'FISONS 670C'.

when ergometrine is given alone and the effect is approximately that of intravenous ergometrine.

As an aid to local anaesthesia in ophthalmology: The solution employed consists of a 2% solution of procaine hydrochloride and 0.4% potassium sulphate. One drop of adrenaline hydrochloride (1:1,000) and approximately 150 international units of Hyalase are added to each 5 ml of the solution.

Two further drops of adrenaline are added for cone injections if this is not contra-indicated.

As an aid to local anaesthesia in fracture reduction:

For Colles' fracture: 20 ml of 1% procaine are mixed with 1,500 international units of Hyalase. Two injections are made: the bulk of the solution is put directly into the fracture haematoma from the extensor aspect of the forearm, and 2-3 ml are infiltrated around the ulnar styloid process. The anaesthetic solution diffuses rapidly all around the injured area and the fracture can be manipulated as soon as the needle is withdrawn.

For Pott's fracture: 40 ml of 1% procaine are mixed with 1,500 international units of Hyalase.

Radiography: The contents of 1 ampoule of Hyalase are dissolved in 1 ml water for injections (a fresh solution must be prepared on each occasion).

Half a millilitre of Hyalase solution is then added to 5 ml of 35% diiodone solution and made up to 15 ml with water for injections.

Fifteen millilitres of the mixture are injected subcutaneously in the scapular region and are followed immediately by a further 15 ml at another site, e.g. the contralateral scapular region.

The area of injection is massaged vigorously to aid dispersion. Normally renal secretion commences five minutes after injection; adequate concentration is obtained in 24-25 minutes and is equal to that obtained by the intravenous method.

Note - The volumes stated are also applicable to children aged from a few weeks to five years provided that renal function is not grossly impaired.

Contra-indications, warnings, etc

Contra-indications: Not to be used to reduce the swelling of bites or stings, or at sites where infection or malignancy is present.

Not to be used for intravenous injections.

Pharmaceutical precautions Store in a cool dry place. Solutions of Hyalase rapidly lose activity and should be used within 12-24 hours of preparation.

Legal category POM.

Package quantities Boxes of 5, 20 and 100 ampoules.

Further information Nil.

Product licence number 0113/5021.

IMFERON®

Presentation Imferon is presented as ampoules containing a dark brown, slightly viscous solution containing iron (50 mg/ml) in the form of a complex of ferric hydroxide with a low molecular weight dextran in a 0.9% sodium chloride solution for injection.

Uses For the rapid and complete correction of proven iron deficiency.

Dosage and administration *Routes of administration:* A series of deep intramuscular injections.

A series of intravenous injections.

One or two large-volume intravenous injections.

Continuous intravenous infusion diluted with normal saline or 5% dextrose solution.

Recommended dosage: Adults and children: The total dose of Imferon required is calculated for each patient individually and is dependent on body weight and haemoglobin level. Tables are provided with each pack of ampoules, and dosage calculators are available on request.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to the product.

The Total Dose Infusion (TDI) method of administration should not be used for patients with a history of asthma. Imferon should not be used in the acute phase of infectious kidney disease.

Warnings: The preparation should be used with extreme care in patients with serious impairment of liver function.

Intramuscular use: In patients with a known history of allergy or chronic infection, a graded series of injection: is strongly recommended, e.g. 0.5 ml, 1 ml then 2 ml until the course is complete.

Intravenous use: Test dose: Undiluted Imferon: Prior to receiving their first Imferon therapeutic dose all patients should be given a *slowly administered* intravenous test dose of not more than 0.5 ml Imferon diluted with patient's own blood. Acute anaphylactoid reactions in these circumstances are usually evident within a few minutes, and this is the *minimum* time period of observation prior to completing the dose - still under strict medical supervision and by slow injection not exceeding 1 ml per minute.

A time interval of an hour or more between test dose and subsequent administration of the complete dose may be desirable in individual circumstances.

The total dose may be divided and given as a series of intravenous injections adopting the same technique.

Test dose: Total dose infusion (TDI): The initial rate of infusion should not exceed 5 drops per minute for 15 minutes *under strict medical supervision*. If this test dose is well tolerated the rate of infusion may be increased to 45 to 60 drops per minute.

Outpatients should be kept under supervision for about an hour after infusion is complete before returning home.

As a high incidence of post-infusion arthralgia has been reported after the total dose infusion method in rheumatoid arthritis, this method of administration should only be used when other forms of iron therapy have been found to be unsuccessful in such patients.

If at any time during the administration of Imferon by TDI or undiluted by the intravenous route signs of hypersensitivity reaction or intolerance are detected stop administration immediately and institute appropriate treatment.

Patients with a history of allergy should be under effective antihistamine therapy at the time of intravenous administration/infusion.

Use in pregnancy: Studies in non-anaemic pregnant animals have indicated that at high single doses of Imferon > 2.5 ml/kg, teratogenic effects may occur. No such effects have been produced at lower levels of 1 ml/kg. For clinical human use the highest dose normally required is in the order of 1 ml/kg or less.

Pharmaceutical precautions Store in cool place. Protect from freezing. Discard four weeks after first opening container.

Legal category POM.

Package quantities Dropper bottle of 5 ml.

Further information Nil.

Product licence number 0113/5090.

FRAMYGEN® EYE OINTMENT

Presentation A smooth, pale yellow ointment containing Framycetin Sulphate BP 0.5% w/w.

Uses The treatment of blepharitis and styes, blepharconjunctivitis, infected conjunctivitis and infected corneal abrasions.

Dosage and administration Direct application to the eye four to six times daily.

Contra-indications, warnings, etc

Contra-indications: Known hypersensitivity to framycetin.

Warnings: Cross sensitivity can occur in neomycin sensitive patients.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Tube of 3.5 g.

Further information Nil.

Product licence number 0113/5069.

GENISOL®

Presentation A clear, golden-yellow liquid containing sodium sulphosuccinated undecylenic monoalkolamide 1% w/v, purified coal-tar fractions 0.25% w/v designed to be therapeutically equivalent to 2% Prepared Coal Tar 3P and comprising:

Phenol	8% w/w	o-Cresol	8% w/w
Quinoline	4% w/w	Pyridine	2% w/w
o-Picoline	2% w/w	Toluene	16% w/w
Xylene	8% w/w	Phenanthrene	32% w/w
Carbazole	20% w/w		

Uses Seborrhoeic dermatitis of the scalp (dandruff) and psoriasis of the scalp.

Dosage and administration To be used once per week or more frequently if required, in the manner of a shampoo. Stir about 10 ml of Genisol into half a tumblerful of warm water. Wet the hair thoroughly, apply half the solution and work into the scalp with the fingers. Rinse and repeat the application. Finally, rinse the hair thoroughly in clean water.

Contra-indications, warnings, etc When washing the hair, care should be taken to keep the solution away from the eyes.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Bottles of 58 ml, 250 ml and 500 ml.

Further information Nil.

Product licence number 0113/5020.

HYALASE®

Presentation A white, fluffy, odourless powder. Each ampoule contains 1,500 international units of Hyaluronidase BP (Ovine).

Uses Hyaluronidase has a temporary and reversible depolymerising action on the polysaccharide hyaluronic acid which is present in the intracellular matrix of connective tissue. This action allows the rapid dispersal and absorption of substances given by subcutaneous or intramuscular injection. Hyaluronidase also facilitates the dispersal of extravasated fluid and haematomatous swellings.

Dosage and administration Adults: *In hypodermoclysis:* a two-way subcutaneous infusion set is required with the fluid container supported about 1 metre above the patient. Suitable hypodermic needles are attached to the connecting tubes after any contained air has been expelled. The needles are then inserted into the subcutaneous tissues at selected sites and the fluid allowed to run in by gravity. The contents of one ampoule of Hyalase (1,500 international units), dissolved in one ml of water for injections, are injected through the rubber tubing about 2 cm from each needle, at the beginning of the infusion.

When this method is employed, approximately 200 ml of fluid can be administered in 20 minutes.

Repeated infusions may be given as required, but it is advisable to change the site of injection.

Injection may alternatively be given from a syringe directly into a site into which 1 ml water for injections containing 1,500 international units of Hyalase has previously been injected. The needle should be maintained in the site adopted throughout the procedure which, in this case, should not be unduly prolonged.

It is not advisable to raise the temperature of the fluid prior to infusion since this has been observed to reduce the rate of absorption.

Site of injection. The possible sites of administration are numerous, irrespective of the position of the patient. Choice may be made, for example, from the axillae, pectoral regions, subscapular and trunk areas, thighs and calves.

In general 1,500 international units of Hyalase are sufficient for the administration of 500–1,000 ml of most fluids. In the case of whole blood, however, 3,000 units may be required.

Obstetric anaesthesia: The anaesthetic mixture is prepared as follows:—

Hyalase – 1,500 international units.

Adrenaline hydrochloride – 0.5 ml of 1:1,000 dilution.

Procaine hydrochloride – 30 ml of 1% solution.

Heins' method is as follows: The needle is passed horizontally to the ischial spine, and 5 ml of the solution is deposited here to anaesthetise the pudendal nerve as it enters Alcock's canal. Next, 5 ml of the mixture is infiltrated in the superior portion of the labia minora to anaesthetise the perineal branches of the ilioinguinal nerve. The same procedure is carried out on both sides of the perineum.

Prevention of post-partum haemorrhage: 1,500 international units of Hyalase are dissolved in 1 ml of a solution containing 0.5 mg ergometrine for intramuscular injection. The injection is given in the thigh at the moment of crowning or delivery of the foetal head. When ergometrine is given with Hyalase in this way, the oxytocic effect is apparent 3–4 minutes earlier than

corticosteroids can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

In infants, long-term continuous topical therapy should be avoided. Adrenal suppression can occur even without occlusion.

Cross sensitivity can occur in neomycin sensitive patients.

Pharmaceutical precautions Store in a cool place. Protect from freezing. Shake well before use. Discard two weeks after first opening container.

Legal category POM.

Package quantities Dropper bottle of 5 ml.

Further information Nil.

Product licence number 0113/5089.

FRAMYCORT* EYE OINTMENT

Presentation Smooth, pale yellow ointment containing:

Framycetin Sulphate BP	0.5% w/w
Hydrocortisone Acetate BP	0.5% w/w

Uses The treatment of superficial bacterial eye infections, conjunctivitis, blepharitis, marginal corneal ulceration.

Dosage and administration To be applied to the eye two or three times daily.

Contra-indications, warnings, etc

Contra-indications: Viral infections. Known hypersensitivity to framycetin.

Precautions: In pregnant animals, administration of corticosteroids can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

In infants, long-term continuous topical therapy should be avoided. Adrenal suppression can occur even without occlusion.

Cross sensitivity can occur in neomycin sensitive patients.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Tube of 3.5 g.

Further information Nil.

Product licence number 0113/5065.

FRAMYCORT* OINTMENT

Presentation Off-white ointment containing:

Framycetin Sulphate BP	0.5% w/w
Hydrocortisone Acetate BP	0.5% w/w

Uses Subacute and chronic eczema-dermatitis complicated by secondary infection, seborrhoeic dermatitis, anogenital pruritus.

Dosage and administration *Topical application:* Rub in gently and thoroughly two to three times daily,

leaving a light surface layer over the affected area. Cover with a light dressing.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to framycetin.

Precautions: In pregnant animals, administration of corticosteroids can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical steroid should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

In infants, long-term continuous topical therapy should be avoided. Adrenal suppression can occur even without occlusion.

Cross sensitivity can occur in neomycin sensitive patients.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Tube of 15 g.

Further information Nil.

Product licence number 0113/5067.

FRAMYGEN* CREAM

Presentation Smooth, white cream containing Framycetin Sulphate BP 0.5% w/w.

Uses All uncomplicated bacterial skin infections including: sycosis barbae, impetigo and other pyogenic infections.

Dosage and administration Topical application smeared directly on to lesions or as a spread on dressing two to three times a day.

Contra-indications, warnings, etc

Contra-indications: Known hypersensitivity to framycetin.

Warnings: Cross sensitivity can occur in neomycin sensitive patients.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Tube of 15 g.

Further information Nil.

Product licence number 0113/5068.

FRAMYGEN* EYE AND EAR DROPS

Presentation A clear, very pale fawn coloured fluid containing Framycetin Sulphate BP 0.5% w/w.

Uses *In ophthalmology:* Treatment of styes, blepharitis, conjunctivitis and other superficial eye infections, corneal abrasions.

In otology: Otitis externa.

Dosage and administration To be applied to the eye or into the auditory canal, 1-4 drops three to four times daily, or as directed by the physician.

Contra-indications, warnings, etc

Contra-indications: Known hypersensitivity to framycetin or benzalkonium chloride.

Warnings: Cross sensitivity can occur in neomycin sensitive patients.

njection BP in 5% dextrose. A sterile solution containing 6% w/v dextrans of weight average molecular weight 10,000 in 5% w/v Dextrose Injection BP.

Dextraven 110 in Saline: a clear, almost colourless, slightly viscous liquid. Dextran 110 Injection BP in 0.9% sodium chloride. A sterile solution containing 6% w/v dextrans of weight average molecular weight 110,000 in Sodium Chloride Injection BP.

Dextraven 150 6% in Dextrose: a clear, almost colourless, slightly viscous liquid. A sterile solution containing 6% w/v dextrans of weight average molecular weight 150,000 in 5% w/v Dextrose Injection BP.

Dextraven 150 6% in Saline: a clear, almost colourless, slightly viscous liquid. A sterile solution containing 6% w/v dextrans of weight average molecular weight 150,000 in Sodium Chloride Injection BP.

Uses For the restoration and maintenance of blood volume where this has been reduced as a result of haemorrhage, extravasation of blood or plasma, accidental or surgical wounds, and in burns. Prophylactically, in major surgery to maintain blood volume and pressure during prolonged operations.

Dosage and administration *Haemorrhage:* In moderate blood loss 500 ml are infused rapidly, taking 15 minutes. A further 500 ml are given more slowly, taking 30–45 minutes. In severe haemorrhage 1,000 ml are infused as rapidly as possible. A further 500 ml may be given more slowly, depending on the clinical condition of the patient and the availability of cross-matched blood.

Crush injuries: The loss of plasma proteins into injured tissues and the consequent attraction of water out of the circulation may be combated by the infusion of 500–1,500 ml of Dextraven 110 or Dextraven 150. The rate of infusion is dictated by the degree of shock. Where this is severe, rapid infusion is necessary.

Burns: As a guiding principle up to 3,000 ml of Dextraven 110 or Dextraven 150 may be given in the first 36–48 hours. Electrolytes, dextrose and possibly blood will also be required according to the clinical situation.

Prophylaxis: Prior to major surgery a Dextraven 110 or Dextraven 150 drip at the rate of 10–20 drops a minute is set up as soon as the patient is anaesthetised. The drip rate may be adjusted to maintain the blood pressure during the operation. It is seldom necessary to continue the infusion after the operation is complete.

Contra-indications, warnings, etc *Anaphylactoid reactions* occur rarely. They are more common and may be more severe in patients with a history of asthma.

The most frequently observed signs of such reactions are hypotension and bronchospasm, progressing on very rare occasions to cardiac arrest. In addition, skin manifestations such as erythema and urticaria may be seen.

In view of the above it is essential to observe patients closely throughout the infusion, particularly during the first few minutes. If there is any suspicion of an anaphylactoid reaction, treatment with Dextraven should be discontinued immediately and appropriate resuscitative measures instituted.

In continuing haemorrhage, whole blood or packed cells may be indicated after 1,000–1,500 ml of Dextraven 110 or Dextraven 150 have been infused. This prevents over-dilution of clotting factors and maintains oxygen-carrying capacity. Where clotting factors are already

reduced (e.g. in hypofibrinogenaemia or thrombocytopenia) correction of this condition must be undertaken prior to or concomitantly with the Dextraven infusion.

Pharmaceutical precautions Do not store in excess of 25°C or expose to undue fluctuations in temperature. Do not use if cloudy or if a deposit is present. Discard any unused solution.

Legal category POM.

Package quantities Bottles of 500 ml.

Further information If blood samples are required for grouping and cross-matching, they should be taken when possible before infusion.

Product licence numbers

Dextraven 110 in Dextrose	0113/5058
Dextraven 110 in Saline	0113/5059
Dextraven 150 6% in Dextrose	0113/5054
Dextraven 150 6% in Saline	0113/5055

DIMYRIL* LINCTUS

Presentation Faintly opalescent, red liquid, each 5 ml of which contains 40 mg isoaminile citrate.

Uses For the treatment of cough associated with acute and chronic bronchitis, influenza, common cold, laryngitis and measles.

Dosage and administration *Oral: Adults:* 5 ml three to five times per day.

Children: 2.5–5 ml three to five times per day.

Infants: As recommended by the physician.

Contra-indications, warnings, etc *Side-effects:* Dizziness, nausea and constipation occur rarely.

Overdosage: Symptoms: Hallucinations and mania. Treatment: Withdrawal of drug; induction of vomiting/gastric lavage if large quantities taken; medical observation and supportive measures as necessary.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Bottle of 150 ml.

Further information Nil.

Product licence number 0113/5012.

FRAMYCORT* EYE AND EAR DROPS

Presentation Clear, very pale fawn coloured supernatant fluid with a fine white deposit which readily disperses on shaking. Contains:

Framycetin Sulphate BP	0.5% w/v
Hydrocortisone Acetate BP	0.5% w/v

Uses Treatment of superficial bacterial eye infections, conjunctivitis, blepharitis, marginal corneal ulceration and otitis externa.

Dosage and administration Direct application to the eye or into the auditory canal, 1–4 drops three to four times daily, or as directed by the physician.

Contra-indications, warnings, etc

Contra-indications: Viral infections. Known hypersensitivity to framycetin or benzalkonium chloride.

Precautions: In pregnant animals, administration of

Fisons plc
Pharmaceutical Division
12 Derby Road
Loughborough, Leics LE11 0BB

FISONS
Pharmaceuticals

ACNIL*

Presentation A smooth, soft, brownish-pink cream containing:

Precipitated Sulphur BP	3.0% w/w
Resorcinol BP	0.5% w/w
Cetrimide BP	0.5% w/w

Uses Acnil is a mild antiseptic and keratolytic for the treatment of acne vulgaris.

Dosage and administration *Adults:* Spread sparingly over the affected area only, twice daily until the spots disappear.

Children: At the discretion of the physician.

Contra-indications, warnings, etc

Contra-indication: Rosacea.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Tube of 25 g.

Further information Nil.

Product licence number 0113/5000.

AURALGICIN*

Presentation A pale yellow, viscous liquid containing:

Benzocaine BP	1.4% w/v
Ephedrine Hydrochloride BP	1.0% w/v
Phenazone BPC	5.5% w/v
Chlorbutol BP	1.0% w/v
Potassium Hydroxyquinoline Sulphate BPC	0.1% w/v
Glycerol BP	to 100%

Uses Antibacterial, analgesic ear drops for the treatment of acute and subacute otitis media.

Dosage and administration *Adults and children:*

1. The patient should be lying on his side – affected ear uppermost.
2. Pour the ear drops from the bottle into the affected ear until the ear is filled. (The patient will find it more soothing if the ear drops are warmed before placing them in the ear. This can be achieved by placing a teaspoon in warm water and then pouring the drops onto the dried warm spoon. The drops can now be applied to the ear from the spoon.)
3. Wait a few minutes before placing a plug of cotton wool into the ear.
4. Repeat the treatment hourly until no further pain is felt.
5. Thereafter the treatment should be repeated three-hourly for a period of 24 hours or until the doctor advises that no further treatment is necessary.

Note: If pain and inflammation persist after 24 hours the doctor should be consulted again.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to benzocaine or other ingredients. Not recommended for use in patients with perforated ear drums.

Pharmaceutical precautions *Important:* Replace the cap immediately after use. Do not use if cloudy as the effectiveness will be reduced.

For external use only.

Legal category P.

Package quantities Bottle of 12 ml.

Further information Appropriate systemic therapy may also be required.

Product licence number 0113/5003.

BARQUINOL* HC

Presentation Smooth, buff cream containing:

Hydrocortisone Acetate BP	0.5% w/w
Clioquinol BP	3.0% w/w

Uses Infective eczema, fungal infections, seborrhoeic dermatitis and pruritis.

Dosage and administration Apply directly to the affected area as a smear or as a spread on a dressing. Apply two or three times daily.

Contra-indications, warnings, etc *Precautions:* In pregnant animals, administration of corticosteroids can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

In infants, long-term continuous topical therapy should be avoided. Adrenal suppression can occur even without occlusion.

Side-effects: Clioquinol may occasionally cause severe irritation.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Tube of 15 g.

Further information Nil.

Product licence number 0113/5004.

DEXTRAVEN* 110 IN DEXTROSE

DEXTRAVEN* 110 IN SALINE

DEXTRAVEN* 150 6% IN DEXTROSE

DEXTRAVEN* 150 6% IN SALINE

Presentation *Dextraven 110 in Dextrose:* a clear almost colourless slightly viscous liquid. *Dextran 110*

oses are required, 3–4 capsules may be given over 24 ours.

Contra-indications, warnings, etc Tetracyclines re selectively absorbed by developing bones and teeth nd may cause dental staining and enamel hypoplasia. r addition, these compounds readily cross the placental rrier and therefore Tetralysal 300 should not be dministered to pregnant women or children below the ge of 8 years unless in the opinion of the physician no ther less toxic agents are available.

As lymecycline is mainly excreted by the kidneys, it hould not be administered to patients with renal ufficiency.

Its use is also contra-indicated in patients sensitive to tetracyclines.

The absorption of tetracyclines may be affected by the imultaneous administration of milk, antacids and iron reparations.

It should also be borne in mind that the prolonged use f broad spectrum antibiotics may result in the appear- nce of resistant organisms and superinfection.

Overdosage: There is no specific treatment, but gastric vage should be performed as soon as possible. upportive measures should be instituted as required, nd a high fluid intake maintained.

Pharmaceutical precautions The capsules should be stored in air-tight containers in a cool place protected from light.

Legal category POM.

Package quantities Tetralysal 300 is available in bottles of 100 capsules.

Further information The active constituent of Tetralysal 300 is lymecycline, tetracycline chemically bonded to the amino acid L-lysine. It has been estimated that Tetralysal 300 (lymecycline 408 mg) is equivalent in its action to 500 mg of tetracycline hydrochloride.

Lymecycline is approximately 5,000 times more soluble than tetracycline base, and unlike tetracycline hydrochloride, it is soluble at all physiological pH values. (A 5% aqueous solution does not precipitate in the presence of serum.)

Product licence number Tetralysal 3433/0044.

**Trade Mark*

other intra-abdominal and intrapelvic infections; gonorrhoea; female genital tract infections; septicaemia; urinary tract infections; respiratory tract infections; bone and joint infections; skin and soft-tissue infections.

Mefoxin is also indicated for adjunctive therapy in the surgical treatment of infections, including abscesses, infection complicating hollow visceral perforations, cutaneous infections, and infections of serous surfaces, whether caused by aerobes, mixed aerobes and anaerobes, or anaerobes.

Clinical experience has demonstrated that Mefoxin can be administered to patients who are receiving carbenicillin, kanamycin, gentamicin, tobramycin, or amikacin.

Prevention: Mefoxin is indicated for the prevention of certain post-operative infections in patients undergoing contaminated or potentially contaminated surgical procedures or where the occurrence of post-operative infection could be serious.

Microbiology: Mefoxin is active in vitro against: Aerobic bacteria: *Gram-positive cocci* including: *Staphylococci*: (including coagulase-positive, coagulase-negative, and penicillinase-producing strains); Group A beta-haemolytic streptococci (*Streptococcus pyogenes*); Group B beta-haemolytic streptococci (*Streptococcus agalactiae*); *Streptococcus pneumoniae* (*Diplococcus pneumoniae*); other streptococci (except group D streptococci including enterococci, most strains of which are resistant, e.g. *Streptococcus faecalis*), *Gram-negative cocci* including: *Neisseria gonorrhoeae* (including penicillinase-producing strains); *Neisseria meningitidis*. *Gram-negative rods (facultative anaerobes)* including: *Escherichia coli*; *Klebsiella pneumoniae*; *Klebsiella spp.*; *Proteus mirabilis*. *Proteus* (indole-positive): *Proteus vulgaris*; *Proteus rettgeri*; *Proteus morganii*; *Haemophilus influenzae*; *Serratia marcescens*; *Providencia spp.*; *Salmonella* and *Shigella spp.*

Anaerobic bacteria: *Gram-positive cocci* including: *Peptococcus spp.*; *Peptostreptococcus spp.*; Microaerophilic streptococcus. *Gram-positive rods* including: *Clostridium perfringens*; *Clostridium spp.*; *Eubacterium spp.*; *Propionibacterium acnes*. *Gram-negative cocci* including: *Veillonella spp.* *Gram-negative rods* including: *Bacteroides fragilis*; *Bacteroides melaninogenicus*; *Bacteroides spp.* (including both penicillin-susceptible and penicillin-resistant strains); *Fusobacterium spp.*

Mefoxin is active against some strains of the following bacteria: *Acinetobacter calcoaceticus* var. *anitratum* (*Herellea vagincola*); *Acinetobacter calcoaceticus* var. *Iwoffi* (*Mima polymorpha*); *Alcaligenes faecalis*; *Citrobacter spp.* and *Flavo-bacterium spp.*; *Enterobacter spp.*

Mefoxin is not active against *Pseudomonas spp.*, most strains of enterococci, many strains of *Enterobacter cloacae*, and methicillin-resistant staphylococci.

Human pharmacology: Mefoxin administered parenterally, produces high serum and urine concentrations. It is excreted virtually unchanged as active Mefoxin by the kidneys, and has a mean terminal serum half-life of approximately one hour. Mefoxin passes rapidly into body fluids such as pleural, bile, and ascitic fluids. Probenecid slows tubular excretion and increases and prolongs blood levels.

Intravenous: Peak serum concentration of Mefoxin following 1 g infused intravenously over three minutes was 125 mcg/ml, infused over 30 minutes was 72 mcg/ml, and infused over 120 minutes was 25 mcg/ml. Following 2 g infused intravenously over

three minutes, peak serum concentration was 221 mcg/ml.

In a number of studies using 0.5 g, 1 g, or 2 g intravenous doses of Mefoxin mean total urinary recovery ranged from 77% to 99% of the cefoxitin dose.

Intramuscular: When Mefoxin was reconstituted for intramuscular injection with 0.5% or 1% lignocaine hydrochloride, the lignocaine had no effect on the absorption or elimination of Mefoxin.

Intramuscular injections of 1 g of Mefoxin in 0.5% lignocaine hydrochloride solution produced a peak serum concentration of 30 mcg/ml at 20 minutes. Approximately 85% of an intramuscular dose is excreted by the kidneys in the first six hours; this results in high urine levels (e.g. >3,000 mcg/ml between one and two hours after a 1 g dose).

Dosage and administration Mefoxin may be administered intravenously or intramuscularly. (See reconstitution directions for each route below.) Dosage and route of administration should be determined by severity of infection, susceptibility of the causative organisms, and condition of the patient.

Therapy may be started while awaiting the results of susceptibility testing.

Adults: Dosage: The usual adult dosage is 1 g or 2 g of Mefoxin every eight hours. (See 'Usual adult dosage' chart.)

In adults with renal insufficiency, an initial loading dose of 1 g to 2 g may be given. After a loading dose, the following recommendations for maintenance dosage may be used as a guide.

In the patients undergoing haemodialysis, the loading dose of 1–2 g should be given after each haemodialysis, and the maintenance dose should be given as indicated in the chart giving 'Maintenance dosage of Mefoxin in adults with reduced renal function'.

Children: Children three months of age and older: the recommended dosage in children of three months of age and older is 80–160 mg/kg of body weight per day divided into 4–6 equal doses. The total daily dosage may be increased to 200 mg/kg but not to exceed 12 g per day for severe infections.

No recommendation is made for children under three months of age.

In children with renal insufficiency dosage frequency should be reduced as indicated for adults.

Uncomplicated urinary tract infections: In uncomplicated urinary tract infections due to susceptible organisms, 1 g intramuscularly twice a day has been shown to be effective.

Uncomplicated gonorrhoea: For single dose therapy of uncomplicated gonorrhoea, including that caused by penicillinase-producing strains, the recommended dose is 2 g of Mefoxin intramuscularly given with 1 g of probenecid by mouth (at the same time or up to one hour before).

Prophylactic administration for adults: 2 g intramuscularly or intravenously just prior to surgery (approximately $\frac{1}{2}$ –1 hour before incision), then 2 g every 6 hours. Prophylactic therapy does not usually continue for more than 24 hours.

Prophylactic administration for children (3 months of age and older): 30–40 mg/kg at the times given for adults.

Caesarean section: 2.0 g intravenously as soon as the umbilical cord is clamped; and 2.0 g intravenously or intramuscularly 4 and 8 hours after the initial dose.

Subsequent doses may be given every six hours with usually no need to continue for more than 24 hours.

Intravenous administration: Reconstitute Mefoxin with Water for Injections BP: 1 g is soluble in 2 ml. Although Mefoxin is very soluble, for intravenous use it is preferable to add 10 ml of Water for Injections BP to the 1 g vial or to the 2 g vial. Shake to dissolve and then withdraw entire contents of vial into syringe.

Solutions of Mefoxin range from clear to light amber in colour. The pH of freshly reconstituted solutions usually ranges from 4.2 to 7.0.

For direct intravenous injection, Mefoxin may be slowly injected into the vein over a period of three to five minutes or may be given through the tubing when the patient is receiving parenteral solutions.

An intermittent intravenous infusion of Mefoxin may be employed when large amounts of fluid are to be given. However, during infusion of the solution containing Mefoxin, it may be advisable temporarily to discontinue administration of any other infusion solution at the same site (by using an appropriate IV infusion set).

A solution of Mefoxin may also be given by continuous intravenous infusion (see overleaf for compatibility and stability).

Intramuscular administration ONLY: Reconstitute Mefoxin 1 g with 2 ml of Water for Injections BP, or 0.5% or 1% lignocaine hydrochloride (without adrenaline) solution. Mefoxin is given by deep injection into a large muscle mass. Avoid injection into a blood vessel.

Note: Some patients may be hypersensitive to lignocaine.

Preparation of solution: The following table is provided for convenience in reconstituting Mefoxin for both intravenous and intramuscular administration.

Strength	Amount of diluent to be added (ml*)	Approximate average concentration (mg/ml)
1 gram vial	2 (Intramuscular)	400
1 gram vial	10 (IV)	95
2 gram vial	10 or 20 (IV)	180 or 95

* Shake to dissolve and let stand until clear.

Compatibility and stability: A solution of Mefoxin in Water for Injections BP may be added to the following solutions: 0.9% Sodium Chloride Injection BP, 5% or 10% Dextrose Injection BP, Dextrose and Sodium Chloride Injection BP (5%/0.9%, 5%/0.45%, or 5%/0.2%), Lactated Ringer's Injection USP, 5% Dextrose Injection in 0.02% sodium bicarbonate solution, 5% Dextrose in Lactated Ringer's Injection, 5% or 10% invert sugar in water, 10% invert sugar in saline solution, 4.2% Sodium Bicarbonate Injection BP, M/6 Sodium Lactate Injection BP, insulin (in normal saline or 10% invert sugar), heparin (100 units/ml and 0.1 units/ml), mannitol (2.5%, 5% and 10%).

Mefoxin has been shown to be chemically and visually compatible with aminoglycosides such as amikacin, gentamicin, kanamycin, and tobramycin mixed in 200 ml of 0.9% sodium chloride or 5% dextrose in water.

Contra-indications, warnings, etc

Contra-indications: Mefoxin is contra-indicated in persons who have shown hypersensitivity to cefoxitin. In the absence of clinical experience, Mefoxin should not be administered to patients who have shown hypersensitivity to cephalosporins.

Usual adult dosage

Type of infection	Dose (g)	Frequency (hrs)	Total daily dosage
Uncomplicated	1	Every 8 (occasionally every 6)	3 g (4 g)
Moderately severe or severe	2	Every 8 (occasionally every 6)	6 g (8 g)
Infections generally needing antibiotics in higher dosage	3 (2)	Every 6 (every 4)	12 g

Maintenance dosage of Mefoxin in adults with reduced renal function

Renal function	Creatinine clearance (ml/min)	Dose (g)	Frequency (hrs)
Mild impairment	50-30	1-2	Every 8-12
Moderate impairment	29-10	1-2	Every 12-24
Severe impairment	9-5	0.5-1	Every 12-24
Essentially no function	<5	0.5-1	Every 24-48

Precautions: There is some clinical and laboratory evidence of partial cross-allergenicity between cephamycins and other beta-lactam antibiotics, penicillins, and cephalosporins. Severe reactions (including anaphylaxis) have been reported with most beta-lactam antibiotics.

Before therapy with Mefoxin, careful inquiry should be made concerning previous hypersensitivity reactions to beta-lactam antibiotics. Mefoxin should be given cautiously to penicillin-allergic patients.

Any patient who has demonstrated some form of allergy, particularly to drugs, should receive antibiotics cautiously. If an allergic reaction to Mefoxin occurs, the drug should be discontinued.

The total daily dosage should be reduced when Mefoxin is administered to patients with transient or persistent reduction of urinary output due to renal insufficiency because high and prolonged serum antibiotic concentrations can occur from usual dosages.

Interference with laboratory tests: A false-positive reaction to glucose in the urine may occur with reducing substances but not with the use of specific glucose oxidase methods.

Using the Jaffe technique, falsely high creatinine values in serum may occur if Mefoxin serum concentrations exceed 100 mcg/ml. Serum samples from patients treated with Mefoxin should not be analysed for creatinine if withdrawn within two hours of drug administration.

Use in pregnancy: Use of the drug in women of childbearing potential requires that the anticipated benefits be weighed against possible hazards. Reproductive and teratogenic studies have been performed in mice and rats and have revealed no evidence of impaired fertility or harm to the foetus due to Mefoxin. There are no controlled studies with Mefoxin in pregnant women.

Nursing mothers: Mefoxin is excreted in human milk.

Infants under three months of age: Clinical trials are proceeding in infants under three months of age. Pending the outcome of these trials, dosage recommendations for such infants remain to be established.

Side-effects: Mefoxin is generally well tolerated. Side-effects rarely require stopping treatment and usually have been mild and transient.

Local reactions: Thrombophlebitis has occurred with intravenous administration. Pain, induration and tenderness after intramuscular injections have been reported.

Allergic: Maculopapular rash, urticaria, pruritus, eosinophilia, fever and other allergic reactions have been noted rarely.

Gastro-intestinal: Nausea, vomiting, and diarrhoea have been reported rarely.

Blood: Transient leucopenia, neutropenia and haemolytic anaemia have been reported. Some individuals, particularly those with azotaemia, may develop positive direct Coombs tests during therapy with Mefoxin.

Liver function: Transient elevations in SGOT, SGPT, serum LDH, and serum alkaline phosphatase have been reported rarely.

Kidney: Elevations in serum creatinine and/or blood urea levels have been observed. The role of Mefoxin in changes in renal function tests is difficult to assess, since factors predisposing to pre-renal azotaemia or to impaired renal function usually have been present.

Treatment of overdosage: No information is available at present.

Pharmaceutical precautions Mefoxin, as reconstituted with Water for Injections BP, Water for Injections BP preserved with parabens or benzyl alcohol, 0.9% Sodium Chloride Injection BP, 5% Dextrose Injection BP, or 0.5% and 1.0% lignocaine hydrochloride (preserved in parabens), maintains satisfactory potency for 24 hours at room temperature, for one week under refrigeration (below 5°C) and for at least 30 weeks in the frozen state and will maintain potency after thawing for at least 24 hours at room temperature.

After reconstitution with Water for Injections BP and subsequent storage in disposable plastic syringes, Mefoxin is stable for 24 hours at room temperature and 48 hours under refrigeration.

After the periods mentioned above, any unused solutions or frozen material should be discarded. Do not refreeze.

Note: Mefoxin in the dry state should be stored below 30°C. Avoid exposure to temperatures above 50°C. The dry material as well as solutions tend to darken, depending on storage conditions; product potency, however, is not adversely affected.

Legal category POM.

Package quantities Sterile Mefoxin is supplied in vials containing 1 g or 2 g of cefoxitin as the sodium salt.

Further information Nil.

Product licence numbers

1 g 0025/0130

2 g 0025/0131

MINTEZOL*

Presentation Orange-coloured chewable tablets,

marked 'MSD 907', containing 500 mg Thiabendazole BPC.

Uses Anthelmintic.

For the following intestinal helminthiases (singly or in combination): enterobiasis (threadworm disease), strongyloidiasis, ascariasis (large roundworm disease), uncinariasis (hookworm disease – *Necator americanus*, *Ancylostoma braziliense*, and *Ancylostoma duodenale*), trichuriasis (whipworm disease), Dracunculiasis (guinea worm).

Mintezol kills adult worms, and also the eggs of threadworm (*Enterobius vermicularis*, sometimes called pinworm), roundworm, and hookworm. It interferes with the embryonation and larval stage development of strongyloides. The anthelmintic activity against whipworm (*Trichuris trichiura*) is not predictable.

Mintezol is also indicated in cutaneous larva migrans (creeping eruption). In trichinosis, Mintezol can relieve symptoms and fever and reduce eosinophilia during the invasion stage, but its effect on the larvae of *Trichinella spiralis* which have migrated to muscle is questionable.

Dosage and administration Dosage depends on the body weight of the patient and is independent of the condition being treated. Usually, 2 doses are given each day. For patients weighing less than 60 kg (132 lb), each dose is based on 25 mg thiabendazole per kg body weight. For patients weighing 60 kg or more, each dose is 1.5 g thiabendazole. The maximum daily dosage for adults weighing 60 kg or more is 3 g.

Mintezol should be taken with meals. Dietary restrictions, complementary medications and cleansing enemas are not necessary.

The table below relates dosage to body weight:

Duration of therapy does depend on the particular nematode infestation, and is as follows:

Enterobiasis: 2 doses on one day, repeated a week later. This regime is intended to reduce the risk of reinfection due to viable eggs in the environment. If this is not practicable, the patient can be given 2 doses a day for two successive days.

Patient's weight		Dose (twice daily)
kg	lb	Tablets (500 mg thiabendazole)
10	22	$\frac{1}{2}$
20	44	1
30	66	1½
40	88	2
50	110	2½
60	132 (or more)	3

Strongyloidiasis, ascariasis, uncinariasis and trichuriasis: 2 doses a day for two successive days. Alternatively, a single dose of 50 mg/kg may be given, but a high incidence of side-effects would be expected.

(Clinical experience with thiabendazole in the treatment of the conditions in the above paragraph in children weighing less than 15 kg has been limited.)

Cutaneous larva migrans: 2 doses a day for two successive days. If active lesions are still present two days after completion of this therapy, a second similar course is recommended.

Trichinosis: 2 doses a day for two to four successive days, according to the response of the patient. The

optimum dosage in trichinosis has not yet been established. (Clinical experience with thiabendazole in the treatment of this condition in children weighing less than 15 kg has been limited.)

Dracunculiasis: 50–100 mg/kg in two equally divided doses for one day. The lower dosage for patients with 1 or 2 visible worms; the higher dosage for patients with multiple infection (3 or more worms). In massive infections (10 worms or more), 50 mg/kg can be given five to eight days after treatment, if required.

Further considerations: In certain patients, 2 doses a day may lead to a higher incidence of side-effects. In these circumstances, 25 mg per kg body weight may be given after the largest meal on the first day and repeated 24 hours later after a similar meal on the second day.

For mass treatment, a single dose of 50 mg/kg after the evening meal is highly effective and most convenient, though a higher incidence of side-effects may be expected.

Contra-indications, warnings, etc

Contra-indications: A history of hypersensitivity to thiabendazole.

Precautions: If any hypersensitivity reactions occur, therapy should be discontinued immediately and not resumed. Erythema multiforme, including a fatal case of Stevens-Johnson syndrome, has been associated with thiabendazole therapy in children.

Mintezol may impair alertness in some patients, who should avoid driving, operating machinery, or other activities made hazardous by diminished alertness.

Ideally, anaemic, dehydrated or malnourished patients should be given supportive therapy before starting treatment with Mintezol. Liver and renal function should be carefully monitored in patients with disorders of these organs.

Use in pregnancy and lactation: Clinical experience and follow-up studies of the effect of thiabendazole in pregnancy and lactation have been limited. The use of Mintezol in these conditions requires that the potential benefits should be weighed against possible hazards to mother or child. It is excreted in the milk of cattle. Reproduction studies of successive generations of mice, rats, pigs, rabbits, cattle and sheep have shown no foetal abnormalities which could be directly attributable to thiabendazole.

Side-effects: The most common are anorexia, nausea, vomiting and dizziness. Diarrhoea, epigastric distress, pruritus, weariness, giddiness, headache and drowsiness occur less often.

Fever, facial flushing, chills, conjunctival injection, angioneurotic oedema, anaphylaxis, lymphadenopathy, erythema multiforme including Stevens-Johnson syndrome, peri-anal rash and skin rash have occurred infrequently; whether these represent hypersensitivity to thiabendazole, to the parasite, or a manifestation of the disease, is uncertain.

Rare side-effects are tinnitus, collapse, abnormal sensation in the eyes, blurring of vision, hyperirritability, numbness, hyperglycaemia, yellow vision, enuresis, hypotension, cholestasis and parenchymal liver damage, and a transitory rise in cephalin flocculation and SGOT. The appearance of live ascaris in the mouth and nose has been reported on rare occasions.

Some patients excrete a metabolite which imparts a characteristic odour to their urine, similar to that which occurs after eating asparagus. This odour lasts for about

one day after therapy is completed. Crystalluria, with and without haematuria, has been reported, but it promptly subsided when therapy was stopped. A few patients on Mintezol have developed transient leucopenia, but a cause and effect relationship has not been established.

Treatment of overdose: Symptomatic and supportive: there is no specific antidote. The stomach should be emptied by emesis or gastric lavage.

Pharmaceutical precautions Keep container tightly closed; store in a cool place, protect from light.

Legal category P.

Package quantities *Tablets:* Packs of 6.

Further information Mintezol should always be taken after a full meal.

Product licence number 0025/5031.

MODURETIC*

Presentation Peach-coloured, half-scored, diamond-shaped tablets, marked 'MSD 917', containing 5 mg amiloride hydrochloride and 50 mg Hydrochlorothiazide BP.

Aniseed/peppermint-flavoured solution containing 5 mg amiloride hydrochloride and 50 mg hydrochlorothiazide BP in each 5 ml.

Uses Potassium-conserving diuretic and anti-hypertensive.

For the treatment of patients with hypertension, congestive heart failure, or hepatic cirrhosis with ascites, in whom potassium depletion might be anticipated. The presence of amiloride hydrochloride in Moduretic minimises the likelihood of excessive potassium loss during vigorous diuresis for long-term therapy. Moduretic is particularly indicated in conditions where potassium balance is especially important, e.g. patients with congestive heart failure receiving digitalis.

In hepatic cirrhosis with ascites, Moduretic usually provides satisfactory diuresis with diminished potassium loss and less risk of metabolic alkalosis.

Dosage and administration The rate of loss of weight and the serum electrolyte levels should determine the dosage. The most satisfactory rate of weight loss after initiation of diuresis is about 0.5–1.0 kg/day.

Moduretic is not recommended for children.

Hypertension: Usually 1 or 2 tablets (or 1 or 2 teaspoonfuls, 5 or 10 ml) once-a-day or in divided doses. The dosage may be increased if necessary, but not exceeding 4 tablets (or 4 teaspoonfuls) a day.

Moduretic may be used alone or as an adjunct to other antihypertensive drugs such as Aldomet* (methyldopa, MSD) or Blocadren* (timolol maleate, MSD). Since Moduretic enhances the action of these agents, the dosage of the antihypertensive drugs may have to be reduced to avoid an excessive drop in blood pressure.

Studies have shown that Blocadren and Moduretic can be used together once daily. The majority of patients will respond to 10–20 mg Blocadren once daily and 1 tablet (or 1 teaspoonful) of Moduretic.

Congestive heart failure: Initially 1 or 2 tablets (or 1 or 2 teaspoonfuls) a day, subsequently adjusted if required, but not exceeding 4 tablets (or 4 teaspoonfuls) a day. Optimal dosage is determined by the diuretic response

and the serum potassium level. Once an initial diuresis has been achieved, reduction in dosage may be attempted for maintenance therapy. Maintenance therapy may be on an intermittent basis.

Hepatic cirrhosis with ascites: Initially 1 tablet (or 1 teaspoonful) a day, increased gradually if necessary until there is effective diuresis, but not exceeding 4 tablets (or 4 teaspoonfuls) a day. A gradual weight reduction is especially desirable in cirrhotic patients, to reduce the likelihood of untoward reactions associated with diuretic therapy. Maintenance dosage may be lower than those required to initiate diuresis; dosage reduction should therefore be attempted when the patient's weight is stabilised.

Contra-indications, warnings, etc

Contra-indications: Hyperkalaemia (serum potassium over 5.5 mEq/litre); other potassium-conserving diuretics, and potassium supplements; anuria; acute renal failure, severe progressive renal disease, diabetic nephropathy; patients with blood urea over 60 mg per 100 ml or serum creatinine over 1.5 mg per 100 ml, in whom serum electrolyte and blood urea levels cannot be monitored carefully and frequently; prior sensitivity to amiloride hydrochloride or hydrochlorothiazide. In renal impairment, use of potassium-conserving agent may result in rapid development of hyperkalaemia. The safety of amiloride hydrochloride for use in children has not been established; Moduretic is therefore not recommended in children. For 'Use in pregnancy and the nursing mother', see 'Precautions'.

Precautions: **Diabetes mellitus:** Hyperkalaemia has commonly occurred in diabetic patients on amiloride hydrochloride, especially those with chronic renal disease or pre-renal azotaemia. The status of renal function should therefore be determined before Moduretic is given to known or suspected diabetics.

Moduretic should be discontinued before giving a glucose-tolerance test, as one patient with poorly controlled diabetes mellitus, who became severely hyperkalaemic while receiving amiloride hydrochloride, died following two repeated intravenous glucose-tolerance tests. The insulin requirements of diabetic patients may need to be changed. Diabetes mellitus which has been latent may become manifest during thiazide administration.

Metabolic or respiratory acidosis: Potassium-conserving therapy should be initiated only with caution in severely ill patients in whom metabolic or respiratory acidosis may occur, e.g. patients with cardiopulmonary disease or decompensated diabetes. Shifts in acid-base balance alter the balance of extracellular/intracellular potassium, and the development of acidosis may be associated with rapid increases in serum potassium.

Hyperkalaemia (serum potassium level over 5.5 mEq/litre): This has been observed in patients receiving amiloride hydrochloride, either alone or with other diuretics, particularly in the aged, in diabetics, and in hospital patients with hepatic cirrhosis or congestive heart failure who had known renal involvement, were seriously ill, or were undergoing vigorous diuretic therapy. Such patients should be carefully observed for clinical, laboratory and ECG evidence of hyperkalaemia (not always associated with an abnormal ECG). Some deaths have been reported in this group of patients. Should hyperkalaemia develop, Moduretic should be discontinued immediately, and if necessary, active measures taken to reduce the serum potassium to normal.

Electrolyte imbalance and blood urea increases: Hypo-natraemia and hypochloreaemia may occur, although the likelihood of hypochloreaemic alkalosis is reduced with Moduretic. Any chloride deficit may be corrected by the use of ammonium chloride (except in patients with liver disease), and largely prevented by a near-normal salt intake.

Reversible increases in blood urea have been reported accompanying vigorous diuresis, especially in seriously ill patients, such as those with hepatic cirrhosis with ascites and metabolic alkalosis or those with resistant oedema; serum electrolyte and blood urea levels should be carefully monitored in these patients.

Moduretic should be used with caution in patients with renal impairment. Special care should be taken to avoid cumulative or toxic effects due to a reduced excretion of its components. In addition, azotaemia may be precipitated or increased by hydrochlorothiazide. If increasing azotaemia and oliguria occur during treatment, Moduretic should be discontinued.

Effects in cirrhotic patients: Oral diuretic therapy is more frequently accompanied by adverse reactions in patients with hepatic cirrhosis and ascites because these patients are intolerant of acute shifts in electrolyte balance, and because they often have pre-existing hypokalaemia as a result of associated aldosteronism. Hepatic encephalopathy, manifested by tremors, confusion and coma, has been reported in patients on amiloride hydrochloride. Patients with liver disease should be observed for this complication when Moduretic is given. In cirrhotic patients receiving amiloride hydrochloride alone, a deepening of jaundice has occurred, but the relationship to amiloride is uncertain.

Other precautions: Sensitivity reactions to thiazides may occur in patients with or without a history of allergy or bronchial asthma. Hydrochlorothiazide potentiates the action of other antihypertensive agents. Therefore the dosage of these agents, especially the ganglionic blockers, may need to be reduced when Moduretic is added to the regimen. Lithium should generally not be given to patients receiving diuretics, since the risk of lithium toxicity is very high in such patients. The possibility that the thiazides may activate or exacerbate systemic lupus erythematosus has been reported.

Hydrochlorothiazide may decrease arterial responsiveness to noradrenaline, but not enough to prevent noradrenaline being effective in therapeutic usage. Thiazides may increase responsiveness to tubocurarine. The antihypertensive effect of thiazides may be enhanced in the post-sympathectomy patient. Orthostatic hypotension may occur, and may be potentiated by alcohol, barbiturates and narcotics.

Calcium excretion is decreased by hydrochlorothiazide and magnesium excretion is increased.

Thiazides may decrease serum PBI levels without signs of thyroid disturbance. Pathological changes in the parathyroid glands, accompanied by hypercalcaemia and hypophosphataemia, have been reported in a few patients receiving prolonged thiazide therapy. The common complications of hyperparathyroidism have not been observed. Thiazides should be discontinued before carrying out tests for parathyroid function.

Hyperuricaemia may occur, or gout may be precipitated, in certain patients receiving thiazides.

As with any drug, patients should be observed regularly for the possible occurrence of liver dysfunction, idiosyncratic reactions, or blood dyscrasias.

Use in pregnancy and the nursing mother: As clinical

experience is limited, Moduretic is not recommended for use during pregnancy. Thiazides appear in breast milk. If use of the drug is deemed essential, the patient should stop nursing. Since thiazides cross the placental barrier and appear in cord blood, the use of Moduretic where pregnancy is present or suspected requires that the benefits of the drug be weighed against possible hazards to the foetus. These hazards include foetal or neonatal jaundice, thrombocytopenia, and possibly other side-effects that have occurred in the adult. The routine use of diuretics in otherwise healthy pregnant women with or without mild oedema is not indicated.

Side-effects: *Gastro-intestinal:* Anorexia, nausea, vomiting, abdominal fullness, gastric irritation, cramps, pain, constipation and diarrhoea. Studies performed in normal subjects have shown no significant effect of amiloride on gastric secretion.

Related to diuresis: Dry mouth, thirst, paraesthesiae, transient blurred vision, salivary gland inflammation, dizziness, vertigo, weakness, susceptibility to fatigue, muscle cramps, orthostatic hypotension.

Other side-effects: Reversible adverse reactions reported with Moduretic are skin rash, pruritus, and such minor psychiatric disturbances as confusion. Transient visual disturbances have also been noted.

Side-effects associated with thiazide therapy are headache, restlessness, jaundice (intrahepatic cholestatic jaundice), pancreatitis, yellow vision, hyperglycaemia, glycosuria, hyperuricaemia. Thrombocytopenia, leucopenia, agranulocytosis, aplastic anaemia, haemolytic anaemia, purpura, rash, urticaria, photosensitivity, necrotising angitis (vasculitis, cutaneous vasculitis), fever, respiratory distress including pneumonitis and anaphylactic reactions have also been reported.

There have been isolated instances of gastro-intestinal bleeding in patients with a history of gastro-intestinal disease receiving amiloride hydrochloride alone; a causal relationship to amiloride has not been established. Rare reversible abnormalities, thought to be related to amiloride hydrochloride, have been observed in liver function tests. One patient with pre-existing partial heart block developed complete heart block after receiving amiloride hydrochloride.

Whenever side-effects are moderate or severe, the dosage of Moduretic should be reduced, or therapy withdrawn.

Treatment of overdosage: Dehydration, electrolyte imbalance and hepatic coma are treated by the established procedures. There is no specific antidote. If ingestion is recent, emesis should be induced or gastric lavage performed. Treatment is symptomatic and supportive. If hyperkalaemia occurs, active measures should be taken to reduce the serum potassium levels. For respiratory impairment, oxygen or artificial respiration should be administered.

Pharmaceutical precautions Keep container tightly closed; store in a cool place, protected from light.

Legal category POM.

Package quantities

Bottles of 100 and 500 tablets.
Bottles of 200 ml solution.

Further information Oral potassium supplements must not be given with Moduretic.

Onset of diuretic action begins within two to four hours after administration of Moduretic, and reaches a

peak at about the fourth hour; there is detectable activity for about 24 hours.

Product licence numbers

Tablets 0025/5016
Solution 0025/0165

PERIACTIN*

Presentation White, half-scored tablets, marked 'MSD 62', containing Cyproheptadine Hydrochloride BP equivalent to 4 mg anhydrous cyproheptadine hydrochloride.

A yellow syrup containing, in each 5 ml, Cyproheptadine Hydrochloride BP equivalent to 2 mg anhydrous cyproheptadine hydrochloride.

Uses *As an appetite stimulant:* Periacetin is recommended for those patients with decreased appetite or poor eating habits with resulting underweight, where stimulation of appetite, with weight gain, is desirable.

In allergy and pruritus: Periacetin has a wide range of anti-allergic and antipruritic activity, and can be used successfully in treatment of acute and chronic allergic and pruritic conditions, such as: dermatitis, including neurodermatitis and neurodermatitis circumscripta; eczema; eczematoid dermatitis; dermatographism; mild, local allergic reactions to insect bites; hay fever and other seasonal rhinitis; perennial allergic and vasomotor rhinitis; allergic conjunctivitis due to inhalant allergies and foods; urticaria; angioneurotic oedema; drug and serum reactions; anogenital pruritus; pruritus of chickenpox.

Periacetin is indicated as adjunctive therapy to adrenaline and other standard measures for the relief of anaphylactic reactions after the acute manifestations have been controlled.

In migraine headache: Periacetin has been reported to have beneficial effects in a significant number of patients having vascular types of headache. Many patients who have responded inadequately to all other agents have reported amelioration of symptoms with Periacetin. The characteristic headache and feeling of malaise may disappear within an hour or two of the first dose.

Dosage and administration There is no recommended dosage for children under 2 years old. Periacetin is not recommended for elderly debilitated patients.

As an appetite stimulant: Daily dosage may be given as a single dose once a day in the evening or alternatively in divided doses. Dosage should be individualised according to the needs and response of the patient.

Adults and adolescents: The usual dosage appears to be 4 mg (1 tablet or two 5 ml spoonfuls) three times a day. Larger doses are neither required nor recommended for appetite stimulation.

Children aged 7-14 years: The dosage should not exceed 12 mg (3 tablets or six 5 ml spoonfuls) a day.

Children aged 2-6 years: The dosage should not exceed 8 mg (2 tablets or four 5 ml spoonfuls) a day.

The effect of Periacetin on appetite and weight gain only occurs during the period of its administration. After therapy is stopped, there may be some weight loss, but usually not to pre-treatment levels.

In allergy and pruritus: Dosage must be determined on an individual basis. The effect of a single dose usually lasts for four to six hours. For continuous effective relief,

the daily requirement should be given in divided doses, three or four times a day, or as often as necessary.

Adults: 4–20 mg a day, most patients requiring 12–16 mg a day.

Maximum: 32 mg a day.

Children aged 7–14 years: Usually 4 mg three times a day, according to the patient's weight and response. Any additional dosage should be given at bedtime. Maximum 16 mg a day.

Children aged 2–6 years: Initially 2 mg three times a day, adjusted according to the patient's weight and response. Any additional dosage should be given at bedtime. Maximum 12 mg a day.

In vascular headache and migraine: For both prophylactic and therapeutic use at an initial dose of 4 mg repeated if necessary after half an hour. Patients who respond usually obtain relief with 8 mg, and this dose should not be exceeded within a 4- to 6-hour period.

Maintenance: 4 mg every four to six hours.

Contra-indications, warnings, etc

Contra-indications: Concurrent use with monoamine oxidase inhibitors; glaucoma; predisposition to urinary retention; stenosed peptic ulcer; pyloroduodenal obstruction; symptomatic prostatic hypertrophy; bladder neck obstruction; during an acute asthmatic attack; elderly debilitated patients; nursing mothers; newborn or premature infants; known sensitivity to cyproheptadine hydrochloride.

Precautions: Antihistamines should not be used to treat lower respiratory tract symptoms including those of acute asthma. Alertness may be impaired in some patients. Driving a car or other activities made hazardous by diminished alertness should be avoided. Antihistamines are more likely to cause dizziness, sedation and hypotension in the elderly; and conversely, occasionally excitation in the young child. Patients receiving Periacin should be warned not to take alcohol or other CNS depressants. When Periacin is considered for patients who present with symptoms of severe loss of appetite, care should be taken to exclude and serious underlying pathology.

Rarely, prolonged therapy with antihistamines may cause blood dyscrasias.

The use of any drug in pregnancy or in women of child-bearing age requires that the potential benefits be weighed against its possible hazards to mother and child.

Drug interactions: MAO inhibitors prolong and intensify the anticholinergic effects of antihistamines.

Patients should be cautioned against taking alcohol and other central nervous system depressants.

Side-effects: The only side-effects that appear frequently are drowsiness and somnolence; many patients who initially complain of these may no longer do so after the first three or four days of continuous therapy. Drowsiness may be desirable in children by decreasing the emotional tension often associated with anorexia; and in patients with dermatitis and pruritus since it tends to increase the threshold of perception and reduce emotional tension. Dry mouth, dizziness, apprehensiveness, faintness, dryness of the mucous membranes, headache, nausea, and allergic manifestations of skin rash and oedema have been reported in low incidence. On rare occasions, CNS stimulation (as manifested by agitation, confusion, visual hallucinations) may occur. Other side-effects reported rarely are fatigue, excitation, disturbed co-ordination, tremor, irritability, insomnia, and vomiting. Also, photo-

sensitivity, epigastric distress, diarrhoea, palpitations, nervousness, restlessness, paraesthesiae, blurred vision, and thrombocytopenia.

Treatment of overdosage: Emesis should be induced or gastric lavage performed. A saline cathartic should be given and respiration maintained. Convulsive stimulants should be avoided. Generally, treatment is symptomatic and supportive.

Pharmaceutical precautions Periacin should be kept in a cool, dry place; the syrup should also be protected from freezing. Periacin Syrup may be diluted with Syrup BP; the mixture should be used within 14 days.

Legal category P.

Package quantities *Tablets:* Bottles of 100 and 500. *Syrup:* Bottles of 200 ml.

Further information Periacin is the first clinically proved appetite stimulant. At the recommended dosage, it increases the desire to eat in a high proportion of patients. Gain in weight usually results from the increased food intake, and is generally seen after the first week of therapy. There is no clinical evidence of fluid retention or disturbance of endocrine function.

Product licence numbers

Tablets 0025/5017
Syrup 0025/5018

SALURIC*

Presentation White, half-scored tablets, marked 'MSD 432', containing 500 mg Chlorothiazide BP.

Uses Thiazide diuretic.

Oedema associated with congestive heart failure, hepatic cirrhosis, premenstrual tension, drug-induced oedema, and in oedema due to various forms of renal dysfunction (i.e. nephrotic syndrome, acute glomerulonephritis and chronic renal failure). Hypertension, either alone or as an adjunct to other hypertensive drugs, such as Aldomet* (methyldopa, MSD) or Blocadren* (timolol maleate, MSD).

Dosage and administration *Adults – for oedema:* Usually 1 or 2 tablets (0.5–1.0 g) once or twice a day. Many patients respond to intermittent therapy: every other day, or three to five consecutive days a week. Intermittent therapy is less likely to produce excessive diuretic response with resulting electrolyte imbalance.

In oedema accompanying premenstrual tension: $\frac{1}{2}$ –1 tablet once or twice a day, from the first morning of symptoms until the onset of the menses.

Adults – for control of hypertension: Initially, usually 0.5 g or 1.0 g a day as a single or divided dose, increased or decreased according to response. Some patients may need 4 tablets (2.0 g) a day (in divided doses).

Thiazides may add to or potentiate the action of other antihypertensives. If Saluric is added to therapy with other antihypertensive agents, dosage reduction of such agents may be necessary to prevent an excessive drop in blood pressure.

Infants and children: Usually 25 mg per kg body weight a day, given in 2 doses. Infants under 6 months may need up to 35 mg per kg a day, in 2 doses.

On this basis, infants up to 2 years of age may be given

125–375 mg of Saluric daily in 2 doses. Children from 2 to 12 years of age may be given 375 mg to 1.0 g daily in 2 doses. Dosage in both age groups should be based on body weight.

Contra-indications, warnings, etc

Contra-indications: Anuria, known hypersensitivity to chlorothiazide. See also 'Use in pregnancy and the nursing mother', under 'Precautions'.

Precautions: Azotaemia may be precipitated or increased by Saluric. Cumulative effects of chlorothiazide may develop in patients with impaired renal function. If increasing azotaemia and oliguria occur during treatment of severe progressive renal disease, Saluric should be discontinued.

Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance, or of serum ammonia, may precipitate hepatic coma.

Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma.

Saluric adds to or potentiates the action of other antihypertensive agents. Potentiation occurs with ganglion- or adrenergic-blocking drugs.

The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

Patients should be carefully monitored for signs of fluid and electrolyte imbalance (hyponatraemia, hypomagnesaemia, hypochlorhaemic alkalosis and hypokalaemia). It is particularly important to make serum and urine electrolyte determinations when the patient is vomiting excessively or receiving parenteral fluids. Warning signs, irrespective of cause, are: dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia and gastro-intestinal disturbances.

Hypokalaemia may develop, especially with brisk diuresis, when severe cirrhosis is present, or during concurrent steroid or ACTH administration. Interference with adequate electrolyte intake will contribute to hypokalaemia. Hypokalaemia can sensitise or exaggerate the response of the heart to the toxic effects of digitalis (e.g. increased ventricular irritability).

Hypokalaemia may be avoided or treated in the adult by concurrent use of Midamor* (amiloride hydrochloride), a potassium-conserving agent. It also may be avoided by giving potassium chloride or foods with a high potassium content. (Note that symptoms and signs which might indicate ulceration or obstruction of the small bowel in patients taking tablets or capsules containing potassium salts are indications for stopping treatment with such preparations immediately.)

Any chloride deficit is generally mild and does not usually require specific treatment except under unusual circumstances (as in liver or renal disease). Dilutional hyponatraemia may occur in oedematous patients in hot weather; except in rare instances when hyponatraemia is life-threatening, appropriate therapy is water restriction rather than administration of salt. In actual salt depletion, appropriate replacement is the therapy of choice.

Thiazides may increase responsiveness to tubocurarine. The antihypertensive effect of the thiazide may be enhanced in the post-sympathectomy patient. Chlorothiazide may decrease arterial responsiveness to noradrenaline, but not enough to prevent noradrenaline being therapeutically useful. Orthostatic hypotension may occur, and may be potentiated by alcohol, barbiturates or narcotics.

Thiazides may decrease serum protein-bound iodine levels without signs of thyroid disturbances.

Saluric decreases calcium excretion.

Pathological changes in the parathyroid glands, with hypercalcaemia and hypophosphataemia, have been observed in a few patients on prolonged thiazide therapy. The common complications of hyperparathyroidism such as renal lithiasis, bone resorption and peptic ulceration have not been seen. Thiazides should be discontinued before carrying out tests for parathyroid function.

Hyperuricaemia may occur, or gout may be precipitated, in certain patients receiving thiazide therapy.

Insulin requirements in diabetic patients may be increased, decreased or unchanged. Latent diabetes mellitus may become manifest during thiazide administration.

Lithium should generally not be given to patients receiving diuretics, since the risk of lithium toxicity is very high in such patients.

Use in pregnancy and the nursing mother: Thiazides appear in breast milk. If use of the drug is deemed essential the patient should stop nursing. Thiazides cross the placental barrier and appear in the cord blood. Therefore, the use of Saluric, when pregnancy is present or suspected, requires that the benefits of the drug be weighed against the possible hazards to the foetus. These hazards include foetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. The routine use of diuretics in otherwise healthy, pregnant women with or without mild oedema is not indicated.

Side-effects: Gastro-intestinal system: Anorexia, gastric irritation, nausea, vomiting, cramps, diarrhoea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis, salivary gland inflammation.

Central nervous system: Dizziness, vertigo, paraesthesiae, headache, yellow vision.

Haematological: Leucopenia, agranulocytosis, thrombocytopenia, aplastic anaemia, haemolytic anaemia.

Cardiovascular: Orthostatic hypotension (may be aggravated by alcohol, barbiturates, narcotics).

Hypersensitivity: Purpura, photosensitivity, rash, urticaria, necrotising angitis (vasculitis, cutaneous vasculitis), fever, respiratory distress including pneumonitis, anaphylactic reactions.

Other: Hyperglycaemia, glycosuria, hyperuricaemia, muscle spasm, weakness, restlessness, transient blurred vision.

Whenever side-effects are moderate or severe, thiazide dosage should be reduced or therapy withdrawn.

Treatment of overdosage: Symptomatic and supportive; no specific antidote. If ingestion is recent the stomach should be emptied by emesis or gastric lavage. Dehydration, electrolyte imbalance, hepatic coma, and hypotension should be corrected by standard methods. For impaired respiration, oxygen or artificial respiration should be given.

Pharmaceutical precautions Keep container tightly closed; store in a cool place, protected from light.

Legal category POM.

Package quantities Bottles of 100 and 500.

Further information Diuresis usually begins within two hours, is at a peak after four hours and persists for six to twelve hours. No rigid dietary salt restriction required.

Product licence number 0025/5019.

SINEMET®

Presentation The standard strength is known as Sinemet-275 and is supplied as dapple-blue, half-scored, oval tablets, marked 'MSD 654', containing 25 mg carbidopa (as carbidopa monohydrate) and 250 mg Levodopa BP.

Sinemet-Plus is available as yellow, half-scored, oval tablets, marked 'SINEMET PLUS', containing 25 mg carbidopa (as carbidopa monohydrate) and 100 mg levodopa.

Sinemet-110 is available as dapple-blue, half-scored, oval tablets, marked 'MSD 647', containing 10 mg carbidopa (as carbidopa monohydrate) and 100 mg Levodopa BP.

Uses Antiparkinsonian agent.

For treatment of Parkinson's disease and syndrome. Sinemet is useful in relieving many of the symptoms of parkinsonism, particularly rigidity and bradykinesia. It is frequently helpful in the management of tremor, dysphagia, sialorrhoea, and postural instability associated with Parkinson's disease and syndrome.

When response to levodopa alone is irregular, and signs and symptoms of Parkinson's disease are not controlled evenly through the day, substitution of Sinemet usually reduces fluctuations in response. By reducing certain adverse reactions produced by levodopa alone, Sinemet permits more patients to obtain adequate relief of the symptoms of Parkinson's disease.

Sinemet may be given to patients with Parkinson's disease and syndrome who are taking vitamin preparations that contain pyridoxine.

Dosage and administration The optimum daily dosage of Sinemet must be determined by careful titration for each patient.

Sinemet Tablets are available as:

Sinemet-110 containing 10 mg carbidopa and 100 mg levodopa.

Sinemet-Plus containing 25 mg carbidopa and 100 mg levodopa.

Sinemet-275 containing 25 mg carbidopa and 250 mg levodopa.

General considerations: Studies show that the peripheral enzyme dopa decarboxylase is fully inhibited (saturated) by carbidopa at doses between 70 and 100 mg a day. The formulations of Sinemet are designed to provide a range of doses with sufficient carbidopa to inhibit peripheral dopa decarboxylase and thus exert optimal therapy.

Patients who require less than 700 mg levodopa given as Sinemet-275 will theoretically not receive sufficient carbidopa to saturate peripheral dopa decarboxylase. Sinemet-Plus may be helpful, especially for patients with nausea and vomiting.

Most patients can be maintained on divided doses of three to six tablets of Sinemet-275 a day. Tablets are scored for easy division should the frequency of daily dosage need to be increased. During the titration period, Sinemet-Plus may be more convenient.

Patients on Sinemet-Plus who need a higher dosage should be switched to Sinemet-275. Dosage with either form should not exceed eight tablets a day. If patients do show a need for higher doses, levodopa should be added.

Because both beneficial and adverse effects are seen more rapidly with Sinemet than with levodopa, patients should be carefully monitored during the dosage adjustment period. Involuntary movements, particularly ble-

pharospasm, is a useful early sign of excess dosage in some patients.

Sinemet-110 can be used as an alternative to Sinemet-Plus.

Patients not receiving levodopa: Dosage may be initiated with one tablet of Sinemet-Plus three times a day, and adjusted as necessary by small increments to a maximum daily dosage of eight tablets. If patients need more levodopa, one tablet of Sinemet-275 should be substituted three or four times a day. If further titration is necessary, the dosage of Sinemet-275 may be increased gradually to a maximum of eight tablets a day.

Patients receiving levodopa: Discontinue levodopa at least twelve hours (24 hours for slow-release preparations) before starting therapy with Sinemet. The easiest way to do this is to give Sinemet as the first morning dose after a night without any levodopa. The dose of Sinemet should be approximately 20% of the previous daily dosage of levodopa.

The suggested starting dose for most patients is one tablet of Sinemet-275 three or four times a day.

Patients requiring less than 1,500 mg levodopa a day should be started on one tablet of Sinemet-Plus three or four times a day.

The dosage may then be adjusted gradually, but this should not exceed eight tablets a day.

Patients receiving levodopa with another decarboxylase inhibitor: When transferring a patient to Sinemet from levodopa combined with another decarboxylase inhibitor, its dosage should be discontinued at least twelve hours before Sinemet is started. Begin with a dosage of Sinemet that will provide the same amount of levodopa as contained in the other levodopa/decarboxylase inhibitor combination.

Patients receiving other antiparkinsonian agents: Current evidence indicates that other standard antiparkinsonian agents may be continued when Sinemet is introduced (as indicated above), though dosage may have to be adjusted.

Contra-indications, warnings, etc

Contra-indications: Concurrent use with monoamine oxidase inhibitors (these must be discontinued at least two weeks before starting Sinemet), narrow-angle glaucoma; known hypersensitivity to this medication.

Because levodopa may activate a malignant melanoma, it should not be used in patients with suspicious undiagnosed skin lesions or a history of melanoma.

See also 'Pregnancy and lactation' under 'Precautions'.

Precautions: Sinemet may be given to patients already receiving levodopa alone; however, the levodopa must be discontinued at least 12 hours before Sinemet is started. Sinemet should be substituted at a dosage that will provide approximately 20% of the previous levodopa dosage (see 'Dosage and administration').

Sinemet is not recommended for the treatment of drug-induced extrapyramidal reactions. Sinemet should be administered cautiously to patients with severe cardiovascular or pulmonary disease, bronchial asthma, renal, hepatic or endocrine disease.

All patients should be monitored carefully for the development of mental changes, depression with suicidal tendencies, and other serious antisocial behaviour. Patients with current psychoses should be treated with caution. Patients with a history of severe involuntary movements or psychotic episodes when treated with levodopa alone should be observed carefully when Sinemet is substituted. These reactions are thought to be

due to increased brain dopamine following administration of levodopa, and use of Sinemet may cause a recurrence. Concomitant administration of psychoactive drugs such as phenothiazines and butyrophenones should be carried out with caution, and the patient carefully observed for loss of antiparkinsonian effect. Patients with a history of convulsions should be treated with caution.

Phenytoin and papaverine have been reported to reverse the beneficial effects of levodopa.

Patients with chronic wide-angle glaucoma may be treated cautiously with Sinemet, provided the intra-ocular pressure is well controlled and the patient monitored carefully for changes in intra-ocular pressure during therapy.

Care should be exercised when Sinemet is administered to patients with a history of myocardial infarction who have atrial, nodal or ventricular arrhythmias. Cardiac function should be monitored with particular care in such patients during the period of initial dosage adjustment.

As symptoms of postural hypotension have occasionally been reported, Sinemet should be given with caution to patients receiving antihypertensive agents. Adjustment of the dosage of the antihypertensive agent may be required when Sinemet is started. (For patients on pargyline, see the contra-indication on monoamine oxidase inhibitors.)

As with levodopa, there is a possibility of upper gastrointestinal haemorrhage in patients with a history of peptic ulcer. If general anaesthesia is required, therapy with Sinemet may be continued as long as the patient is permitted to take fluids and medication by mouth. If therapy is interrupted temporarily, the usual daily dosage may be administered as soon as the patient is able to take oral medication.

Transient abnormalities in laboratory test results may occur, but have not been associated with clinical evidence of disease. These include elevated blood urea, SGOT, SGPT, LDH, bilirubin, alkaline phosphatase, and protein-bound iodine levels.

Positive Coombs tests have been reported, both with Sinemet and levodopa alone, but haemolytic anaemia is extremely rare.

Usage in children: The safety of Sinemet in patients under 18 years of age has not been established.

Pregnancy and lactation: Although the effects of Sinemet on human pregnancy and lactation are unknown, both levodopa and combinations of carbidopa and levodopa have caused visceral and skeletal malformations in rabbits. Therefore, use of Sinemet in women of child-bearing potential requires that the anticipated benefits of the drug be weighed against possible hazards should pregnancy occur. Sinemet should not be given to nursing mothers.

Drug interactions: Clinical experience with concurrent administration of Sinemet and other standard antiparkinsonian drugs, e.g. benzotropine mesylate, benzhexol hydrochloride, is limited. To date, however, there has been no indication of interactions that would preclude concurrent use. No adverse reactions have been reported that do not occur with the various agents alone.

Side-effects: Side-effects that occur frequently with Sinemet are those due to the central neuropharmacological activity of dopamine. These reactions can usually be diminished by dosage reduction. The most common are choreiform, dystonic and other involuntary movements. Muscle twitching and blepharospasm may be taken as early signs to consider dosage reduction.

Less common are mental changes, including paranoid ideation and psychotic episodes; depression, with or without development of suicidal tendencies; and dementia. Convulsions have occurred, but a causal relationship has not been established.

Less frequent side-effects are cardiac irregularities and/or palpitations, orthostatic hypotensive episodes, bradykinetic episodes (the 'on-off' phenomenon), anorexia, nausea, vomiting and dizziness.

Gastro-intestinal bleeding, development of duodenal ulcer, hypertension, phlebitis, leucopenia and agranulocytosis have occurred rarely.

Positive Coombs tests have been reported both with Sinemet and with levodopa alone, but haemolytic anaemia is extremely rare.

Other side-effects that have been reported include:

Psychiatric: Euphoria, lethargy, sedation, stimulation, fatigue and malaise, confusion, insomnia, nightmares, hallucinations and delusions, agitation and anxiety.

Neurological: Ataxia, faintness, headache, increased hand tremor, trismus, oculogyric crisis, weakness, numbness, bruxism.

Gastro-intestinal: Constipation, diarrhoea, epigastric and abdominal distress and pain, flatulence, hiccups, sialorrhoea, difficulty in swallowing, bitter taste, dry mouth, burning sensation of the tongue.

Dermatological: Sweating, oedema, hair loss, rash, unpleasant odour, dark sweat.

Respiratory: Hoarseness, bizarre breathing pattern.

Urogenital: Urinary retention, incontinence, haematuria, dark urine, priapism.

Special senses: Blurred vision, diplopia, dilated pupils, activation of latent Horner's syndrome.

Other: Hot flushes, weight gain or loss, flushing, abnormalities in laboratory tests (see 'Precautions').

Treatment of overdosage: General supportive measures should be employed, along with immediate gastric lavage. Intravenous fluids should be administered judiciously, and an adequate airway maintained. ECG monitoring should be instituted, and the patient carefully observed for the possible development of arrhythmias; if required, appropriate anti-arrhythmic therapy should be given.

The possibility that the patient may have taken other drugs as well as Sinemet should be taken into consideration. To date, no experience has been reported with dialysis, and hence its value in the treatment of overdosage is not known. Pyridoxine has no effect in reversing the effects of Sinemet.

Pharmaceutical precautions Keep container tightly closed; store in a cool place, protected from light.

Legal category POM.

Package quantities Bottles of 100.

Further information Levodopa relieves the symptoms of Parkinson's disease, presumably by being decarboxylated to dopamine in the brain. Carbidopa, which does not cross the blood-brain barrier, inhibits only the extracerebral decarboxylation of levodopa, making more levodopa available for transport to the brain and subsequent conversion to dopamine. This obviates the need for large doses of levodopa at frequent intervals. The lower dosage reduces or eliminates many adverse reactions, some of which are attributable to dopamine being formed in extracerebral tissues.

ce numbers

0025/0085

0025/0150

0025/0084

11 PARA-AMINOHIPPURATE

Preparation A clear, colourless to slightly yellow solution for intravenous injection, containing in each ml of sterile solution 2 g sodium para-aminohippurate. Active ingredient: Sodium Hydroxide BP.

Uses As a diagnostic agent for the estimation of effective renal plasma flow (RPF). In research procedures, for the measurement of the functional capacity of the renal tubular secretory mechanism (Tm_{PAH}).

Dosage and administration For intravenous use only.

For the measurement of RPF, the concentration of sodium para-aminohippurate in the plasma is maintained at 2 mg per 100 ml. As a research procedure for the measurement of Tm_{PAH} , the plasma level of sodium para-aminohippurate must be sufficient to saturate the capacity of the tubular secretory cells. Concentrations of from 40 to 60 mg per 100 ml are necessary.

Contra-indications, warnings, etc

Precautions: Intravenous solutions must be administered with caution in patients with low cardiac reserve, since a rapid increase in plasma volume can precipitate congestive heart failure.

For measurement of RPF, small doses of sodium para-aminohippurate are used. However, in research procedures for Tm_{PAH} determinations high plasma levels are required to saturate the capacity of the tubular cells. During these procedures the intravenous administration of sodium para-aminohippurate solutions should be carried out slowly and with caution. The patient should be continuously observed for any adverse reactions.

Renal clearance measurement of sodium para-aminohippurate cannot be made with any significant accuracy in patients receiving sulphonamides, procaine or thiazolesulphone. These compounds interfere with chemical colour development essential to the analytical procedures.

Probenecid depresses tubular secretion of certain weak acids such as sodium para-aminohippurate. Therefore patients receiving probenecid will have erroneously low RPF and Tm_{PAH} values.

Effects: Vasomotor disturbances, flushing, tingling, vomiting, cramps. Patients may have a sensation of heat or the desire to defaecate or urinate during or after the administration of a primary dose.

Effect of overdosage: Not applicable.

Precautions No special requirements.

Form POM.

Containers Vials of 10 ml and 50 ml.

Instructions for use Methods of calculating renal plasma flow found in the package leaflet.

Product number 0025/5080.

Trade name

colourless to light yellow, sterile

Uses

glaucoma, reduction of intra-ocular pressure, conditions, hypertension, coma, including secondary glaucoma

Dosage and administration

is one drop 0.25% solution 4 times a day.

If clinical response is not obtained, the dose may be changed to one drop 0.5% solution 4 times a day. If needed, the dose may be increased with miotics, adrenaline or sympathomimetics, but not with carbonic anhydrase inhibitors.

Intra-ocular pressure should be reassessed approximately four weeks after starting treatment because response to Timoptol may take a few weeks to stabilise.

Provided that the intra-ocular pressure is maintained at satisfactory levels, many patients can then be placed on once-a-day therapy. Because of naturally occurring diurnal variations in intra-ocular pressure, satisfactory response is best determined by measuring the intra-ocular pressure at different times during the day.

Transfer from other agents: When only a single antiglaucoma agent is being used, continue the agent and add one drop of 0.25% Timoptol in each affected eye twice a day. On the following day, discontinue the previous agent completely, and continue with Timoptol. If a higher dosage of Timoptol is required, substitute one drop of 0.5% solution in each affected eye twice a day.

When several antiglaucoma agents are being used, the patient should be assessed individually. It may be possible to discontinue some or all the other agents; adjustments should be made to one agent at a time.

Clinical trials have shown the addition of Timoptol to be useful in patients who respond inadequately to maximum antiglaucoma drug therapy.

Contra-indications, warnings, etc

Contra-indications: Bronchospasm, including bronchial asthma, or chronic obstructive pulmonary disease; uncontrolled cardiac failure; and hypersensitivity.

Precautions: Like other topically applied ophthalmic drugs, Timoptol may be absorbed systemically. Timoptol should be used with caution in patients with known contra-indications to systemic use of beta-adrenergic receptor blocking agents. These include sinus bradycardia and greater than first degree heart block; cardiogenic shock; diabetes, especially labile diabetes. Cardiac failure should be adequately controlled before beginning therapy with Timoptol. Patients with a history of severe cardiac disease should be watched for signs of cardiac failure and have their pulse rates checked.

Patients who are already on an oral beta-adrenergic blocking agent should be observed for a potential additive effect on either intra-ocular pressure or the known systemic effects of beta-blockade when given Timoptol.

Although Timoptol alone has little or no effect on pupil size, mydriasis has occasionally been reported when Timoptol is given with adrenaline.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic receptor blocking drugs. The reported incidence is small and is

When treatment with the drug should be initiated, it is not otherwise explicitly contraindicated by involving beta-blockade.

Contraindications: Timoptol has not been studied in pregnancy. The use of Timoptol requires that the potential benefit be weighed against possible hazards.

Use in children: Since clinical studies in children have not been conducted, Timoptol is not currently recommended for use in children.

Side-effects: Timoptol is usually well tolerated.

Signs and symptoms of ocular irritation, including conjunctivitis, blepharitis, and keratitis have been reported occasionally. Visual disturbances including refractory changes (due to withdrawal of miotic therapy) have been reported infrequently.

Hypersensitivity reactions, including localised and generalised rash, and urticaria, have been reported rarely.

Aggravation or precipitation of certain cardiovascular, pulmonary and other disorders have been reported, presumably related to the effects of beta blockade. These include bradyarrhythmia, hypotension, syncope, and bronchospasm (predominantly in patients with pre-existing bronchospastic disease). Respiratory failure, congestive heart failure and masked symptoms of hypoglycaemia in insulin-dependent diabetes have been reported rarely. In clinical trials, slight reduction of the resting heart rate in some patients (mean reduction 2.9 beats/minute, standard deviation 10.2) has been observed.

The following adverse effects have been reported rarely, and a causal relationship to Timoptol has not been established: aphakic cystoid macular oedema, headache, dry mouth, anorexia, dyspepsia, nausea, dizziness, CNS effects, (fatigue, confusion, depression, somnolence, and anxiety), palpitation, and hypertension.

Pharmaceutical precautions Timoptol is stable at room temperature.

Legal category POM.

Package quantities Both the 0.25% and 0.5% w/v solution of timolol maleate are presented in special metered-dose Ocumeter® dispensers, each containing 5 ml.

Further information Unlike miotics, Timoptol reduces IOP with little or no effect on accommodation or pupil size. In patients with cataracts, the inability to see around lenticular opacities when the pupil is constricted is avoided. When changing patients from miotics to Timoptol a refraction might be necessary when these effects of the miotic have passed.

Diminished response after prolonged therapy with Timoptol has been reported in some patients.

Timoptol has been generally well tolerated in glaucoma patients wearing conventional hard contact lenses. Timoptol has not been studied in patients wearing lenses made with material other than polymethylmethacrylate (PMMA).

Product licence numbers

0.25% Ophthalmic Solution	0025/0134
0.5% Ophthalmic Solution	0025/0136

TYROZETS®

Presentation Pink, aniseed-flavoured lozenges,

marked 'MSD' one side and Tyrozets the other, containing 1 mg tyrothricin and 5 mg Benzocaine.

Uses Antibiotic and local analgesic-anaesthetic.

For minor mouth and throat irritations; irritation following tonsillectomy and other oral and throat surgery.

Dosage and administration *Usual dosage:* 1 lozenge every three hours; maximum, 8 lozenges in 24 hours. An adequate response is not evident within two hours; consider stopping Tyrozets.

To allow maximum contact with inflamed tissue Tyrozets should not be chewed or swallowed whole, but allowed to dissolve slowly in the mouth.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to tyrothricin or to benzocaine. If evidence of sensitivity occurs during therapy, Tyrozets should be discontinued.

Precautions: The use of antibiotics may cause overgrowth of non-susceptible organisms. If new infections due to bacteria or fungi appear during therapy, Tyrozets should be stopped and appropriate measures taken.

Topical use of Tyrozets as an aid to prevention of local infection in no way alters the need for adequate systemic therapy if an infection should develop.

Side-effects: Blackness or soreness of the tongue may occur, but usually disappears when therapy is stopped.

Treatment of overdose: Symptomatic and supportive; emesis should be induced or gastric lavage performed.

Pharmaceutical precautions Store in a cool, dry place.

Legal category P.

Package quantities Vials of 12 lozenges.

Further information Since tyrothricin is used only locally and has a low index of sensitisation and toxicity, cross-sensitisation with antibiotics used systemically in more serious infections is unlikely.

Product licence number 0025/5072.

VIRVINA®

Presentation Dark-brown elixir containing, in 5 ml, 0.676 mg Thiamine Hydrochloride BP (Vitamin B₁), 0.338 mg Riboflavin BP (Vitamin B₂), 0.02 mg Pyridoxine Hydrochloride BP (Vitamin B₆), 5 mg Nicotinamide BP, 21.5 mg calcium glycerophosphate, 43.5 mg sodium glycerophosphate, 4 mg of potassium glycerophosphate, and 2.5 mg manganese glycerophosphate, in a palatable base containing 17% alcohol.

Uses Tonic.

For the prevention or treatment of Vitamin B deficiency (but not pernicious anaemia).

Dosage and administration *Adults:* 15 ml three times a day before meals.

Children, 6 years old or over: 5-10 ml three times a day before meals.

Contra-indications, warnings, etc Hypersensitivity to any of the ingredients, or to alcohol, has been reported.

Overdosage: Should be treated symptomatically. Severe effects may be expected if taken together with symptomatic treatment for excessive heat.

Pharmaceutical precautions Store in a cool, dry place, closed, and protected from light.

Product licence numbers

Sinemet-275 0025/0085

Sinemet-Plus 0025/0150

Sinemet-110 0025/0084

SODIUM PARA-AMINOHIPPURATE

Presentation A clear, colourless to slightly yellow solution for intravenous injection, containing in each 10 ml of sterile solution 2 g sodium para-aminohippurate. Inactive ingredient: Sodium Hydroxide BP.

Uses As a diagnostic agent for the estimation of effective renal plasma flow (RPF). In research procedures, for the measurement of the functional capacity of the renal tubular secretory mechanism (Tm_{PAH}).

Dosage and administration For intravenous use only.

For the measurement of RPF, the concentration of sodium para-aminohippurate in the plasma is maintained at 2 mg per 100 ml. As a research procedure for the measurement of Tm_{PAH} , the plasma level of sodium para-aminohippurate must be sufficient to saturate the capacity of the tubular secretory cells. Concentrations of from 40 to 60 mg per 100 ml are necessary.

Contra-indications, warnings, etc

Precautions: Intravenous solutions must be administered with caution in patients with low cardiac reserve, since a rapid increase in plasma volume can precipitate congestive heart failure.

For measurement of RPF, small doses of sodium para-aminohippurate are used. However, in research procedures for Tm_{PAH} determinations high plasma levels are required to saturate the capacity of the tubular cells. During these procedures the intravenous administration of sodium para-aminohippurate solutions should be carried out slowly and with caution. The patient should be continuously observed for any adverse reactions.

Renal clearance measurement of sodium para-aminohippurate cannot be made with any significant accuracy in patients receiving sulphonamides, procaine or thiazolesulphone. These compounds interfere with chemical colour development essential to the analytical procedures.

Probenecid depresses tubular secretion of certain weak acids such as sodium para-aminohippurate. Therefore, patients receiving probenecid will have erroneously low RPF and Tm_{PAH} values.

Side-effects: Vasomotor disturbances, flushing, tingling, nausea, vomiting, cramps. Patients may have a sensation of warmth or the desire to defaecate or urinate during or shortly after the administration of a primary dose.

Treatment of overdosage: Not applicable.

Pharmaceutical precautions No special requirements.

Legal category POM.

Package quantities Vials of 10 ml and 50 ml.

Further information Methods of calculating renal function are to be found in the package leaflet.

Product licence number 0025/5080.

TIMOPTOL®

Presentation Clear, colourless to light yellow, sterile

eye drops, available as a 0.25% and 0.5% w/v solution of timolol maleate.

Uses Timoptol Ophthalmic Solution is a beta-adrenergic receptor blocking agent used topically in the reduction of elevated intra-ocular pressure in various conditions including the following: patients with ocular hypertension; patients with chronic open-angle glaucoma including aphakic patients; some patients with secondary glaucoma.

Dosage and administration Recommended therapy is one drop 0.25% solution in the affected eye twice a day.

If clinical response is not adequate, dosage may be changed to one drop 0.5% solution in each affected eye twice a day. If needed, Timoptol may be used with miotics, adrenaline or systemically-administered carbonic anhydrase inhibitors.

Intra-ocular pressure should be reassessed approximately four weeks after starting treatment because response to Timoptol may take a few weeks to stabilise.

Provided that the intra-ocular pressure is maintained at satisfactory levels, many patients can then be placed on once-a-day therapy. Because of naturally occurring diurnal variations in intra-ocular pressure, satisfactory response is best determined by measuring the intra-ocular pressure at different times during the day.

Transfer from other agents: When only a single antiglaucoma agent is being used, continue the agent and add one drop of 0.25% Timoptol in each affected eye twice a day. On the following day, discontinue the previous agent completely, and continue with Timoptol. If a higher dosage of Timoptol is required, substitute one drop of 0.5% solution in each affected eye twice a day.

When several antiglaucoma agents are being used, the patient should be assessed individually. It may be possible to discontinue some or all the other agents; adjustments should be made to one agent at a time.

Clinical trials have shown the addition of Timoptol to be useful in patients who respond inadequately to maximum antiglaucoma drug therapy.

Contra-indications, warnings, etc

Contra-indications: Bronchospasm, including bronchial asthma, or chronic obstructive pulmonary disease; uncontrolled cardiac failure; and hypersensitivity.

Precautions: Like other topically applied ophthalmic drugs, Timoptol may be absorbed systemically. Timoptol should be used with caution in patients with known contra-indications to systemic use of beta-adrenergic receptor blocking agents. These include sinus bradycardia and greater than first degree heart block; cardiogenic shock; diabetes, especially labile diabetes. Cardiac failure should be adequately controlled before beginning therapy with Timoptol. Patients with a history of severe cardiac disease should be watched for signs of cardiac failure and have their pulse rates checked.

Patients who are already on an oral beta-adrenergic blocking agent should be observed for a potential additive effect on either intra-ocular pressure or the known systemic effects of beta-blockade when given Timoptol.

Although Timoptol alone has little or no effect on pupil size, mydriasis has occasionally been reported when Timoptol is given with adrenaline.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic receptor blocking drugs. The reported incidence is small and in

most cases the symptoms have cleared when treatment was withdrawn. Discontinuation of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy involving beta-blockade should be gradual.

Use in pregnancy: Timoptol has not been studied in human pregnancy. The use of Timoptol requires that the anticipated benefit be weighed against possible hazards.

Use in children: Since clinical studies in children have not been conducted, Timoptol is not currently recommended for use in children.

Side-effects: Timoptol is usually well tolerated.

Signs and symptoms of ocular irritation, including conjunctivitis, blepharitis, and keratitis have been reported occasionally. Visual disturbances including refractory changes (due to withdrawal of miotic therapy) have been reported infrequently.

Hypersensitivity reactions, including localised and generalised rash, and urticaria, have been reported rarely.

Aggravation or precipitation of certain cardiovascular, pulmonary and other disorders have been reported, presumably related to the effects of beta blockade. These include bradyarrhythmia, hypotension, syncope, and bronchospasm (predominantly in patients with pre-existing bronchospastic disease). Respiratory failure, congestive heart failure and masked symptoms of hypoglycaemia in insulin-dependent diabetes have been reported rarely. In clinical trials, slight reduction of the resting heart rate in some patients (mean reduction 2.9 beats/minute, standard deviation 10.2) has been observed.

The following adverse effects have been reported rarely, and a causal relationship to Timoptol has not been established: aphakic cystoid macular oedema, headache, dry mouth, anorexia, dyspepsia, nausea, dizziness, CNS effects, (fatigue, confusion, depression, somnolence, and anxiety), palpitation, and hypertension.

Pharmaceutical precautions Timoptol is stable at room temperature.

Legal category POM.

Package quantities Both the 0.25% and 0.5% w/v solution of timolol maleate are presented in special metered-dose Ocumeter® dispensers, each containing 5 ml.

Further information Unlike miotics, Timoptol reduces IOP with little or no effect on accommodation or pupil size. In patients with cataracts, the inability to see around lenticular opacities when the pupil is constricted is avoided. When changing patients from miotics to Timoptol a refraction might be necessary when these effects of the miotic have passed.

Diminished response after prolonged therapy with Timoptol has been reported in some patients.

Timoptol has been generally well tolerated in glaucoma patients wearing conventional hard contact lenses. Timoptol has not been studied in patients wearing lenses made with material other than polymethylmethacrylate (PMMA).

Product licence numbers

0.25% Ophthalmic Solution	0025/0134
0.5% Ophthalmic Solution	0025/0136

TYROZETS®

Presentation Pink, aniseed-flavoured lozenges,

marked 'MSD' one side and Tyrozets the other, containing 1 mg tyrothricin and 5 mg Benzocaine BP.

Uses Antibiotic and local analgesic-anaesthetic.

For minor mouth and throat irritations; secondary irritation following tonsillectomy and other mouth and throat surgery.

Dosage and administration *Usual dosage:* 1 lozenge every three hours; maximum, 8 lozenges in 24 hours. If an adequate response is not evident within two days consider stopping Tyrozets.

To allow maximum contact with inflamed tissues, Tyrozets should not be chewed or swallowed whole, but allowed to dissolve slowly in the mouth.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to tyrothricin or to benzocaine. If evidence of sensitivity occurs during therapy. Tyrozets should be discontinued.

Precautions: The use of antibiotics may cause overgrowth of non-susceptible organisms. If new infections due to bacteria or fungi appear during therapy, Tyrozets should be stopped and appropriate measures taken.

Topical use of Tyrozets as an aid to prevention of local infection in no way alters the need for adequate systemic therapy if an infection should develop.

Side-effects: Blackness or soreness of the tongue may occur, but usually disappears when therapy is stopped.

Treatment of overdose: Symptomatic and supportive; emesis should be induced or gastric lavage performed.

Pharmaceutical precautions Store in a cool, dry place.

Legal category P.

Package quantities Vials of 12 lozenges.

Further information Since tyrothricin is used only locally and has a low index of sensitisation and toxicity, cross-sensitisation with antibiotics used systemically in more serious infections is unlikely.

Product licence number 0025/5072.

VIRVINA®

Presentation Dark-brown elixir containing, in each 5 ml, 0.676 mg Thiamine Hydrochloride BP (Vitamin B₁), 0.338 mg Riboflavin BP (Vitamin B₂), 0.017 mg Pyridoxine Hydrochloride BP (Vitamin B₆), 5 mg Nicotinamide BP, 21.5 mg calcium glycerophosphate, 43.5 mg sodium glycerophosphate, 4 mg of potassium glycerophosphate, and 2.5 mg manganese glycerophosphate, in a palatable base containing 17% alcohol.

Uses Tonic.

For the prevention or treatment of Vitamin B deficiency (but not pernicious anaemia).

Dosage and administration *Adults:* Usually 10–15 ml three times a day before meals.

Children, 6 years old or over: 5–10 ml three times a day before meals.

Contra-indications, warnings, etc No side-effects have been reported.

Overdose: Should be treated as for ethyl alcohol, together with symptomatic and supportive measures.

Pharmaceutical precautions Keep container tightly closed, and protected from sunlight and excessive heat.

Legal category P.

Package quantities Bottles of 200 ml and 1,000 ml.

Further information Nil.

Product licence number 0025/5073.

ZINAMIDE*

Presentation White, half-scored tablets, marked 'MSD 504', containing 500 mg Pyrazinamide BP.

Uses Antituberculous agent.

Indicated in patients with active tuberculosis in whom problems of drug resistance or patient intolerance preclude therapy with some combination of isoniazid, streptomycin and/or para-aminosalicylic acid. Zinamide should be given only with other effective antituberculous agents.

Dosage and administration *Usual adult dosage:* 20–35 mg/kg a day divided into three or four doses; the maximum daily dosage is 3 g regardless of body weight. Zinamide should be administered with at least one other effective antituberculous drug. The use of Zinamide in combination therapy does not modify the accepted dosages of other antituberculous agents.

Contra-indications, warnings, etc

Contra-indications: Severe hepatic damage. Safety for use in children has not been established (see also 'Precautions').

Precautions: Zinamide should only be used when close daily observation of the patient is possible, and when laboratory facilities are available for performing frequent liver function tests and blood uric acid determinations. Pre-treatment examinations should include *in vitro* sensitivity tests of recent cultures of *M. tuberculosis* from the patient as measured against the usual antituberculous drugs. Liver function tests, especially serum glutamic pyruvic transaminase (SGPT) and serum glutamic oxaloacetic transaminase (SGOT) determinations, should be carried out prior to therapy, and then every two to four weeks during therapy. Therapy with Zinamide should be withdrawn and not reinstated if signs of hepatocellular damage occur.

If hyperuricaemia accompanied by an acute gouty arthritis occurs, therapy should be discontinued and not reinstated. Zinamide should be used with caution in

patients with a history of gout or diabetes mellitus, as their management may become more difficult.

The safety of Zinamide for use in children has not been established. Because of its potential toxicity, the use of Zinamide in children should be avoided unless it is considered crucial.

There has been one report that the use of Zinamide increased the incidence of fatal haemoptysis. Despite the absence of evidence confirming this, the possibility of an adverse effect on blood clotting time or vascular integrity should be considered.

Side-effects: A hepatic reaction is the most common side-effect of Zinamide. This varies from a symptomless abnormality of hepatic cell function, detectable only by laboratory tests, through a mild syndrome of fever, anorexia, malaise, liver tenderness, hepatomegaly and splenomegaly, to more serious reactions such as clinical jaundice, and rare cases of progressive fulminating acute yellow atrophy and death.

Other side-effects – active gout, sideroblastic anaemia, arthralgias, anorexia, nausea and vomiting, dysuria, malaise, fever, urticaria, aggravation of peptic ulcer.

Treatment of overdosage: The stomach should be emptied by emesis or gastric lavage. Short-acting barbiturates may be given for manifestations of CNS stimulation, anaesthetics for coma, and artificial respiration and oxygen for respiratory failure. In the event of shock, a vasopressor agent (e.g. Aramine, metaraminol tartrate, MSD – see separate entry) should be given.

Pharmaceutical precautions Keep container tightly closed; store in a cool place, protected from light.

Legal category POM.

Package quantities Bottles of 100 and 500. Pure pyrazinamide powder, for sensitivity tests, is available on request.

Further information Zinamide has been used with other 'second line' agents, such as ethionamide and cycloserine, in cases where all three 'standard' drugs were contra-indicated. The use of such combinations has produced sputum conversion in a high proportion of patients able to continue therapy for at least six months.

Product licence number 0025/5038.

*Trade Mark

Merrell Pharmaceuticals Limited
Meadowbank
Bath Road
Hounslow
Middlesex TW5 9QY

Merrell

CLOMID*

Presentation Beige, round, flat, bevelled tablets. The upper surface bisected and the lower surface engraved 'M' within two circles. Each tablet contains 50 mg Clomiphene Citrate BP.

Uses The treatment of ovulatory failure in women wishing to become pregnant. Clomid is indicated only in patients with ovarian dysfunction. Commonly associated diagnoses include polycystic ovary syndrome, lactation amenorrhoea syndrome, psychogenic amenorrhoea, and certain cases of secondary amenorrhoea of undetermined aetiology. An additional diagnosis is post-oral contraceptive amenorrhoea.

Dosage and administration The recommended dose for the first course of Clomid is 50 mg (1 tablet) daily for five days. When ovulation occurs at this dosage there is no advantage in increasing the dose in subsequent cycles of treatment. If ovulation occurs at this dosage but is not followed by pregnancy, subsequent courses for a total maximum of 6 cycles of Clomid treatment may be administered.

If ovulation appears not to have occurred after the first course of therapy, a second course of 100 mg daily (two 50 mg tablets given as a single daily dose) for five days should be given. If ovulatory menses do not occur, this dose may be repeated for two additional cycles, but failure to induce ovulation after 3 consecutive cycles at this dosage should constitute an adequate therapeutic trial. If, however, ovulation does occur at this dosage but is not followed by pregnancy, subsequent courses for a total maximum of 6 cycles of Clomid treatment may be administered. The importance of properly timed coitus cannot be overemphasised.

Therapy may be started at any time in a patient who has had no recent uterine bleeding; but if progestin-induced bleeding is planned, or if spontaneous uterine bleeding occurs prior to therapy, the course of Clomid should be started on or about the fifth day of the cycle.

Contra-indications *Pregnancy:* Although there is no evidence that Clomid has a harmful effect on the human foetus, Clomid does damage rat and rabbit foetuses when given in high doses to the pregnant animal. Therefore, Clomid should not be administered during pregnancy. To avoid inadvertent Clomid administration during early pregnancy, the basal body temperature should be recorded throughout all treatment cycles, and the patient should be carefully observed to determine whether ovulation occurs. If the basal temperature following Clomid is biphasic and is not followed by menses, the patient should be examined carefully and should have a pregnancy test.

Liver disease: Clomid should not be given to patients with known liver disease or a history of liver dysfunction.

Abnormal uterine bleeding: Clomid should not be given until the cause of the bleeding has been determined. It is most important to ensure that neoplastic lesions are not overlooked.

Precautions *Visual symptoms:* Patients should be advised that blurring or other visual symptoms may occasionally occur during Clomid therapy. The significance of these symptoms is not yet understood. If they do occur, Clomid should be discontinued; and a complete ophthalmological evaluation should be made. No further courses of Clomid should be administered.

Diagnosis prior to Clomid therapy: Careful evaluation and selection of patients, and close attention to dosage instructions, contra-indications and side-effects, are mandatory. Since Clomid is indicated only in patients with ovarian dysfunction, other possible causes of infertility should be excluded or treated before giving Clomid.

Pelvic examination should be made before each course of Clomid is given.

Overstimulation of the ovary during Clomid therapy: Since Clomid stimulates the ovaries, it may cause abnormal ovarian enlargement due to overstimulation in some patients. With the exception of patients with polycystic ovary syndrome, Clomid should not be given in the presence of an ovarian cyst, since further enlargement of the ovary may occur. Patients known to have polycystic ovaries should be given the smallest dose possible of Clomid with expectation of favourable results. It should be borne in mind that maximal ovarian enlargement may not occur until several days after the treatment cycle is completed. Patients who complain of pelvic pain after receiving Clomid should be examined with care. If enlargement of the ovary occurs, additional courses of Clomid should not be given until the ovaries have returned to pre-treatment size, and then a shorter course or smaller dose should be administered. Ovarian enlargement and cyst formation that are occasionally associated with Clomid therapy regress spontaneously within a few days or weeks after discontinuing treatment. Unless surgical indication for laparotomy exists, such cystic enlargement should be managed conservatively.

Multiple pregnancy: The incidence of multiple pregnancy is increased when conception takes place during a cycle in which Clomid is given. In a large series of closely monitored patients who became pregnant after receiving Clomid, there were 6.9% (165) twins, 0.5% (11) triplets, 0.3% (7) quadruplets and 0.13% (3) quintuplets. Of these multiple pregnancies, 357 live infants were born of 165 multiple births. After excluding 60 neonatal deaths, 297 survived, including 27 of 61 live infants from triplet, quadruplet and quintuplet pregnancies. In addition, one sextuplet pregnancy has been reported in a patient treated with Clomid. Patients (and their husbands)

should be advised of the possibility and potential complications of multiple pregnancy associated with Clomid therapy.

Side-effects Side-effects are not prominent and infrequently interfere with treatment when the recommended dosage of Clomid is given.

Side-effects are dose-related, being more frequent and more severe when higher doses of Clomid are administered.

The more common side-effects are hot flushes, abdominal discomfort (distension, bloating, pain or soreness), ovarian enlargement and visual blurring. The vasomotor symptoms resembling menopausal hot flushes are not usually severe and disappear soon after treatment is discontinued. Abdominal symptoms are most often related to ovulatory (*mittelschmerz*) or premenstrual phenomena, or to ovarian enlargement. At recommended dosage the normal variation in ovarian size may be exaggerated. Rare instances of massive ovarian enlargement and rupture of a lutein cyst with haemoperitoneum have been reported.

Visual symptoms, described usually as 'blurring' or spots or flashes (scintillating scotomata), increased in incidence with increasing total dose and disappeared within a few days or weeks after Clomid was discontinued. These symptoms appear to be due to intensification and prolongation of after-images. Symptoms often first appear or are accentuated with exposure to a more brightly lit environment. While measured visual acuity has not generally been affected, one patient taking 200 mg daily developed visual blurring on the seventh day of treatment, which progressed to severe diminution of visual acuity by the tenth day. No other abnormality was found and the visual acuity returned to normal on the third day after treatment was stopped. One patient treated during clinical studies developed scotomata during prolonged Clomid administration, which disappeared by the 32nd day after stopping therapy.

The following conditions have been reported in association with Clomid therapy: relationship of cause and effect has neither been proved nor disproved; Ophthalmologically definable scotomata and retinal cell function (electroretinographic) changes have also been reported.

Posterior capsular cataract (4, all in investigational studies), detachment of the posterior vitreous (1), spasm of retinal arteriole (1), in original 2,369 investigational pregnancies.

Other less frequently reported symptoms included nausea or vomiting, increased nervous tension, depression, fatigue, dizziness or lightheadedness, insomnia, headache, breast soreness, heavier menses, intermenstrual spotting, weight gain, urticaria and allergic dermatitis, increased urinary frequency and moderate reversible hair loss.

Defects at birth have been reported in 58 infants from 2,369 delivered pregnancies in mothers treated with Clomid. Four of the infants were in the abortion/stillbirth category, 14 were from multiple pregnancies, and the remaining were single births. The defects have included Down's syndrome (5 infants), congenital heart lesions (8 infants), microcephaly (2 infants), harelip and cleft palate (2 infants), hypospadias (3 infants), undescended testes (2 infants), club foot (4 infants), gastro-intestinal malformations (4 infants), congenital hip (2 infants) and polydactyly (both of twins).

Eight of the total of 58 infants were born to 7 of 158

mothers who received (inadvertently) a course of Clomid during the first six weeks after conception.

Clomid, when given continuously for prolonged periods, may interfere with cholesterol synthesis. Serum from patients treated in this way appears to have elevated desmosterol levels. In patients taking recommended doses of Clomid serum sterol patterns are not significantly altered.

Bromsulphthalein (BSP) retention of greater than 5% has been reported in 32 of 141 patients in whom it was measured. Other liver function tests were usually normal. Retention was usually minimal unless associated with prolonged continuous Clomid administration or with apparently unrelated liver disease. In some patients, pre-existing BSP retention decreased even though Clomid therapy was discontinued. One patient developed jaundice on the 14th day of Clomid treatment; liver biopsy revealed bile stasis without evidence of hepatitis. Clomid has not been reported to cause significant abnormality in the haematopoietic or renal systems, the protein-bound iodine or in serum cholesterol.

Overdosage There is no experience of overdosage with Clomid.

Pharmaceutical precautions Clomid tablets should be protected from light, moisture and excessive heat.

Legal category POM.

Package quantities Clomid is obtainable in packs of 30 and 100 tablets in blister packs.

Further information Clomid is prescribable under the supervision of an appropriate specialist.

Pharmacological classification: Clomid is a triarylethylene compound (related to chlorotrianisene and triparanol). It is a non-steroidal agent taken by mouth which stimulates ovulation in a high percentage of appropriately selected anovulatory women.

Actions: The ovulatory response to cyclic Clomid therapy appears to be mediated through increased output of pituitary gonadotrophins, which in turn stimulates the maturation and endocrine activity of the ovarian follicle and the subsequent development and function of the corpus luteum. The role of the pituitary is indicated by increased urinary excretion of gonadotrophins and the response of the ovary is manifested by increased urinary oestrogen excretion.

Product licence number 4425/5900.

DEBENDOX*

Presentation White, round, biconvex tablet containing:

Decapryn (doxylamine succinate USNF 1975)	10 mg
Pyridoxine Hydrochloride BP	10 mg

in a special timed-release coating designed to release active ingredients four to six hours after ingestion.

Uses Debendox is indicated for nausea and vomiting of pregnancy which are unresponsive to conservative measures and are sufficiently distressing to require drug intervention.

Dosage and administration Two tablets at bedtime. In severe cases or when nausea occurs during the day, 1 additional tablet on arising and another in mid-afternoon.

Contra-indications, warnings, etc *Contra-indications:* Known idiosyncrasy to any of the ingredients.

Precautions: Because of potential drowsiness, patients should be warned not to engage in activities requiring mental alertness such as operating motor vehicles or other machinery, or perform hazardous work, while taking Debendox.

There have been a large number of epidemiological studies of Debendox. Although there have been some reports of congenital malformations associated with its administration in early pregnancy, a causal relationship has not been established.

For no medicinal product can a small risk of teratogenic effect be excluded with absolute certainty and so the use of any drug during early pregnancy should be avoided if at all possible.

Side-effects: Doxylamine succinate may cause drowsiness; vertigo; nervousness; epigastric pain; headache; palpitation; diarrhoea; disorientation; or irritability. Pyridoxine hydrochloride is a vitamin that is generally recognised as having no adverse effects.

Overdosage: The tablets are designed to release their active ingredients four to six hours after ingestion. On one occasion intense purging produced recognisable tablets per rectum. Gastric lavage, emetics, and Universal Antidote (activated charcoal 2 parts, tannic acid 1 part, magnesium oxide 1 part) are recommended.

Because of the delayed release characteristics of Debendox, symptoms of overdosage may not become evident for some hours after ingestion of the tablets. It is recommended that patients who have or may have taken an overdose be admitted without delay to hospital for treatment or observation.

Pharmaceutical precautions Debendox Tablets should be stored in a cool dry place.

Legal category POM.

Package quantities Blister strips of 25 in packs of 50.

Further information Nil.

Product licence number 4425/5901.

DESTOLIT* ▼

Presentation Plain white tablet containing 150 mg ursodeoxycholic acid.

Uses Destolit is indicated for the dissolution of radiolucent (i.e. non-radio opaque) cholesterol gallstones in patients with a functioning gallbladder.

Dosage and administration The daily dose for most patients is 3 or 4 tablets of 150 mg according to body weight. This dose should be divided into 2 administrations after meals, with one administration always to be taken after the evening meal.

A daily dose of about 8 to 10 mg/kg will produce cholesterol desaturation of bile in the majority of cases. The measurement of the lithogenic index on bile-rich duodenal drainage fluid after 4-6 weeks of therapy may be useful for determining the minimal effective dose. The lowest effective dose has been found to be 4 mg/kg.

The duration of treatment required to achieve gallstone dissolution will usually not be extended beyond 2 years and should be monitored by regular cholecystograms. Treatment should be continued for 3-4 months after the radiological disappearance of the gallstones.

Any temporary discontinuation of treatment, if prolonged for 3-4 weeks, will allow the bile to return to a state of supersaturation and will extend the total time required for litholysis. In some cases stones may recur after successful treatment.

Contra-indications, warnings, etc In common with all drugs, it is advised that ursodeoxycholic acid should not be given during the first trimester of pregnancy. (In the rabbit, embryotoxicity has been observed, but this has not been seen in the rat.) Treatment in women of child-bearing age should only be undertaken if measures to prevent pregnancy are used. Non-hormonal contraceptive measures are recommended. In cases of conception during treatment, therapy should be discontinued. Active gastric or duodenal ulcers are contra-indications, as are hepatic and intestinal conditions interfering with the enterohepatic circulation of bile acids (ileal resection and stoma, regional ileitis, extra and intra-hepatic cholestasis, severe, acute, and chronic liver diseases). A product of this class has been found to be carcinogenic in animals. The relevance of these findings to the clinical use of ursodeoxycholic acid has not been established.

Excessive dietary intake of calories and cholesterol should be avoided; a low cholesterol diet will probably improve the effectiveness of Destolit tablets. It is also recommended that drugs known to increase cholesterol elimination in bile, such as oestrogenic hormones, oral contraceptive agents and certain blood cholesterol lowering agents should also not be prescribed concomitantly.

Side-effects: Destolit is normally well tolerated. Diarrhoea has been found to occur only occasionally. No significant alterations have so far been observed in liver function.

Overdosage: It is unlikely that overdosage will cause serious adverse effects. Diarrhoea may occur and it is recommended that liver function tests be monitored. Ion-exchange resins may be useful to bind bile acids in the intestines.

Pharmaceutical precautions Destolit tablets have a shelf life of 3 years under normal room temperature storage conditions.

Legal category POM.

Package quantities Blister packs of 60 tablets.

Further information Nil.

Product licence number 4425/0045.

KOLANTICON* GEL

Presentation Kolanticon Gel is a white, viscous, peppermint-flavoured suspension, each 5 ml containing:

Merbentyl* (Dicyclamine Hydrochloride BP)	2.5 mg
Dried Aluminium Hydroxide Gel BP	200 mg
Light Magnesium Oxide BP	100 mg
Dimethylsiloxane BPC	20 mg

Uses Kolanticon is an antacid-antiflatulent-anti-spasmodic-demulcent indicated for the treatment and prophylaxis of symptoms of peptic ulcer and functional dyspepsia especially in patients in whom gastric distress results from hyperacidity, smooth muscle spasm and flatulence. Also indicated for symptomatic relief in oesophagitis, hiatus hernia, gastritis and iatrogenic gastritis.

Dosage and administration Two to four 5 ml spoonfuls every four hours as required.

Contra-indications Known idiosyncrasy to any of the ingredients.

Precautions Magnesium salts, in the presence of renal insufficiency, may cause central nervous system depression. Aluminium hydroxide, in the presence of low phosphorus diets, may cause phosphorus deficiency. Aluminium hydroxide may reduce absorption of tetracyclines when given concomitantly. Products containing dicyclomine hydrochloride should be used with caution in any patient with or suspected of having, glaucoma. Use with care in patients with hiatus hernia associated with reflux oesophagitis because anticholinergic drugs may aggravate this condition.

Side-effects In particularly sensitive patients dicyclomine hydrochloride may cause atropine-like side-effects such as dry mouth, blurred vision, urinary retention or constipation.

Overdosage Signs and symptoms of dicyclomine hydrochloride overdose include: headache, nausea and vomiting, blurred vision, dilated pupils, hot dry skin, dizziness, vertigo, dryness of mouth, difficulty in swallowing, and CNS stimulation.

Treatment should include: Universal Antidote (activated charcoal 2 parts, tannic acid 1 part, magnesium oxide 1 part), emetics, gastric lavage, barbiturates for sedation, pilocarpine 0.01 g subcutaneously every half-hour until the mouth becomes moist.

Pharmaceutical precautions *Kolanticon Gel*: Store in a cool place. Shake well before use.

Legal category P.

Package quantities *Kolanticon Gel*: Amber glass bottles of 125 ml and 500 ml.

Further information Nil.

Product licence number 4425/0032.

KOLANTYL* GEL AND TABLETS

Presentation *Kolantyl Gel* is a white, viscous, peppermint-flavoured suspension, each 5 ml containing:

Merbentyl* (Dicyclomine Hydrochloride BP)	2.5 mg
Dried Aluminium Hydroxide Gel BP	200 mg
Light Magnesium Oxide BP	100 mg

Kolantyl Tablets are white, round tablets, marked 'K' inside two concentric circles. Each tablet contains:

Merbentyl (Dicyclomine Hydrochloride BP)	5 mg
Magnesium Trisilicate BP	90 mg
Dried Aluminium Hydroxide Gel BP	240 mg
Magnesium Hydroxide BPC	144 mg

Uses Antacid and antispasmodic for the treatment of symptoms of peptic ulcer and for prophylaxis in the ulcer-prone patient: for the relief of symptoms of gastric hyperacidity with or without pylorospasm in conditions such as: oesophagitis, hiatus hernia, and acute, iatrogenic and chronic gastritis.

Dosage and administration *Kolantyl Gel*: Two to four 5 ml spoonfuls every four hours as required.

Kolantyl Tablets: 1-2 chewed or allowed to dissolve in the mouth every four hours as required.

Contra-indications Known idiosyncrasy to any of the ingredients.

Precautions Magnesium salts, in the presence of renal insufficiency, may cause central nervous system depression. Aluminium hydroxide, in the presence of low phosphorus diets, may cause phosphorus deficiency. Aluminium hydroxide may reduce absorption of tetracyclines when given concomitantly. Products containing dicyclomine hydrochloride should be used with caution in any patient with, or suspected of having glaucoma. Use with care in patients with hiatus hernia associated with reflux oesophagitis because anticholinergic drugs may aggravate this condition.

Side-effects Side-effects are uncommon. When they occur, they are usually related to the dicyclomine hydrochloride in the formula, which, in a few susceptible individuals, may cause atropine-like side-effects. Such side-effects rarely necessitate a discontinuance of the drug.

Overdosage Universal Antidote (activated charcoal 2 parts, tannic acid 1 part, magnesium oxide 1 part), emetics, gastric lavage. Barbiturates and pilocarpine may be helpful when indicated.

Pharmaceutical precautions *Kolantyl Gel*: Store in a cool place. Shake well before use.

Kolantyl Tablets: None.

Legal category P.

Package quantities *Kolantyl Gel*: Bottles of 500 ml.

Kolantyl Tablets: Blister packs of 50.

Further information Nil.

Product licence numbers

<i>Kolantyl Gel</i>	0027/5002
<i>Kolantyl Tablets</i>	4425/0033

LURSELLE* ▼

Presentation Lurselle is presented as plain white, non-coated tablets imprinted on one face with the name 'Lurselle,' each tablet containing 250 mg probucol [4-4' (iso-propyldenedithio) bis (2,6-di-t-butylphenol)].

Uses Lurselle is indicated as ancillary therapy to diet for the reduction of elevated serum cholesterol in patients with hypercholesterolaemia, or in patients with combined hypercholesterolaemia and hypertriglyceridaemia where levels of cholesterol are a cause of concern.

Dosage and administration The recommended dose for adults is two tablets of 250 mg twice a day with the morning and evening meals.

Paediatric dosage has not yet been established.

Contra-indications, warnings, etc Reproduction studies in animals have not demonstrated any impairment of fertility or any harm to the foetus or offspring due to Lurselle. As yet there are no adequate studies in pregnant women, and the use of Lurselle during pregnancy is therefore not recommended. If a patient wishes to become pregnant, it is recommended that the drug be withdrawn and birth control procedures should be continued for at least six months due to the persistence of the drug in the fatty tissues of the body.

In animals it has been shown that some of the drug is excreted in the milk. It is recommended that nursing mothers should not be treated with Lurselle.

Before instituting therapy with Lurselle an attempt should be made to control elevated serum cholesterol by appropriate dietary regimens, weight reduction, and the treatment of any underlying disorder which might be the cause of the hypercholesterolaemia. Serum cholesterol and triglyceride levels should be monitored during the first months of treatment with Lurselle and periodically thereafter.

A favourable trend in cholesterol reduction should be evident during the first two months of Lurselle administration. An assessment should be made by the sixth month whether adequate reduction is being attained. A discontinuation in Lurselle treatment is usually followed by a gradual return of cholesterol to pre-treatment values.

If a marked sustained rise in serum triglycerides occurs during Lurselle therapy, consideration should be given to improving dietary compliance; alcohol abstinence; further restriction of calories, or adjustment of carbohydrate intake. If hypertriglyceridaemia persists, Lurselle should be discontinued.

Overdosage: In cases of overdosage symptomatic treatment and supportive measures should be instituted according to the individual symptoms.

Side-effects: The side effects associated with Lurselle are generally mild to moderate and of short duration. They include diarrhoea, which occurs in about one in 10 patients, flatulence, abdominal pain, nausea and vomiting. These reactions are usually transient and seldom require the drug to be discontinued.

During the clinical studies in which patients have been treated for as long as 9 years, Lurselle had to be discontinued in less than 3 percent of the patients because of adverse gastrointestinal reactions.

Angio-neurotic oedema has been observed very occasionally and a single hypersensitivity reaction with dizziness, palpitation and syncope has been reported.

Concomitant Therapy

The dosage of hypoglycaemic agents and oral anticoagulants need not usually be modified when given with Lurselle and these drugs do not alter the effect of Lurselle on serum cholesterol.

Administration of Lurselle with a second lipid lowering drug has been shown to produce further significant reductions in serum cholesterol. The most effective combinations were Lurselle with either ion exchange resins or nicotinic acid.

Pharmaceutical precautions Lurselle tablets should be stored in a well closed container, protected from light, heat and moisture.

Legal category POM.

Package quantities 120 tablets.

Further information Absorption of Lurselle from the gastrointestinal tract is limited; food intake improves absorption and consequently induces higher and less variable peak blood levels. Lurselle is eliminated slowly from the body; the major pathway of excretion is the biliary tract.

Studies in man on the mode of action of Lurselle are still underway but they have shown that Lurselle lowers serum cholesterol by increasing the excretion of bile acids and by inhibiting an early stage of cholesterol biosynthesis. In addition there may be a slight decrease in absorption of dietary cholesterol.

Studies with Lurselle have shown no evidence of biliary tract pathology or related gallstone formation.

Product licence number 4425/0043.

MERALEN*

Presentation Hard gelatin capsule with light blue body and dark blue cap. Both halves printed Merrell. Each 100 mg capsule contains Flufenamic Acid BP 100 mg.

Uses Meralen is an anti-inflammatory analgesic for the relief of pain in rheumatoid arthritis, osteoarthritis and ankylosing spondylitis.

Dosage and administration *Adults:* 600 mg daily, in divided doses, preferably with food. After four weeks continuous therapy, reduced maintenance dosage of 400 mg daily may be satisfactory in some patients. For those weighing less than 45 kg (100lb) dosage should not exceed 10 mg per kg body weight daily.

Children: Meralen should not be given to children of 14 years or less.

Contra-indications, warnings, etc Contra-indicated in pregnancy; in inflammatory bowel disease and in patients suffering from gastric and/or intestinal ulceration; and in renal or hepatic disease.

Precautions: Concurrent therapy with other plasma protein binding drugs, e.g. anticoagulants, may necessitate a modification in dosage.

Side-effects: Discontinue administration of Meralen if diarrhoea or abnormalities in liver function tests occur.

The commonest side-effect is gastro-intestinal upset, characterised by nausea, vomiting, or epigastric discomfort. If gastro-intestinal intolerance occurs and the physician attributes this to the drug, the dose of Meralen may be reduced by one half. If signs and symptoms do not subside, the drug may need to be completely discontinued. The physician may be able to increase the daily dosage of Meralen again, once these symptoms have subsided. In some patients the gastro-intestinal symptoms subside spontaneously without reduction of dosage of Meralen.

Meralen should be discontinued in the event of rash suspected to be a sensitivity reaction.

One case of purpura and four of leucopenia have been reported; one of the latter had been diagnosed as spontaneous leucopenia before Meralen therapy had commenced.

Bronchospasm may be precipitated in patients suffering from, or with a previous history of, bronchial asthma or allergic disease.

Overdosage: Gastric lavage in the conscious patient and intensive supportive therapy where necessary; activated charcoal has been shown to be a powerful absorbent for Meralen and its metabolites. Studies in experimental animals showed that a 5 to 1 ratio of charcoal resulted in considerable suppression of absorption of the drug.

Pharmaceutical precautions No special storage precautions.

Legal category POM.

Package quantities 100 mg capsules available in a pack of 100 capsules.

Further information Nil.

Product licence number 4425/0016R.

MERBENTYL* TABLETS AND SYRUP

Presentation Merbentyl Tablets are white, round, plain bi-convex tablets, stamped 'M' in two concentric circles, containing Dicyclomine Hydrochloride BP 10 mg.

Merbentyl Syrup is light red, bitter and raspberry flavoured. Each 5 ml contains 10 mg Dicyclomine Hydrochloride BP.

Uses Merbentyl is a smooth muscle antispasmodic primarily indicated for the treatment of *functional* conditions involving *smooth muscle spasm* of the gastrointestinal tract. The commonest of these are: irritable colon (mucous colitis, spastic colon), spastic constipation, infant colic.

Merbentyl can also be used as *adjunctive medication* in a number of organic gastro-intestinal conditions to relieve associated smooth muscle spasm, e.g. colitis, diverticulosis and diverticulitis, regional enteritis, gastritis, peptic ulcer, ulcerative colitis, cholelithiasis and cholecystitis (but not biliary colic).

Dosage and administration *Adults:* 1–2 tablets or one to two 5 ml spoonfuls (10–20 mg) three times daily before or after meals.

Children (2–12 years): 1–2 tablets or one to two 5 ml spoonfuls (10–20 mg) according to age, three times daily.

Children (6 months–2 years): 5–10 mg three or four times daily, 15 minutes before feeds. Do not exceed a daily dose of 40 mg. If it is necessary to dilute Merbentyl Syrup this may be done using Syrup BP or if diluted immediately prior to use with water.

Infants (up to 6 months): 5 mg three or four times daily, 15 minutes before feeds. Do not exceed daily dose of 20 mg. If it is necessary to dilute Merbentyl Syrup this may be done using Syrup BP or if diluted immediately prior to use with water.

Contra-indications Known idiosyncrasy to Dicyclomine Hydrochloride BP.

Precautions Products containing dicyclomine hydrochloride should be used with caution in any patient with, or suspected of having, glaucoma or prostatic hypertrophy. Use with care in patients with hiatal hernia associated with reflux oesophagitis because anticholinergic drugs may aggravate the condition.

There are rare reports of infants, 6 weeks of age and under, administered dicyclomine hydrochloride syrup, who have evidenced respiratory symptoms (breathing difficulty, shortness of breath, breathlessness, respiratory collapse, apnoea), as well as seizures, syncope, asphyxia, pulse rate fluctuations, muscular hypotonia and coma. The above symptoms have occurred within minutes of ingestion and lasted 20–30 minutes. The timing and nature of the reactions suggest that they were a consequence of local irritation and/or aspiration, rather than to a direct pharmacological effect. No known deaths or permanent adverse effects have been reported. Merbentyl Syrup should be used with caution in this age group.

Side-effects Side-effects seldom occur with Merbentyl. However, in susceptible individuals, dry mouth, thirst

and dizziness may occur. On rare occasions, fatigue, sedation, blurred vision, rash, constipation, anorexia, nausea and vomiting, headache, and dysuria have also been reported.

Overdosage Symptoms of Merbentyl overdosage are headache, dizziness, nausea, dry mouth, difficulty in swallowing, dilated pupils and hot dry skin. Treatment may include Universal Antidote (activated charcoal 2 parts, tannic acid 1 part, magnesium oxide 1 part), emetics, gastric lavage, pilocarpine 0.01 g subcutaneously every half-hour until mouth becomes moist. Barbiturates for sedation.

Pharmaceutical precautions *Merbentyl Tablets:* None.

Merbentyl syrup: Should be stored and dispensed in amber glass bottles.

Legal category POM.

Package quantities *Merbentyl Tablets:* Packs of 50 and 250 tablets.

Merbentyl Syrup: Amber glass bottles of 125 ml and 500 ml.

Further information Nil.

Product licence numbers

Merbentyl Tablets 0027/5007

Merbentyl Syrup 0027/5008

MEROCAINE*

Presentation Merocaine lozenges are green, round, slightly domed lozenges with 'M' indented on both sides. Each lemon/lime flavoured lozenge contains:

Cetylpyridinium Chloride BP 1.4 mg (1:1500)
Benzocaine Ph Eur 10 mg

Uses Merocaine lozenges provide rapid and profound local anaesthetic action and topical antibacterial effects for the temporary relief of pain and discomfort in sore throat and superficial mouth infections. Indicated for relief of minor throat irritations and, adjunctively, for symptomatic relief of pain and discomfort in more serious throat infections, such as tonsillitis and pharyngitis, and following dental procedures involving oral mucosa and gingival surfaces.

Dosage and administration Allow to dissolve slowly in the mouth. One lozenge every 2 hours as needed but not more than 8 lozenges in 24 hours. Not indicated for children under 12 years of age.

Contra-indications, warnings, etc

Contra-indications: Idiosyncrasy to any of the ingredients.

Side-effects: Allergic reactions and methaemoglobinemia have been reported with Benzocaine.

Overdosage: There is no experience of overdosage but normal procedures of gastric lavage and maintenance of respiration and circulation (using vasopressor drugs if necessary) should apply.

Pharmaceutical precautions None.

Legal category P.

Package quantities 3 strips of 8 lozenges per carton.

Further information Nil.

Product licence number 4425/0028.

MEROCKET* SOLUTION

Presentation Merocet Solution is a pale yellow, cinnamon-peppermint flavoured solution containing 1 : 2,000 Cetylpyridinium Chloride BP, Ethanol (96%) BP 14%, phosphate buffers and aromatics.

Uses Cetylpyridinium Chloride BP is a surface-active quaternary compound with bactericidal and anti-fungal properties. Merocet Solution is indicated for the symptomatic treatment of sore throat. It is also indicated for minor irritations of the mouth and throat and for use prophylactically in dentistry and after dental operations. Merocet Solution can also be used for daily oral hygiene.

Dosage and administration *Adults and children over six years:* The solution may be used full strength or diluted with an equal volume of water – warm if desired – every three hours, or as often as required.

Contra-indications, warnings, etc Known idiosyncrasy to cetylpyridinium chloride.

Precautions: None.

Side-effects: Infrequent and transient complaints of a burning sensation of the mouth.

Overdosage: There is no experience of overdosage.

Pharmaceutical precautions Avoid storage at low temperatures.

Legal category GSL.

Package quantities White flint-glass bottles of 200 ml.

Further information Nil.

Product licence number 4425/0017.

NETHAPRIN DOSPAN*

Presentation Nethaprin Dospan Tablets are white, round, flat, bevelled tablets, scored on one side and engraved 'N' on the other. Each tablet contains:

Nethamine* (etafedrine hydrochloride)	50 mg
Butaphyllamine* (bufylline)	180 mg
Decapryn* (doxylamine succinate USNF)	25 mg
Phenylephrine Hydrochloride BP	25 mg

Uses Nethaprin Dospan is a bronchodilator, anti-histamine, mild sedative, decongestant indicated for bronchospasm (wheezing) associated with chronic bronchitis, bronchial asthma or emphysema. Also useful in allergic cough.

Dosage and administration *Adults and children over 12 years:* For relief of mild to moderate attacks and for 12-hour protection: one tablet every 12 hours as required.

Children 6–12 years: $\frac{1}{2}$ tablet every 12 hours as required. Not recommended for children under 6 years.

Contra-indications Do not administer concurrently with monoamine oxidase inhibitors. Hypersensitivity.

Precautions This preparation may cause drowsiness; patients should be advised not to drive or operate machinery if affected.

It is dangerous to exceed the stated dose.

Side-effects While significant sympathomimetic side-effects have not been reported, an occasional sensitive patient may experience side-effects characteristic of this

class of medicine. Nausea or other gastro-intestinal upsets have been reported occasionally.

Overdosage Nethaprin Dospan is a sustained release formulation and releases active ingredients over 10–12 hours. Signs and symptoms of overdosage include salivation, diuresis, dryness of the mouth, excitement, hypertension, dilated pupils, convulsions, insomnia and tachycardia. Treatment may include emetics, gastric lavage, barbiturates, and the patient should be kept cool and quiet.

Pharmaceutical precautions Store in a cool dry place.

Legal category POM.

Package quantities Amber glass bottles of 50.

Further information Nil.

Product licence number 0027/5013.

NETHAPRIN* EXPECTORANT

Presentation Nethaprin Expectorant is an orange-red syrup, with a bitter-ginger flavour, each 5 ml containing:

Nethamine* (etafedrine hydrochloride)	20 mg
Butaphyllamine* (bufylline)	60 mg
Decapryn* (doxylamine succinate USNF)	6 mg
Glyceryl guaiacolate (USNF 1970)	100 mg

Uses Nethaprin Expectorant is a bronchodilator, anti-histamine, mild sedative, expectorant mixture indicated for the treatment of unproductive cough or excessive mucus production associated with bronchospasm (wheezing).

Dosage and administration *Adults and children over 12 years:* One to two 5 ml spoonfuls every three to four hours.

Children 6–12 years: One 5 ml spoonful every three to four hours.

Not recommended for children under 6 years.

Contra-indications Do not administer concurrently with monoamine oxidase inhibitors. Hypersensitivity.

Precautions This product may cause drowsiness; patients should be advised not to drive or operate machinery if affected.

It is dangerous to exceed the stated dose.

Side-effects While significant sympathomimetic side-effects have not been reported, an occasional sensitive patient may experience symptoms characteristic of this class of medicine. Nausea and other gastro-intestinal upsets have been reported occasionally.

Overdosage Signs and symptoms of overdosage include salivation, diuresis, dryness of the mouth, excitement, hypertension, dilated pupils, convulsions, insomnia and tachycardia. Treatment may include emetics gastric lavage, and barbiturates. The patient should be kept cool and quiet.

Pharmaceutical precautions Avoid extremes of temperature.

Legal category POM.

Package quantities Amber glass bottles of 125 ml and 500 ml.

Further information Nil.

Product licence number 0027/5014.

PEXID*

Presentation White, round, flat-faced, bevelled edge tablets. There is a concentric circle 'M' design and on the other side a scored bisect line. Each tablet contains 100 mg of perhexiline maleate.

Uses Pexid is indicated to reduce the frequency of moderate to severe attacks of angina pectoris in patients with coronary artery disease. It is not intended for the treatment of the acute attack. Pexid may be valuable even in patients who do not respond adequately to therapy with other anti-anginal drugs. Sublingual nitroglycerin should be used concomitantly as necessary, for the acute anginal episode if it occurs.

Pexid is also indicated for the management of ventricular extra-systoles in patients with coronary artery disease. It has been proven effective in the elimination or reduction of the extra-systoles, and in the prevention of their recurrence. Until its safety and efficacy have been demonstrated in the acute phase following a myocardial infarction, Pexid should not be used to treat arrhythmias which occur during this period.

Dosage and administration The usual dosage at the beginning of treatment is 100–200 mg per day which may be given in two divided doses. This dosage is to be adjusted progressively up or down at 2 or 4 week intervals based on the results obtained.

It is generally advised not to administer more than 300 mg a day but in certain patients it has been necessary to use 400 mg daily.

The maintenance dose must be the minimum dose which is effective and well-tolerated.

Contra-indications Pexid is contra-indicated in patients with impaired hepatic or renal function and in patients with a known hypersensitivity to the drug.

Precautions During the administration of Pexid, patients must be regularly examined, especially for the appearance of the signs or symptoms described below.

The following clinical and laboratory observations are particularly recommended before and during treatment:

1. Tests for signs and symptoms of peripheral neuropathy, such as paresthesiae, muscle weakness, etc. If the patient complains of visual disturbances, during treatment with Pexid, a complete ophthalmological investigation must be undertaken.
2. Observation for clinical signs of hepatic involvement (weakness, loss of appetite, loss of weight).
3. Determination of serum enzymes (SGPT, SGOT, alkaline phosphatase, LDH) and bilirubin.
4. Determination of blood glucose.
5. Determination of weight.
6. Fundoscopy and tests of visual acuity.

If such medical monitoring proves impractical, Pexid should not be prescribed. Treatment with Pexid should be discontinued in the following instances:

1. Appearance of peripheral neuropathy papilloedema, retinal haemorrhage, or impairment of vision.
2. Appearance of clinical signs of hepatic disease.
3. Persistent elevations in serum enzymes or abnormalities of specific liver function tests.

4. Persistent or marked hypoglycaemia.
5. Excessive weight loss.
6. Other serious side-effects.

Although animal reproductive studies have not indicated adverse effects, Pexid, like most medications, should not be used during the first trimester of pregnancy or during lactation unless, in the opinion of the physician, the potential benefits outweigh the potential risks.

The use of Pexid during the acute phase of myocardial infarction (the period during which clinical and laboratory findings are not stable) has not been established.

Because reported side-effects such as dizziness, lightheadedness and gait disorders may be related to Pexid administration and could be accompanied by syncope or falling, patients with such symptoms should be cautioned about activities such as driving or operating machinery. These symptoms disappear with the cessation of treatment. In many cases, a decrease of the daily dose may cause the side-effects to lessen or disappear.

Pexid should be administered with caution to patients with diabetes.

The effects of Pexid on premature ventricular contractions are consistent with its action on the intraventricular conduction system. Its effects on the same system may also have the potential of producing or aggravating ventricular conduction disturbances.

Pexid has been prescribed with the following medications: nitroglycerin, anticoagulants, digitalis, diuretics, hypolipemics, antihypertensives, tranquilisers and other products.

The safety of concomitant administration with the above products has not yet been established, with the exception of nitroglycerin used in controlled clinical experiments.

In view of the fact that hypoglycaemia has been reported in association with the administration of Pexid, special attention must be paid in the case of concomitant administration of products which could provoke hypoglycaemia, such as antidiabetics and beta-blockers.

In cases where Pexid is discontinued, and another therapy substituted, account must be taken of the half-life of the compound.

Pexid administered orally is rapidly absorbed. It is principally metabolised through hepatic hydroxylation, but the liver has a limited capacity for biotransformation. The metabolites, partially in conjugated form, are eliminated in the urine and faeces. The elimination half-life is in general, two to six days, but may surpass 30 days in certain cases.

Side-effects Adverse reactions may occur in the initial weeks of treatment or the onset may be delayed. Side-effects may be transient and may disappear spontaneously in two to four weeks. More often, they recede only after the dosage is reduced, but sometimes treatment must be discontinued. In general, the appearance and severity of adverse reactions seem to be dose-dependent.

Reported most often are dizziness or a 'drunken' sensation, gait disorders, unsteadiness, as well as nausea, vomiting, headache, anorexia and moderate weight loss (2 to 4 kg).

Frequently reported are moderate and generally transient elevations of serum enzymes (SGOT, SGPT, alkaline phosphatase, LDH) and bilirubin. Increases in total lipids and triglycerides, moderate hypoglycaemia and alterations of the ECG (slight depression of the T-wave and prolongation of the Q-T interval) have also been noted.

Less frequently reported are: profound weakness,

nervousness, lassitude, insomnia, tremors, paraesthesiae, syncope, impaired hearing, genitourinary disorders, changes in libido, flushing or sweating, rash or urticaria.

Rarely reported and not necessarily drug related are: diplopia, visual disturbances, transient loss of vision, papilloedema in the absence of peripheral neuropathy, abdominal pain, extra-pyramidal syndromes, epileptiform seizures, pulmonary alveolitis, autonomic neuropathy, proximal myopathy and jaundice. Delayed nerve conduction velocities have been reported in patients with and without clinical evidence of neuropathy.

Occasionally, more serious side-effects have been reported in patients being treated with Pexid:

Sensori-motor polyradiculoneuritis which can affect the four limbs and which may be accompanied by papillitis and papilloedema and an increase in the protein (albumin) content of the cerebrospinal fluid. This polyradiculoneuritis first appears as paraesthesiae of the extremities, and/or weakness of the legs with difficulty in walking. In addition, signs and symptoms thought to be manifestations of benign intracranial hypertension (pseudotumour cerebri) have been reported. These include papilloedema, decreased visual acuity, retinal haemorrhages and exudates and, in rare instances, sixth nerve palsy, optic atrophy and loss of vision. In such instances Pexid must be discontinued promptly and appropriate treatment instituted.

Polyradiculoneuritis, hypoglycaemia and weight loss usually regress with suspension of treatment with Pexid.

Hepatic disorders, including some cases similar in type to subacute alcoholic hepatitis, which have occasionally shown cirrhotic changes. The state of the liver before treatment with Pexid and the influence of concomitant therapy or aetiological factors such as alcohol and viral hepatitis are not known.

In rare cases, hepatic damage or hypoglycaemia have led to the death of the patient. Intracellular lipid inclusions have been observed by electron microscopy in tissue specimens from some patients with neuropathy and/or hepatitis.

Overdosage Gastric lavage, emetics, and Universal Antidote (activated charcoal 2 parts, tannic acid 1 part, magnesium oxide 1 part) are recommended.

Pharmaceutical precautions Pexid tablets should be protected from light and kept in a cool dry place.

Legal category POM.

Package quantities Blister strips of 25 in cartons of 50 tablets.

Further information Nil.

Product licence number 4425/0019.

RIFADIN*

Presentation Rifadin capsules (blue and red) marked 'Lepetit', containing 150 mg rifampicin.

Rifadin capsules (red) marked 'Lepetit', containing 300 mg rifampicin.

Rifadin syrup (raspberry colour and flavour), containing 100 mg rifampicin in each 5 ml.

Uses Rifadin, used in combination with other active antituberculosis drugs, is indicated in the treatment of all forms of tuberculosis, including fresh, advanced, chronic and drug-resistant cases. It is also effective against many atypical strains of mycobacteria. Rifadin is active *in vitro* at low concentrations against Gram-positive organisms

and at higher concentrations against Gram-negative organisms.

Dosage and administration The daily dose of Rifadin, calculated from the patient's body weight, should preferably be taken before meals to ensure rapid and complete absorption. Rifadin should be given with other effective antituberculosis drugs to prevent the possible emergence of rifampicin-resistant strains of mycobacteria.

Adults: A single, daily oral dose of 600 mg has been found in clinical practice to be well tolerated, effective and safe for adult patients. A more precise daily dosage can be calculated on the basis of 8–12 mg/kg body weight. Doses towards the lower end of this scale are recommended for frail and elderly patients. A daily dose of 8 mg/kg body weight should not be exceeded in patients with impaired liver function.

Children: In children, oral doses of up to 20 mg/kg body weight daily are recommended, although a total daily dose should not usually exceed 600 mg.

Contra-indications, warnings, etc

Contra-indications: Rifadin is contra-indicated in the presence of jaundice. Rifadin is contra-indicated during the first trimester of pregnancy, and should only be used during the second and third trimesters after careful appraisal of all aspects of the patient's condition. Rifadin is contra-indicated in patients who are hypersensitive to the rifamycins.

Precautions: Patients with impaired liver function should be given Rifadin only in cases of necessity, and then with caution and under close medical supervision. Lower doses of rifampicin and monitoring of liver function are recommended in these cases. In patients with impaired liver function, elderly patients, malnourished patients, and, possibly, children under two years of age, caution is particularly recommended when instituting therapeutic regimens in which isoniazid is to be used concurrently with Rifadin. It is rarely necessary, in the absence of clinical findings, to increase the frequency of performing routine liver function tests in patients with normal pretreatment liver function. An isolated report showing a moderate rise in the serum bilirubin and/or transaminase level is not usually in itself an indication for interrupting treatment; rather the decision should be made after repeating the tests, noting the trends in the levels, and considering them in conjunction with the patient's clinical condition. It has been possible in many patients in whom alterations to liver function prompted interruption of Rifadin therapy, to reinstate the drug without ill-effect.

If *p*-aminosalicylic acid and Rifadin are both included in the treatment regimen, they should be given not less than eight hours apart to ensure satisfactory blood levels.

Rifadin has been shown in animals and man to have liver enzyme inducing properties and may reduce the activity of anticoagulants, corticosteroids, digitalis preparations, oral contraceptives and oral hypoglycaemic agents. It may be necessary to adjust the dosage of these drugs if they are given concurrently with Rifadin, particularly when it is initiated or withdrawn.

Patients on oral contraceptives should be advised to use alternative, non-hormonal methods of birth control during Rifadin therapy.

Side-effects: Apart from occasional gastric intolerance and hypersensitivity reactions, Rifadin is generally very well tolerated and accepted by patients.

Eosinophilia and leucopenia have been reported to occur in a small percentage of patients but no clinical significance has been attributed to this. In some patients hyperbilirubinaemia, resulting from competition between Rifadin and bilirubin for the excretory pathways of the liver at cellular level, can occur in the early days of treatment. A rise in serum transaminase levels may also occur at this time but a return to pretreatment levels is to be expected as the liver adjusts to the metabolic handling of Rifadin. Cases of hepatocellular damage associated with antituberculosis drug regimens that have included rifampicin have been reported. The available evidence suggests that the incidence and severity of this may be higher in those patients with pre-existing liver impairment who are simultaneously receiving isoniazid. However, animal toxicology studies and pharmacokinetic investigations in humans have failed to disclose any significant or consistent interaction between the two substances. Side-effects, probably of immunological/allergic origin, such as fever, skin rashes, occasional renal dysfunction and haematological abnormalities (e.g. thrombocytopenia) have been reported, particularly in connection with intermittent, interrupted or repeated treatment.

Occasional disturbances of the menstrual cycle have been reported in women receiving long term antituberculosis chemotherapy using regimens containing rifampicin. The effectiveness of oral contraceptives may also be reduced.

Rifadin may produce a reddish discolouration of the urine, sputum and tears. The patient should be forewarned of this.

Overdosage: In cases of overdosage with Rifadin, gastric lavage should be performed as soon as possible. Intensive supportive measures should be instituted and individual symptoms treated as they arise. Although it has not been observed in man, animal studies suggest a possible neuro-depressant action associated with very high doses of Rifadin.

Pharmaceutical precautions Rifadin capsules have a shelf life of four years when stored below 25°C. Rifadin Syrup has a shelf life of three years. Rifadin syrup should not be diluted. It should be dispensed in clear or amber glass bottles.

If it proves necessary to open a blister pack, Rifadin capsules should be dispensed in amber glass or plastic containers. Protect from moisture.

Legal category POM.

Packaging quantities

Rifadin capsules 150 mg Bottles of 100 capsules.

Rifadin capsules 300 mg Bottles of 100 capsules.

Rifadin syrup 100 mg/5 ml Bottles of 120 ml.

Further information An oral dose of 450–600 mg Rifadin produces therapeutically effective levels in the blood, with the peak concentrations being observed approximately 2 hours after administration. There is good distribution of Rifadin into body tissues and fluids, including lung, bone, lymph nodes and inflammatory exudates. Rifadin is excreted mainly in the bile and urine, and high concentrations are reached in both these fluids. No cross resistance has been shown between Rifadin and other antituberculosis drugs. Rifadin is compatible with other antituberculosis drugs and has been shown clinically to be particularly effective in combination with isoniazid and ethambutol.

Product licence numbers

Rifadin capsules 150 mg 4425/5915

Rifadin capsules 300 mg 4425/5916
Rifadin syrup 4425/5917

RIFINAH*

Presentation *Rifinah 300*: orange, capsule-shaped tablets containing 300 mg rifampicin and 150 mg isoniazid – marked RH 300.

Rifinah 150: cyclamen, round biconvex tablets containing 150 mg rifampicin and 100 mg isoniazid – marked RH 150.

Uses Rifinah 300 and Rifinah 150 are indicated in the treatment of all forms of tuberculosis, including fresh, advanced and chronic cases.

Dosage and administration The daily dose of Rifinah 300 or Rifinah 150 should preferably be taken before meals to ensure rapid and complete absorption. Another antituberculosis drug may be given concurrently until the susceptibility of the infecting organism to rifampicin and isoniazid has been confirmed.

Adults: For patients of 50 kg (8 stone) and over.

Two Rifinah 300 tablets to be taken in a single daily dose before a meal. The patient receives 600 mg rifampicin and 300 mg isoniazid.

For patients of less than 50 kg (8 stone):

Three Rifinah 150 tablets to be taken in a single daily dose before a meal. The patient receives 450 mg rifampicin and 300 mg isoniazid.

Contra-indications, warnings, etc

Contra-indications: Rifinah 300 and Rifinah 150 are contra-indicated in the presence of jaundice. Rifinah 300 and Rifinah 150 are contra-indicated during the first trimester of pregnancy and should only be used during the second and third trimesters after careful appraisal of all aspects of the patient's condition. Rifinah 300 and Rifinah 150 are contra-indicated in patients who are hypersensitive to the rifamycins or isoniazid.

Precautions: Patients with impaired liver function should be given Rifinah 300 or Rifinah 150 only in cases of necessity and then with caution and under close medical supervision. Careful monitoring of liver function is recommended for these patients. Similar care should be exercised in elderly patients, malnourished patients, and children under two years of age. It is rarely necessary in the absence of clinical findings to increase the frequency of performing routine liver function tests in patients with normal pretreatment liver function. An isolated report showing a moderate rise in the serum bilirubin and/or transaminase level is not usually in itself an indication for interrupting treatment; rather the decision should be made after repeating the tests, noting the trends in the levels, and considering them in conjunction with the patient's clinical condition. Experience has shown that in many cases these changes are transient and usually revert towards normal pretreatment levels in about two weeks, even when the treatment is continued. Where alterations in liver function cause treatment with Rifinah 300 or Rifinah 150 to be interrupted it may be possible after an interval to reinstate the drug without ill-effect. If *p*-aminosalicylic acid and Rifinah 300 or Rifinah 150 are both included in the treatment regimen they should be given not less than eight hours apart to ensure satisfactory blood levels. Rifinah has been shown in animals and man to have liver enzyme inducing properties and may reduce the activity of anticoagulants, corticosteroids, digitalis preparations, oral contraceptives and

oral hypoglycaemic agents. It may be necessary to adjust the dosage of these drugs if they are given concurrently with Rifinah, particularly when it is initiated or withdrawn.

Patients on oral contraceptives should be advised to use alternative, non-hormonal methods of birth control during Rifinah therapy.

Side-effects: Rifampicin and isoniazid, the component drugs in Rifinah 300 and Rifinah 150, are well tolerated at the recommended dosage. Occasional gastro-intestinal disturbances and hypersensitivity reactions may occur. Polyneuritis associated with isoniazid, presenting as paraesthesia, muscle weakness, loss of tendon reflexes etc., is unlikely to be associated with the 300 mg of isoniazid contained in the daily adult dose of Rifinah 300 and Rifinah 150. Various haematological disturbances have been associated with isoniazid, including eosinophilia, agranulocytosis and anaemia.

Eosinophilia and leucopenia have been reported to occur in a small percentage of patients treated with rifampicin but no clinical significance has been attached to this. In some patients hyperbilirubinaemia, resulting from competition between rifampicin and bilirubin for the excretory pathways of the liver at cellular level, can occur in the early days of treatment. A rise in serum transaminase levels may also occur at this time but a return to pretreatment levels is to be expected as the liver adjusts to the metabolic handling of rifampicin. Cases of hepato-cellular damage associated with anti-tuberculosis drug regimens that have included rifampicin and isoniazid have been reported. The available evidence suggests that the incidence and severity of this may be higher in those patients with pre-existing liver impairment. However, animal toxicology studies and pharmacokinetic investigations in humans have failed to disclose any significant or consistent interaction between the two substances.

Side-effects associated with rifampicin, probably of immunological/allergic origin, such as fever, skin rashes, occasional renal dysfunction and haematological abnormalities (e.g. thrombocytopenia) have been reported, particularly in connection with intermittent, interrupted or repeated treatment. Occasional disturbances of the menstrual cycle have been reported in women receiving long term anti-tuberculosis chemotherapy using regimens containing rifampicin. The effectiveness of oral contraceptives may also be reduced.

The rifampicin in Rifinah 300 and Rifinah 150 may produce a reddish discolouration of the urine, sputum and tears and the patient should be forewarned of this.

High doses of isoniazid can cause convulsions. Although this is unlikely to happen with the recommended dose of Rifinah 300 or Rifinah 150, the possibility that the frequency of fits may be increased in patients with epilepsy should be borne in mind. Symptoms due to isoniazid occur more frequently in slow inactivators of the drug.

Overdosage: In cases of overdosage with Rifinah 300 or Rifinah 150, gastric lavage should be performed as soon as possible. Intensive supportive measures should be instituted and individual symptoms treated as they arise. Parenteral pyridoxine (Vitamin B₆) should be given. Symptoms are more likely to be related to isoniazid, including coma, respiratory distress, hyperglycaemia and metabolic ketoacidosis.

Although it has not been observed in man, animal studies suggest a possible neuro-depressant action associated with very high doses of rifampicin.

Pharmaceutical precautions Rifinah 300 and Rifi-

nah 150 tablets have a shelf life of four years when stored below 25°C.

If it proves necessary to open a blister pack, Rifinah 300 and Rifinah 150 should be dispensed in amber glass or plastic containers. Protect from moisture.

Legal category POM.

Package quantities

Rifinah 300 4 weeks calendar packs – 56 tablets
Bottles of 100 tablets.
Rifinah 150 4 weeks calendar pack – 84 tablets
Bottles of 100 tablets.

Further information The recommended daily dose of Rifinah 300 or Rifinah 150 produces therapeutically effective blood levels of rifampicin and isoniazid, two of the most powerful anti-tuberculosis drugs. Serum concentrations and the biological half-life of the two component drugs do not differ significantly from values obtained when the drugs are given alone.

Product licence numbers

Rifinah 300 0341/0016.
Rifinah 150 0341/0015.

SYNDOL®

Presentation Syndol Tablets are yellow, round, flat-faced, bevelled-edge tablets. On one side there is an incised 'S' design and on the other a scored bisect line. Each tablet contains:

Paracetamol BP	450 mg
Codeine Phosphate BP	10 mg
Decapryn® (Doxylamine Succinate USNF)	5 mg
Caffeine BP	30 mg

Uses For the treatment of mild to moderate pain and as an antipyretic. Syndol is recommended for the symptomatic relief of headache, including muscle-contraction or tension headache, migraine, neuralgia, toothache, sore throat, dysmenorrhoea, muscular and rheumatic aches and pains, and for post-operative analgesia following surgical or dental procedures.

Dosage and administration *Adults and children over 12 years:* 1 or 2 tablets every four or six hours as needed for relief. Total dosage over a 24-hour period should not normally exceed 8 tablets.

Not recommended for children under 12 years.

Contra-indications, warnings, etc Idiosyncrasy to any of the ingredients.

Precautions: May cause drowsiness; if affected, patients should be advised not to drive or operate machinery.

Side-effects: Doxylamine succinate may cause drowsiness or dizziness in some patients. Mild constipation may occur associated with the codeine component of Syndol. Agranulocytosis is a very rare complication of treatment with paracetamol.

Overdosage: Treat symptomatically as for paracetamol and codeine.

Pharmaceutical precautions None.

Legal category POM.

Package quantities Blister strips of 10 in packs of 50 tablets.

Further information Nil.

Product licence number 4425/0018.

Product licence number

Tace Tablets 0027/5015

TACE*

Presentation Tace Tablets are off-white, round, convex tablets, scored one side and stamped 'T' in two concentric circles on the reverse. Each tablet contains Chlorotrianisene BP 24 mg.

Uses Tace is an oestrogen indicated for:

1. *Oestrogen deficiency states* – primarily the *menopausal syndrome* (when periods have stopped).
2. *Postpartum breast engorgement* – for prevention and treatment of *painful breast engorgement* in patients who do not nurse their baby.
3. *Prostatic cancer* – for palliative control.

Dosage and administration

1. *Oestrogen deficiency states* (when periods have stopped). One tablet daily for a 30-day course. Often 1 course is sufficient, but in severe cases 2 or more courses, repeated as needed, may be required.
2. *Postpartum breast engorgement* – 2 tablets three times a day for four days. Begin treatment as soon after delivery as possible for best results.
3. *Prostatic cancer* – for palliative control. One tablet daily.

Contra-indications Patients with, or suspected of having, oestrogen-dependent carcinoma of the breast or genital organs.

Warning: Prolonged exposure to unopposed oestrogens may increase the risk of the development of endometrial carcinoma.

Side-effects Tace is well tolerated and side-effects are uncommon when it is used in the recommended dosage. Prolonged continuous administration can lead to endometrial hyperplasia and break-through bleeding. Withdrawal bleeding has also been reported. Gynaecomastia (seldom painful) and reduced potency have occurred in the male. Gastro-intestinal side-effects (nausea and vomiting), often associated with oestrogen therapy, have only occasionally been described with Tace. Although oedema is rare, caution should be exercised when oestrogens must be given to patients whose renal function reserve is low, such as those with borderline cardiac decompensation. Urticarial and other cutaneous reactions have occasionally been reported with Tace.

Overdosage Signs and symptoms of overdosage in the *female* include nausea and vomiting, headache, abdominal distress, anorexia, fluid retention, uterine bleeding; and in the *male*, gynaecomastia, loss of libido and atrophy of sexual organs. Treatment of acute overdosage should include supportive therapy, gastric lavage, diuretics (as indicated) and progestin therapy for uterine bleeding.

Pharmaceutical precautions None.

Legal category POM.

Package quantities Amber glass bottles of 50.

Further information Nil.

TENUATE*

Presentation Tenuate Dospan* Tablets are white, flat, bevelled, oblong tablets, scored on one side and stamped 'Merrell' on the other side. Each contains diethylpropion hydrochloride BP 75 mg in a hydrophilic colloid gum designed to release the ingredient over a 10-hour period.

Uses Anorectic agent indicated for overweight and obesity.

Dosage and administration *Adults and children over 12 years:* One 75 mg tablet swallowed whole in mid-morning.

Not recommended for children under 12 years.

Current medical opinion supports intermittent use of an appetite suppressant. Courses of Tenuate may be given over periods of six to eight weeks, with intervening periods of one month without treatment. Tenuate should be discontinued when patients stop losing weight.

Contra-indications Diethylpropion hydrochloride should not be given concurrently with monoamine oxidase inhibitors, nor should it be given to patients hypersensitive to diethylpropion hydrochloride or to emotionally unstable individuals who are known to be susceptible to drug abuse.

Precautions Although diethylpropion hydrochloride is generally safer than the amphetamines, it should be used with caution in severe hypertension and severe cardiovascular disease. Although rat and human reproductive studies have not indicated adverse effects, diethylpropion hydrochloride, like all medicines, should not be used during the first trimester of pregnancy, unless, in the opinion of the prescribing doctor, the potential benefits outweigh the potential risks.

Since the introduction of diethylpropion in 1958 it has been used by more than 33,000,000 patients. Against this background of extensive clinical use, reports of abuse have been extremely uncommon. Most of the subjects had previously abused other drugs such as amphetamine and phenmetrazine and many were described as having unstable personalities. Addicts have reported relatively little euphoria, and dissatisfaction in the few cases where diethylpropion was administered intravenously. Other abusers after oral administration of diethylpropion have shown marked anxiety and agitation as the effects wore off. After diethylpropion had been taken for 24–72 hours, additional doses did not produce euphoria but agitation and anxiety instead. Hallucinations occurred rarely following relatively high doses of the drug.

Several cases of toxic psychosis have been reported following the excessive use of diethylpropion and a very small number have been reported in which the recommended dose appears not to have been exceeded. The psychosis was temporary and cleared up after the drug was discontinued.

Side-effects Rarely severe enough to require discontinuation of therapy, side-effects associated with diethylpropion hydrochloride have been reported to occur in relatively low incidence. These have included insomnia, nervousness, dryness of the mouth, depressive reactions, headache, tachycardia, constipation, and

allergic rashes. Infrequent occurrences of nausea and vomiting have been noted, but diarrhoea is exceedingly rare.

Overdosage A few unsuccessful suicidal attempts by deliberate overdosage of diethylpropion hydrochloride have been reported. Dosage ranged from 450 to 2,250 mg. Transient sequelae included semicoma or coma, lethargy, increased irritability and nausea.

Accidental overdosage has been reported in several children, 6 months to 3½ years old. Known doses ranged from 50 to 1,100 mg. The most frequent effects were motor hyperactivity, excitability, tachycardia, rapid respiration, pupillary dilatation, and flushing. Treatment usually consisted of gastric lavage, sedation and close observation. Recovery occurred in all patients except one, in whom treatment with a large intravenous dose of sodium amobarbital was implicated.

Pharmaceutical precautions Store in a cool dry place.

Legal category POM.

Package quantities Tenuate Dospan Tablets are in blister strips of 10 in cartons of 100.

Further information Nil.

Product licence number
Tenuate Dospan Tablets 0027/5018.

TRILUDAN* ▼

Presentation White, round, flat faced, bevel edge tablets with 'M' in two concentric circles on one side and a scored bisect line with the code 084 on the other. Each tablet contains 60 mg terfenadine.

Uses Triludan is an antihistamine which is indicated for the symptomatic relief of hay fever, allergic rhinitis and allergic skin conditions.

Dosage and administration *Adults and children over 12 years:* one tablet twice daily.

Children aged 6–12 years: ½ tablet twice daily.

Contra-indications, warnings, etc None known.

Precautions: Although animal reproductive studies have not indicated adverse effects, Triludan, like most medications, should not be used during pregnancy nor during lactation unless, in the opinion of the physician, the potential benefits outweigh any possible risk.

Side-effects: In clinical trials of one or more weeks duration at therapeutic doses drowsiness, usually slight, has been observed, generally with an incidence equal to or less than that observed with placebo in the same trials. Headache, sweating and mild gastro-intestinal disturbances have also been infrequently reported.

Overdosage: There is no experience of overdosage (doses of 600 mg daily have been tolerated with only minor symptoms). Gastric lavage and symptomatic management are advised.

Pharmaceutical precautions None.

Legal category POM.

Package quantities Blister strips of 10 in cartons of 50 tablets.

Further information Nil.

Product licence number 4425/0024.

* *Trade Mark*

Thomas Morson Pharmaceuticals

Division of Merck Sharp & Dohme Limited

Hertford Road, Hoddesdon
Hertfordshire EN11 9BU



ATTENUVAX* ▼

Presentation Lyophilised powder for injection. When reconstituted, each dose of Attenuvax Injection contains not less than the equivalent of 1,000 TCID₅₀ (tissue culture infectious doses) of measles virus vaccine expressed in terms of the assigned titre of the FDA Reference Measles Virus. Attenuvax is a more attenuated line of measles virus derived from Enders' attenuated Edmonston strain.

Uses For general immunisation against measles.

Children: The Department of Health recommends that children 12 months of age or older be vaccinated against measles. (Please refer to 'Contra-indications'.)

Attenuvax given immediately after exposure to natural measles may provide some protection. If, however, the vaccine is given a few days before exposure, substantial protection may be provided.

Dosage and administration After suitably cleansing the injection site, the total volume of reconstituted vaccine should be injected subcutaneously, preferably into the outer aspect of the arm. Attenuvax must not be given intravenously.

The dose of vaccine is the same for all patients.

Warning: A sterile syringe and Adrenaline Injection BP (1:1,000) should be ready for immediate use should an anaphylactoid reaction occur.

Contra-indications, warnings, etc *Contra-indications:* Infants below 15 months of age may fail to respond to the vaccine due to the presence of residual measles antibody of maternal origin; the younger the infant, the lower the chance of seroconversion. Children below the age of 12 months should not normally be given Attenuvax unless they are at special risk. Where immunisation below the age of 12 months is deemed necessary, a second dose should be given after the child has reached 15 months of age.

Any active or suspected infection is reason for delaying vaccination. Active untreated tuberculosis. Malignant disease.

Attenuvax should not be given to those with impaired immunoresponsiveness occurring naturally, or as a result of treatment with steroids, radiotherapy, cytotoxic drugs or other agents. This contra-indication does not apply to patients receiving corticosteroids for replacement therapy, e.g. Addison's disease.

Hypersensitivity to neomycin (each dose of reconstituted vaccine contains approximately 25 mcg of neomycin).

Hypersensitivity to eggs, chicken or chicken feathers: Attenuvax is essentially devoid of potentially allergenic substances derived from host tissues (chick embryo). However, since this vaccine is propagated in cell cultures of chick embryos, the benefits of its use in patients hypersensitive to eggs, chicken or chicken feathers must be weighed against the potential risks of hypersensitivity reactions. Significantly, children with known allergies

experienced no reactions other than those already seen in non-allergic children.

Pregnancy: Do not give Attenuvax to pregnant women, because the possible effects of the vaccine on foetal development are unknown at this time. It is recommended that pregnancy at the time of vaccination be ruled out, and that the possibility of pregnancy occurring in the three months following vaccination must be prevented by medically acceptable methods.

Warnings and adverse effects: Attenuvax is for subcutaneous injection only; it must not be given intravenously.

Attenuvax may be given simultaneously with monovalent or trivalent poliovirus vaccine, live, oral, with Meruvax* II (Rubella Virus Vaccine, Live) and/or Mumpsax* (Mumps Virus Vaccine, Live). Attenuvax should not be given less than one month before or after immunisation with other live virus vaccines.

Children with a history of convulsions, or with parental history of epilepsy (non-traumatic) are considered to be at greater risk of convulsions.

In these cases, it is recognised that the simultaneous administration of normal immune globulin (0.6 mg/lb [1.3 mg/kg] bodyweight) could be beneficial, although it should be recognised that the administration of immunoglobulin might increase the proportion of failures to immune.

It may therefore be necessary to undertake a serological test to determine whether immunisation has been successful.

Attenuvax should not normally be given within three months of a transfusion with blood, or human plasma, or treatment with human immunoglobulin. If any of these substances have been used near to the time of vaccination, a test for the presence of measles antibody should be made at a later date.

It has been reported that live attenuated measles virus vaccine may result in a temporary depression of tuberculin skin sensitivity. If a tuberculin test is to be done, it should be administered either before or with Attenuvax.

Children under treatment for tuberculosis have not experienced exacerbation of the disease when immunised with live measles virus vaccine, and no studies have been reported on the effect of measles virus vaccines on untreated tuberculous children.

The occurrence of thrombocytopenia and purpura associated with live virus measles vaccines has been extremely rare.

Because the vaccine is slightly acidic (pH 6.2-6.6), patients may complain of burning and/or stinging at the injection site for a short time.

Moderate fever and rash may occur during the month after vaccination. Rarely, high fever or local reaction may occur. Children developing fever may, on rare occasions, exhibit febrile convulsions.

There have been isolated reports of ocular palsies and Guillain-Barre syndrome occurring after immunisation with vaccines containing live attenuated measles virus. The ocular palsies have occurred approximately 3-24

days following vaccination. No definite causal relationship has been established between either of these events and vaccination.

There have been reports of subacute sclerosing panencephalitis (SSPE) in children who did not have a history of natural measles but did receive measles vaccine. Some of these cases may have resulted from unrecognised measles in the first year of life or possibly from the measles vaccination. Based on estimated nationwide measles vaccine distribution in the USA, the association of SSPE cases to measles vaccination is about one case per million vaccine doses distributed. This is far less than the association with natural measles: 5–10 cases of SSPE per million cases of measles.

Local reactions characterised by marked swelling, redness and vesiculation at the injection site of attenuated live virus measles vaccines have occurred in children who have previously received killed measles vaccine. Allergic reactions such as wheal and flare at the injection site have been reported.

Treatment of overdose: Not applicable.

Pharmaceutical precautions Prior to reconstitution, the vaccine should be shipped and stored between 2°–8°C. *Protect from light.*

Studies have shown that the vaccine contains a minimum of 1,000 TCID₅₀ per dose after storage at any one of the following temperatures for the stated time period:

<i>Dried Vaccine</i>	<i>Retention of Potency</i>
<i>Storage Temperature</i>	<i>1,000 TCID₅₀ per dose</i>
2°–8°C	2 years
20°–25°C	4 months
37°C	2 weeks
45°C	6 days

The vaccine should be reconstituted using only the diluent provided, and used immediately after reconstitution.

Colour: The vaccine when reconstituted is yellow. It is acceptable for use only when clear.

Legal category POM.

Package quantities A single-dose vial of lyophilised, vaccine, packed with an ampoule containing diluent.

Further information Experience from more than 80 million doses of all live measles vaccines given in the USA through 1975 indicates that significant central nervous system reactions such as encephalitis and encephalopathy, occurring within 30 days after vaccination, have been temporally associated with measles vaccine approximately once for every million doses. In no case has it been shown that reactions were actually caused by vaccine. The risk of such serious neurological disorders following live measles virus vaccine administration remains far less than that for encephalitis and encephalopathy caused by natural measles (one per thousand reported cases).

A study suggests that the overall effect of measles vaccine has been to protect against SSPE by preventing measles with its inherent higher risk of SSPE.

Product licence number 0025/0070.

DOLOBID®

Presentation Peach-coloured, capsule-shaped, film-coated tablets, marked 'DOLOBID', containing 250 mg

diflunisal; and orange-coloured, film-coated tablets, marked 'DOLOBID', containing 500 mg diflunisal.

Uses Dolobid is indicated for the relief of pain.

Dolobid is also indicated in the relief of pain and inflammation associated with osteoarthritis and rheumatoid arthritis.

Dosage and administration The initial dosage is 500 mg given twice daily. For longer-term therapy, dosage can be adjusted to 250 mg or 500 mg given twice daily. Dosage should be adjusted to the nature and intensity of the pain being treated and should be given twice a day. Even if the initial dose is taken in the afternoon, a second dose should be taken at bedtime. Tablets should be swallowed whole, not crushed or chewed. The highest dose studied in patients was 1500 mg daily.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to the drug.

In patients who have previously experienced acute asthmatic attacks precipitated by aspirin or non-steroidal anti-inflammatory agents.

The drug should not be administered to patients with active gastro-intestinal bleeding.

The use of Dolobid should be avoided in patients with active peptic ulcer.

Dolobid should not be given to pregnant women, since the safety for this use has not been established. Nursing mothers should not take Dolobid, or should stop nursing.

Precautions: Dolobid should be used with caution in patients having a history of gastro-intestinal haemorrhage or ulcers.

Use with caution in patients receiving anticoagulant therapy since concomitant administration may prolong the prothrombin time.

Co-administration of aluminium hydroxide suspension significantly decreases the absorption of Dolobid by approximately 40%.

The dosage of Dolobid may need to be reduced in patients with renal functional impairment since the major route of excretion is via the kidney. In patients with severe renal impairment, the drug should not be used.

No evidence of renal toxicity has been seen at therapeutic dose levels in man. In rats and dogs, high oral doses of diflunisal (50–200 mg/kg/day) as with aspirin, produced similar pathological changes (gastro-intestinal ulceration and renal papillary oedema). These dosages are approximately 3 to 12 times the maximum dosages recommended in man.

Transient elevations of bilirubin and other routine liver function tests have occurred rarely. The clinical significance of these transient elevations has not been determined.

Since paediatric indications and dosage have not yet been established, Dolobid should not be given to children.

Side-effects: Dolobid is generally well tolerated.

Those side-effects experienced are usually mild, the most common being related to the upper gastro-intestinal tract.

Digestive system: Gastric pain, dyspepsia, nausea, and vomiting.

Isolated cases of gastro-intestinal ulcer and bleeding have been reported.

Central nervous system: Vertigo, somnolence, and rarely mild tinnitus, have been reported infrequently.

Skin: Pruritus and rash have been reported rarely. Cross-sensitivity with aspirin was suspected in two patients. A few cases of erythema multiforme, including the Stevens-Johnson syndrome, have been reported. A causal relationship with Dolobid has not been established.

Treatment of overdosage:

The initial plasma half-life following single oral doses of diflunisal seems to be dose dependent, ranging from approximately 7.5 hours for a 250 mg dose to 11 hours for a 500 mg dose.

When an acute overdose is taken, the stomach should be emptied by vomiting or lavage, though little drug will likely be recovered if more than an hour has elapsed since ingestion.

To facilitate urinary elimination of the drug, attempt to maintain renal function. Because of the high degree of protein binding, haemodialysis is not recommended.

Pharmaceutical precautions Store in a cool place, protected from light.

Legal category POM.

Package quantities Dolobid 250 mg tablets are supplied in packs of 50, 100 and 1,000 tablets; the 500 mg tablets in packs of 100.

Further information Following a single therapeutic dose, significant relief of pain usually occurs within the first hour. Dolobid has a prolonged duration of action and is therefore administered twice daily.

Dolobid has a dose-related effect on platelet function. In normal volunteers given Dolobid over eight days, 250 mg twice daily had no effect on platelet function and 500 mg twice daily affected platelet function only slightly. However, 1,000 mg twice daily inhibited platelet function. In contrast to acetylsalicylic acid, these effects were reversible.

Bleeding time was unaffected by 250 mg twice daily, slightly increased at 500 mg twice daily, and the greater increase at 1,000 mg twice daily was not statistically significant from placebo.

Faecal blood loss is significantly less following treatment with Dolobid (250 mg b.d.) than that associated with aspirin (600 mg q.i.d.).

Product licence numbers

250 mg tablet 0025/0128
500 mg tablet 0025/0146

H-B-VAX* ▼

Presentation Available as 1 ml vials of sterile suspension containing 20 mcg of Hepatitis B surface antigen adsorbed on to alum.

Uses H-B-Vax is indicated for immunisation against infection caused by hepatitis B virus, including all known subtypes.

The incidence of infection varies greatly in different parts of the world, and the vaccination strategy should be adjusted accordingly.

In areas of low prevalence, vaccination should be limited to those who are at increased risk of infection, such individuals would be found among:

Health care personnel: Dentists; physicians and surgeons; nurses and hospital ancillary workers; dental hygienists; laboratory personnel handling blood products from known carriers; health care students, especially those treating known carriers.

Patient and patient contacts: Patients in haemodialysis, haematology and oncology units; patients who need frequent and/or large-volume blood transfusions and clotting factor concentrates; residents and staff of mental institutions; intimate contacts of persons with persistent hepatitis B antigenaemia.

Plasma fractionation workers.

Persons at increased risk due to their sexual practices: Homosexually active males; prostitutes; persons who repeatedly contract sexually transmitted diseases.

Users of illicit injectable drugs.

Those living for prolonged periods in countries where Hepatitis B is endemic.

Dosage and administration H-B-Vax is for intramuscular use only; it must not be given intravenously, subcutaneously or intradermally.

Shake well before use. After thorough agitation H-B-Vax is an opaque, white suspension.

The immunisation regimen consists of three doses of vaccine given intramuscularly.

1st dose: at elected date

2nd dose: 1 month later

3rd dose: 6 months after first dose, as a 'booster'

The volume of dose to be given on each occasion is:

Group	Initial	1 month	6 months
Children 6 months to 10 years	0.5 ml (10 mcg)	0.5 ml (10 mcg)	0.5 ml (10 mcg)
Adults and children over 10 years	1.0 ml (20 mcg)	1.0 ml (20 mcg)	1.0 ml (20 mcg)
Dialysis and immunocompromised	Dose to be determined from ongoing studies		

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to any component of the vaccine.

Warnings: Because of the prolonged incubation period of hepatitis B, infection may be present at the time of vaccination. H-B-Vax may be ineffective in such patients.

Patients with immuno-deficiency or those receiving immuno-suppressive therapy may need larger doses of H-B-Vax.

Although study is still needed to determine the effectiveness of H-B-Vax after infection with hepatitis B, it has been shown that an injection of up to 3 ml of hepatitis B immunoglobulin does not interfere with the action of H-B-Vax injected at a different site.

Precautions: Adrenaline Injection BP (1:1000) should be available for immediate use should an anaphylactoid reaction occur.

Any serious active infection is reason for delaying vaccination unless, in the physician's opinion, this delay might entail even greater risk.

Caution should be exercised in administering H-B-Vax to individuals in whom a febrile or systemic reaction could pose a significant risk such as in patients with a severely compromised cardio-pulmonary status.

Nursing mothers: Because it is not known whether H-B-Vax is excreted in human milk, the physician should exercise caution before vaccinating nursing mothers with H-B-Vax.

Children: The safety and efficacy of H-B-Vax has not been determined in infants under 6 months of age. H-B-Vax is not recommended for infants of this age.

Pregnancy: H-B-Vax is not recommended for pregnant women. Animal reproduction studies have not been

conducted with the vaccine. It is also not known whether H-B-Vax can cause foetal harm when administered to pregnant women, or can affect reproductive capacity.

Adverse reactions: In studies involving over 1,000 adult volunteers, approximately 25% reported some local or systemic complaint. The most commonly occurring reactions are local soreness and erythema at the injection site. Local swelling, warmth, or induration are reported less frequently, and subside within two days of vaccination.

Low grade fever (less than 101°F) occurs occasionally and is usually confined to the 48-hour period following vaccination. Although uncommon, fever over 102°F has been reported.

Systemic complaints including malaise, fatigue, headache, nausea, myalgia, and arthralgia are infrequent and have been limited to the first few days following vaccination. Rash has been reported rarely.

Treatment of overdose: Not applicable.

Pharmaceutical precautions Store unopened and opened vials at 2–8°C (35.6–46.4°F). DO NOT FREEZE. The vaccine is used directly as supplied; no dilution or reconstitution is necessary. Thiomersal in 1:20,000 dilution is present in the vaccine as a preservative.

Legal category POM.

Package quantities One-ml vials of sterile suspension containing vaccine.

Further information The protective efficacy of H-B-Vax has been demonstrated in human populations. In a study involving individuals with a high risk of contracting hepatitis B virus infection, H-B-Vax has been shown to reduce the incidence of infection by over 90%. The vaccine protected against acute hepatitis B, asymptomatic infection, and chronic antigenaemia. There was evidence of immunity (neutralising antibody) in 87% of vaccinated subjects after administration of two doses of the 3-dose vaccine regimen. However, the third dose (booster dose) was necessary for both a high percentage of responses (96%), and long-term protective effect (i.e. vaccine-induced antibody persisting during the entire 24-month follow-up period).

Although the duration of protective effect of H-B-Vax is unknown at present, available data suggest that immunity will last for about 5 years in patients who have received all three doses, after which time a single booster dose of vaccine might be necessary to maintain immunity.

Product licence number 0025/0164.

INDOCID*

Presentation Ivory, opaque capsules containing 25 mg or 50 mg indomethacin BP, marked 'INDOCID 25' and 'INDOCID 50' respectively.

Ivory, opaque-based, transparent-headed capsules carrying white and blue pellets containing 75 mg indomethacin BP in sustained-release form, marked 'INDOCID R 693'.

A fruit-flavoured suspension containing in each 5 ml, 25 mg indomethacin BP.

Polyethylene glycol suppositories containing 100 mg indomethacin BP.

Uses Non-steroidal anti-inflammatory agent with analgesic properties.

For the active stages of: rheumatoid arthritis; osteoarthritis; degenerative joint disease of the hip; ankylosing

spondylitis; acute peri-articular disorders such as bursitis, tendinitis, synovitis, tenosynovitis, capsulitis of the shoulder, sprains and strains; low-back pain (commonly called 'lumbago'); gout.

Also indicated in inflammation, pain and oedema following orthopaedic procedures; and the treatment of dysmenorrhoea and reduction of associated symptoms.

Indocid is not a simple analgesic, its use should be limited to the above conditions, and particularly those cases not responding to conservative measures.

Indocid Suppositories may be used where night pain and morning stiffness are prominent. One suppository at bedtime will frequently give relief from pain and stiffness for 13 to 16 hours after administration. Indocid Suppositories may reduce, but not always abolish, gastrointestinal side-effects of indomethacin therapy.

Indocid-R: Indocid-R may be substituted for all the indications of 'Indocid' except gout, as clinical evidence is not currently available for this dosage form in this condition.

Dosage and administration The dosage of Indocid should be carefully adjusted to suit the needs of the individual patient.

Oral therapy: In order to reduce the possibility of gastrointestinal disturbances, *Indocid/Indocid-R Capsules and Suspension should always be taken with food, milk or an antacid.* (Note, however, that Indocid Suspension should not be mixed with an antacid, but should be taken separately, because indomethacin is unstable in an alkaline medium.) Indocid Suspension should not be diluted.

In chronic conditions, starting therapy with a low dosage, increasing this gradually as necessary, and continuing a trial of therapy for an adequate period (in some cases, up to one month) will give the best results with a minimum of unwanted reactions.

The recommended oral dosage range is 50–200 mg daily. Paediatric dosage not established.

Dosage in dysmenorrhoea: Up to 75 mg a day, starting with onset of cramps or bleeding, and continuing for as long as the symptoms usually last.

Suppositories: Adults: 1 suppository to be inserted once or twice a day. One should be used at bedtime. If another is necessary, it should be used in the morning.

Dosage for Indocid-R: The sustained-release capsule may be given once or twice a day, depending on patient needs and response.

Contra-indications, warnings, etc

Contra-indications: Children (conditions for safe use not established); active peptic ulcer; a recurrent history of gastro-intestinal lesions; sensitivity to indomethacin or aspirin. Safety for use during pregnancy or lactation has not been established. Indocid Suppositories are contra-indicated in patients with a recent history of proctitis.

Precautions Headache, sometimes accompanied by dizziness and lightheadedness, may occur, usually early in treatment. Starting therapy with a low dosage and increasing it gradually will minimise the incidence of headache. These symptoms frequently disappear on continuing therapy or reducing the dosage, but if headache persists despite dosage reduction, Indocid should be withdrawn. Patients should be warned that they may experience dizziness and, if they do, should not drive a car or undertake potentially dangerous activities needing alertness. Indocid should be used cautiously in

patients with psychiatric disorders, epilepsy, or parkinsonism, as it may tend to aggravate these disorders.

Gastro-intestinal disturbances may be minimised by giving Indocid orally with food, milk or an antacid. They usually disappear on reducing the dosage; if not, the risks of continuing therapy should be weighed against the possible benefits. Indocid Suppositories may reduce gastro-intestinal disturbances.

Peptic ulcer has been reported in a small proportion of patients. Haemorrhage and perforation have occurred in a small proportion of patients, usually with a history of peptic ulcer or those receiving corticosteroids or salicylates concurrently. In some cases, however, there was no history of peptic ulcer, or of other agents being used. If gastro-intestinal bleeding does occur, Indocid should immediately be discontinued.

Tenesmus and irritation of the rectal mucosa (sigmoidoscopic examination of a number of patients showed no mucosal changes) have been reported with Indocid Suppositories.

Indocid may mask the signs and symptoms of infection, and antibiotic therapy should be initiated promptly if an infection occurs during therapy with Indocid. It should be used cautiously in patients with existing but controlled infection.

During prolonged therapy, periodic ophthalmological examinations are recommended, as corneal deposits and retinal disturbances have been reported.

Patients should be carefully observed to detect any unusual manifestations of drug sensitivity. Indocid should be used with particular care in the older patient, who may be more prone to adverse reactions.

Indocid Suppositories should be used with caution in patients with a recent history of rectal bleeding.

Drug interactions: Controlled clinical studies have shown that Indocid did not influence the hypoprothrombin-aemia produced by anticoagulants in patients and healthy subjects. Nevertheless, if Indocid is added to the treatment of patients receiving anticoagulant therapy, they should be observed closely for alterations of the prothrombin time.

When Indocid is given to patients receiving probenecid, the plasma levels of indomethacin are likely to be increased. Therefore, a lower total daily dosage of Indocid may produce a therapeutic effect, and when increases in the dose are made, they should be made cautiously and in small increments.

Warnings and adverse reactions: CNS reactions – headache, dizziness, and lightheadedness. Mental confusion, syncope, drowsiness, convulsions, coma, peripheral neuropathy, depression and other psychiatric disturbances such as depersonalisation may occur as transient reactions that often disappear with continued or reduced dosage. However, occasionally, severe reactions require stopping therapy.

Gastro-intestinal – the more frequent reactions are nausea, anorexia, vomiting, epigastric distress, abdominal pain and diarrhoea. Others are ulceration (single or multiple) of oesophagus, stomach, duodenum or elsewhere in the small intestine, sometimes with haemorrhage and perforation (a few fatalities have been reported); gastro-intestinal bleeding without obvious ulcer formation; increased abdominal pain in patients with pre-existing ulcerative colitis. Rarely, intestinal ulceration followed by stenosis and obstruction has been reported. Reactions occurring infrequently are stomatitis; gastritis; bleeding from the sigmoid colon (occult or from a diverticulum); perforation of pre-existing sigmoid

lesions such as diverticula and carcinomata; ulcerative colitis and regional ileitis (causal relationship not established). With suppositories, tenesmus and irritation of the rectal mucosa have occasionally been reported, but sigmoidoscopic examination in a number of cases has not revealed mucosal changes.

Hepatic – rarely, toxic hepatitis and jaundice (some fatalities reported).

Cardiovascular/renal – oedema, increased blood pressure, and haematuria (all infrequent).

Dermatological/hypersensitivity – pruritus, urticaria, angioneurotic oedema, angitis, erythema nodosum, skin rash, loss of hair, rapid fall in blood pressure resembling a shock-like state, and acute respiratory distress including sudden dyspnoea and asthma (all infrequent). Bronchospasm may be precipitated in patients suffering from or with a history of bronchial asthma or allergic disease.

Haematological – infrequently, blood dyscrasias may occur including leucopenia, purpura, aplastic and haemolytic anaemia, and particularly thrombocytopenia. Rarely, agranulocytosis and bone-marrow depression. Because some patients may develop anaemia secondary to obvious or occult gastrointestinal bleeding, appropriate blood determinations are recommended.

Ocular – infrequently, blurred vision, and orbital and peri-orbital pain. Corneal deposits and retinal disturbances including those of the macula reported in patients with rheumatoid arthritis on prolonged therapy, but similar changes seen in patients with rheumatoid arthritis who had not received Indocid.

Aural – infrequently, tinnitus (rarely, deafness).

Miscellaneous – vaginal bleeding, hyperglycaemia, glycosuria, epistaxis, ulcerative stomatitis.

The following adverse reactions have been associated with use of Indocid Suppositories: tenesmus; proctitis; rectal bleeding, burning, pain, discomfort, and itching.

Treatment of overdosage: If ingestion is recent, gastric lavage should be performed. Otherwise therapy is supportive; the progress of the patient should be followed for several days, as gastro-intestinal ulceration and haemorrhage are reported side-effects of indomethacin. Antacids may be helpful.

Pharmaceutical precautions Keep container well closed; store in a cool place, protected from light. Indocid Suspension should also be protected from freezing.

Indocid/Indocid-R Capsules and Suspension should always be taken with food, milk or an antacid. (Note, however, that Indocid Suspension should not be mixed with an antacid but should be taken separately because indomethacin is unstable in an alkaline medium.) Indocid Suspension should not be diluted.

Legal category POM.

Package quantities *Capsules:* 25 mg, bottles of 100 and 500; 50 mg, bottles of 100; 75 mg, bottles of 100.

Suppositories: Boxes of 10.

Suspension: Bottles of 200 ml.

Further information Nil.

Product licence numbers

25 mg	0025/0111
50 mg	0025/0112
75 mg	0025/0125
Suppositories	0025/0062
Suspension	0025/0120

MERUVAX* II ▼

Presentation Lyophilised powder for injection. When reconstituted, Meruvax II Injection contains in each dose not less than the equivalent of 1,000 TCID₅₀ (tissue culture infective doses) of rubella virus vaccine expressed in terms of the assigned titre of the FDA (USA) Reference Rubella Virus. It is prepared from the Wistar Institute RA 27/3 strain of live attenuated rubella virus, adapted to and propagated in human diploid cell (WI-38) culture.

Uses Immunisation against rubella.

Children between 12 months of age and puberty: Meruvax II is indicated for immunisation against rubella in boys and girls from 12 months of age to puberty. No booster is needed. It is not recommended for infants less than a year old because they may retain maternal rubella-neutralising antibodies which may interfere with the immune response. Children in kindergarten and the first years at infants' school deserve priority for vaccination because they often are epidemiologically the major source of virus dissemination in the community. A history of rubella illness is usually not reliable enough to exclude children for immunisation.

Unimmunised children of susceptible pregnant women should receive live attenuated rubella vaccine. By this protection, children are less likely to acquire natural rubella and introduce the virus into the household.

Adolescent and adult males: Vaccination of adolescent or adult males may be useful in preventing or controlling outbreaks of rubella in circumscribed population groups.

Post-pubertal females: Pregnant women **MUST NOT** be given live attenuated rubella virus vaccine.

Non-pregnant adolescent and adult females: Since it is not known to what extent infection of the foetus with attenuated virus might take place following vaccination, or whether damage to the foetus could result, routine immunisation of post-pubertal females of unknown rubella immune status should not be undertaken because of the danger of inadvertently administering vaccine before pregnancy becomes evident.

Post-pubertal females should be considered for vaccination individually. Vaccine should only be given if subjects are shown to be rubella-susceptible by serological testing (see below), if they are not pregnant at the time of vaccination, and if they agree that they will not become pregnant within three months following vaccination.

This cautious approach to the vaccination of post-pubertal females is indicated because of the potential risk from vaccination during pregnancy, and because congenital abnormalities occur in up to 7% of all live births. Their chance appearance after vaccination could lead to serious misinterpretation.

It has been found convenient, in many instances, to vaccinate rubella-susceptible women in the immediate post-partum period.

If vaccination of a post-pubertal female is contemplated, the following is recommended:

1. She should be tested for susceptibility to rubella by the single radial haemolysis (radial diffusion) test.
2. If immune, as evidenced by a specific rubella antibody titre of 15 international units (1 : 16) or greater, vaccination is unnecessary.
3. If susceptible, she may be vaccinated only if she agrees not to become pregnant for the next three months. (This precaution also applies to women in the immediate post-partum period.)

4. She should be informed of the frequent occurrence of self-limiting arthralgia and possibly of self limiting arthritis beginning two to four weeks after vaccination.

As with any vaccine, inoculation of susceptibles does not result in seroconversion in all the vaccinees.

Revaccination: Based on available evidence, there is no reason to revaccinate children who were vaccinated originally when 12 months of age or older; however, children vaccinated when younger than 12 months of age should be revaccinated. (Meruvax II is not recommended in infants less than 12 months of age.)

Use with other live virus vaccines: There are no data available concerning simultaneous use of Meruvax II with monovalent or trivalent poliovirus vaccine, live, oral, or with killed poliovirus vaccines. However serological evidence shows that when M-M-R* (Measles, Mumps and Rubella Virus Vaccine, Live, MSD), containing the HPV-77 rubella strain, is given simultaneously with trivalent poliovirus vaccine, live, oral, antibody responses can be expected to be comparable to those which follow administration of the vaccines at different times. From this it follows that when Meruvax II is given simultaneously with either monovalent or trivalent poliovirus vaccine, oral, Attenuvax* (Measles Virus Vaccine, Live, Attenuated) and/or Mumpsax* (Mumps Virus Vaccine, Live) antibody responses can be expected to be comparable to those which follow administration of the vaccines at different times.

Note: M-M-R is not currently available in the United Kingdom.

Dosage and administration The total volume reconstituted from the single-dose pack should be injected subcutaneously, preferably into the outer aspect of the upper arm, after suitably cleansing the immunisation site.

Meruvax II should not be injected intravenously, or administered intranasally.

Do not give immune serum globulin (ISG) with Meruvax II.

Reconstitution: To reconstitute the vaccine, all the diluent provided should be injected into a vial of lyophilised vaccine, and this agitated to ensure thorough mixing. All the reconstituted vaccine is then withdrawn into the syringe and injected subcutaneously.

Contra-indications, warnings, etc

Contra-indications: Do not give Meruvax II to pregnant females; the possible effects of the vaccine on foetal development are unknown at this time. When vaccination of post-pubertal females is undertaken, pregnancy must be avoided for three months following vaccination.

Hypersensitivity to neomycin. (Each dose of reconstituted vaccine contains approximately 25 mcg of neomycin.)

Any febrile respiratory illness, or other active or suspected infection.

Patients receiving therapy with ACTH, corticosteroids, irradiation, alkylating agents, or antimetabolites. This contra-indication does not apply to patients who are receiving corticosteroids as replacement therapy, e.g. for Addison's disease.

Individuals with blood dyscrasias, leukaemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic systems.

Primary immuno-deficiency states, including cellular immune deficiencies, hypogammaglobulinaemic and dysgammaglobulinaemic states.

History of convulsions. Parental history of non-traumatic epilepsy.

Precautions: Meruvax II is for subcutaneous administration; it must not be given intravenously.

Adrenaline should be available for immediate use should an anaphylactoid reaction occur.

Meruvax II may be given with monovalent or trivalent poliovirus vaccine, live, oral, with Attenuvax* (Measles Virus Vaccine, Live, Attenuated) and/or Mumpsax* (Mumps Virus Vaccine, Live).

Meruvax II should not be given less than one month before or after immunisation with other live virus vaccines.

Excretion of small amounts of live attenuated rubella virus from the nose and throat has occurred in the majority of susceptible individuals 7–28 days after vaccination. There is no definitive evidence to indicate that such virus is transmitted to susceptible persons who are in contact with vaccinated individuals. Consequently, transmission, while accepted as a theoretical possibility, has not been regarded as a significant risk.

Ideally, however, children should be vaccinated when there is no practical possibility of pregnancy in their mother.

There is no evidence that live rubella virus vaccine given after exposure will prevent illness. There is, however, no contra-indication to vaccinating children already exposed to natural rubella.

Vaccination should be deferred for at least three months following blood or plasma transfusions or administration of human immune serum globulin. However, susceptible post-partum patients who received blood products may receive Meruvax II prior to discharge provided that a recent HI titre is drawn 6–8 weeks after vaccination to insure seroconversion. Similarly, although studies with other live rubella virus vaccines suggest that Meruvax II may be given in the immediate post-partum period to those non-immune women who have received anti-Rh₀ (D) globulin (human) without interfering with vaccine effectiveness, a follow-up post-vaccination HI titre should also be determined.

It has been reported that live attenuated rubella vaccine may temporarily depress tuberculin skin sensitivity. If a tuberculin test is to be done, therefore, it should be administered before or simultaneously with Meruvax II.

Adverse reactions: Because the vaccine is slightly acidic (pH 6.2–6.6), patients may complain of burning and/or stinging at the injection site for a short time.

Adverse reactions are uncommon, but symptoms of the same kind as those seen following natural rubella may occur after vaccination. These include regional lymphadenopathy, urticaria, rash, malaise, sore throat, fever, headache, polyneuritis, and occasionally temporary arthralgia that is infrequently associated with signs of inflammation. Local pain, induration, wheal and flare, and erythema may occur at the injection site.

Moderate fever (38.3° to 39.3°C/101° to 102.9°F) occurs occasionally, and high fever (above 39.4°C/103°F) occurs less commonly.

Reactions are usually mild and transient.

In children, joint reactions are rare and of brief duration if they do occur. In women, incidence rates for arthritis and arthralgia are generally higher than those seen in children (children: 0–3%; women: 12–20%) and the reactions tend to be more marked and of longer duration. Rarely, symptoms may persist for a matter of months. In adolescent girls, the reactions appear to be intermediate in incidence between those seen in children and in adult women. Even in older women (35–45 years) these

reactions are generally well tolerated and rarely interfere with normal activities.

Clinical experience with Meruvax II indicates that encephalitis and other nervous system reactions have occurred very rarely. A cause-and-effect relationship has not been established.

In view of the decreases in platelet counts that have been reported, thrombocytopenic purpura is a theoretical hazard.

Pharmaceutical precautions During shipment, to insure that there is no loss of potency, the vaccine must be maintained at a temperature of 10°C (50°F) or less.

Before reconstitution, Meruvax II should be stored at 2° to 8°C (35.6° to 46.4°F), and protected from light. Only the diluent supplied should be used for reconstitution. The vaccine should be used immediately after reconstitution.

Colour: The vaccine when reconstituted is yellow.

Legal category POM.

Package quantities Single-dose vials of lyophilised vaccine with ampoules of sterile diluent.

Further information Meruvax II has been shown to induce rubella haemagglutination-inhibiting (HI) antibodies in over 97% of susceptible subjects.

Vaccine induced antibody levels have been shown to persist for at least six years without substantial decline. If the present pattern continues, it will provide a basis for the expectation that immunity following the vaccine will be permanent. However, continued surveillance will be required to demonstrate this point.

Product licence number 0025/0149.

MIDAMOR*

Presentation Yellow, diamond-shaped tablets, marked 'MSD 92', containing 5 mg amiloride hydrochloride.

Uses Potassium-conserving agent; diuretic.

Although Midamor has mild natriuretic, diuretic and antihypertensive activity when used alone which may be additive to the effects of thiazides and other saluretic-antihypertensive agents, its principal indication is as concurrent therapy with thiazides or more potent diuretics to conserve potassium during periods of vigorous diuresis and during long-term maintenance therapy.

In congestive heart failure, the positive effect of Midamor on potassium balance may be especially useful for patients also receiving digitalis, who are particularly sensitive to lowered potassium levels. In hypertension, it is used as an adjunct to therapy with thiazides and similar agents to prevent potassium depletion. When combined with hydrochlorothiazide, Midamor gives an additive antihypertensive action. In hepatic cirrhosis with ascites, Midamor usually provides adequate diuresis with diminished potassium loss and less risk of metabolic alkalosis, when used alone. It may be used with more potent diuretics when a greater diuresis is required.

Dosage and administration *Midamor alone:* The initial dosage should be 10 mg (as a single dose or 5 mg twice a day). This may be increased if necessary, but must not exceed 20 mg (4 tablets) a day. After diuresis has been achieved, the dosage may be reduced by 5 mg increments to the least amount required.

Midamor usually begins to act within two hours. Its effect upon electrolyte excretion reaches a peak between

six and ten hours, and lasts about 24 hours. Most patients respond during the first day of treatment, but maximum therapeutic effect may not be seen for several days. As in all diuretic therapy, the rate of weight loss and the serum electrolyte levels should determine the dosage. The most satisfactory rate of weight loss is generally about 0.5–1.0 kg a day.

Midamor with other diuretic therapy: When Midamor is used with a diuretic which is given on an intermittent basis, it should be given at the same time as the diuretic.

Congestive heart failure: Initially, 5 or 10 mg (1 or 2 tablets) a day, together with the usual dosage of the diuretic concurrently employed. If diuresis is not achieved with minimal dosage of both agents, the dosage of both may be gradually increased, but that of Midamor should not exceed 20 mg (4 tablets) a day. Once diuresis has been achieved, reduction in dosage of both agents may be attempted for maintenance therapy. The dosage of both drugs is determined by the diuresis and the level of serum potassium.

Hypertension: 5 or 10 mg (1 or 2 tablets) a day, together with the usual antihypertensive dosage of the thiazide concurrently employed. It is not usually necessary to exceed 10 mg of Midamor a day; in any event, not more than 20 mg (4 tablets) of Midamor a day should be given.

Hepatic cirrhosis with ascites: When used with another diuretic, treatment should be started with a small dose of Midamor, i.e. 5 mg (1 tablet), plus a low dosage of the other diuretic agent. If necessary, dosage of both agents may be increased gradually until there is effective diuresis.

The dosage of Midamor should not exceed 20 mg (4 tablets) a day. Maintenance doses may be lower than those required to initiate diuresis; reduction in the daily dosage should therefore be attempted when the patient's weight is stabilised. Gradual weight reduction in cirrhotic patients is especially desirable to reduce the likelihood of untoward reactions associated with diuretic therapy.

Contra-indications, warnings, etc

Contra-indications: Hyperkalaemia (serum potassium over 5.5 mEq/l); other potassium-conserving agents or potassium supplements; anuria, acute renal failure, severe progressive renal disease, diabetic nephropathy; patients with blood urea over 60 mg per 100 ml or serum creatinine over 1.5 mg per 100 ml should not receive amiloride hydrochloride without careful frequent monitoring of serum electrolytes and blood urea levels; prior sensitivity to amiloride hydrochloride. In renal impairment, use of a potassium conserving agent may result in rapid development of hyperkalaemia. Safety for use in children not established. See also 'Use in pregnancy' under 'Precautions'.

Precautions – Diabetes mellitus: Hyperkalaemia has commonly occurred in diabetic patients, especially those with chronic renal disease or pre-renal azotaemia. The status of renal function should therefore be determined before Midamor is given to known or suspected diabetic patients. Midamor should be discontinued before a glucose-tolerance test, as one patient with poorly controlled diabetes mellitus, who became severely hyperkalaemic while receiving amiloride hydrochloride, died following two repeated intravenous glucose-tolerance tests.

Metabolic or respiratory acidosis: Potassium-conserving therapy should be initiated only with caution in severely

ill patients in whom metabolic or respiratory acidosis may occur, e.g. patients with cardiopulmonary disease of decompensated diabetes. Shifts in acid-base balance alter the balance of extracellular-intracellular potassium, and the development of acidosis may be associated with rapid increases in serum potassium.

Hyperkalaemia (serum potassium level over 5.5 mEq/litre): This has been observed in patients receiving amiloride hydrochloride, alone or with other diuretics, particularly in the aged, in diabetics, and in hospital patients with hepatic cirrhosis or cardiac oedema who had known renal involvement, were seriously ill, or were undergoing vigorous diuretic therapy. Such patients should be observed carefully for clinical, laboratory, and ECG evidence of hyperkalaemia (not always associated with an abnormal ECG). Some deaths have been reported in this group of patients. If hyperkalaemia develops, Midamor should be discontinued immediately, and if necessary, active measures taken to reduce the serum potassium to normal.

Electrolyte imbalance and blood urea increases: Hyponatraemia and hypochloraemia may occur when amiloride hydrochloride is used with other oral diuretics. Reversible increases in blood urea levels have been reported accompanying vigorous diuresis, especially when diuretic combinations were used in seriously ill patients, such as those with hepatic cirrhosis with ascites and metabolic alkalosis, or those with resistant oedema. Careful monitoring of serum electrolytes and blood urea levels should therefore be carried out when Midamor is given with oral diuretics to such patients.

Effects in cirrhotic patients: Oral diuretic therapy is more frequently accompanied by adverse reactions in patients with hepatic cirrhosis and ascites, because these patients are intolerant of acute shifts in electrolyte balance, and because they often already have hypokalaemia as a result of associated aldosteronism. Hepatic encephalopathy, manifested by tremors, confusion and coma, has been reported. In cirrhotic patients, jaundice associated with the underlying disease process has deepened in a few instances, but the relationship to amiloride is uncertain.

Other precautions: As with any drug, patients should be observed regularly for the possible occurrence of liver dysfunction, idiosyncratic reactions or blood dyscrasias.

Use in pregnancy: Because clinical experience is limited, Midamor is not recommended for use during pregnancy. The potential benefits of the drug must be weighed against possible hazards to a foetus if it is administered to a woman of childbearing age.

Side-effects – Gastro-intestinal: Anorexia, nausea, vomiting, abdominal fullness, pain, constipation, diarrhoea.

Related to diuresis: Dry mouth and thirst, paraesthesiae, dizziness, weakness, susceptibility to fatigue, muscle cramps, orthostatic hypotension.

Other: Reversible adverse reactions reported with amiloride hydrochloride are skin rash, pruritus, and such minor psychiatric disturbances as confusion; transient visual disturbances have also been noted.

There have been isolated instances of gastro-intestinal bleeding in patients with a history of gastro-intestinal disease receiving amiloride hydrochloride alone; a relationship with amiloride has not been established.

Rare reversible abnormalities, thought to be related to amiloride hydrochloride, have been observed in liver

function tests. One patient with pre-existing partial heart block developed complete heart block following use of amiloride hydrochloride.

Treatment of overdosage: Dehydration, electrolyte imbalance and hepatic coma are treated by the established procedures. There is no specific antidote. Emesis should be induced or gastric lavage performed. Treatment is symptomatic and supportive. If hyperkalaemia occurs, active measures should be taken to reduce the serum potassium levels.

Pharmaceutical precautions Keep container well closed; store in a cool place, protected from light.

Legal category POM.

Package quantities Bottles of 100.

Further information Potassium supplements and other potassium-conserving agents are contra-indicated with Midamor.

Product licence number 0025/5015.

MODUCREN* ▼

Presentation Blue, square, half-scored tablets, marked 'MODUCREN', containing 25 mg hydrochlorothiazide, 2.5 mg amiloride hydrochloride, and 10 mg timolol maleate.

Uses Mild to moderate hypertension.

Dosage and administration 1 to 2 tablets once a day.

Contra-indications, warnings, etc

Contra-indications: Bronchospasm (including bronchial asthma), severe chronic obstructive pulmonary disease, sinus bradycardia (less than 50 beats per minute), second- and third-degree AV block, congestive heart failure, right ventricular failure secondary to pulmonary hypertension, significant cardiomegaly, and cardiogenic shock. Hyperkalaemia (serum potassium greater than 5.5 mEq/litre). Anuria, acute and chronic renal insufficiency, severe or progressive renal disease (blood urea more than 60 mg %, BUN more than 30 mg %, serum creatinine more than 1.5 mg %), diabetic nephropathy.

Anaesthetic agents causing myocardial depression, hypersensitivity to any component of Moducren or to sulphonamide-derived drugs. Use of other potassium-conserving agents or potassium supplements except in severe and/or refractory cases of hypokalaemia.

Precautions: *Congestive cardiac failure:* Care should be exercised before and during treatment of patients with cardiomegaly or history of cardiac failure. *Cardiac arrhythmias:* Patients at risk of congestive heart failure should be carefully observed for bradycardia, AV block and respiratory distress. If congestive cardiac failure persists, Moducren should be withdrawn. Moducren should be withdrawn gradually in patients with angina pectoris because abrupt withdrawal of beta blockers has been associated with increase in pain, and reports of myocardial infarction, and ventricular arrhythmias. *Elective or emergency surgery:* Moducren should also be gradually withdrawn prior to elective surgery of anginal patients. Agonists such as isoprenaline or noradrenaline may be used to counter the effects of beta-blockade in emergency surgery. *Renal and hepatic disease and electrolyte disturbances:* Moducren should be used with caution in patients with renal or hepatic disease and in

those patients in whom fluid and electrolyte balance is critical. Acid-base balance should be monitored frequently in severely ill patients at risk of respiratory acidosis. Serum and urine electrolyte determinations should be made in patients vomiting excessively or receiving parenteral fluids. Dilutional hyponatraemia may occur in patients with oedema in hot weather that calls for appropriate therapy; hypochloreaemia requires specific treatment only under exceptional circumstances. Hypokalaemia or hyperkalaemia may occur. *Diabetes mellitus, hypoglycaemia:* Moducren should be given with caution to diabetic patients and to patients subject to spontaneous hypoglycaemia as the symptoms and signs of acute hypoglycaemia may be masked. Moducren should only be used in diabetic patients after determining the status of renal function. Moducren should be discontinued at least three days before glucose tolerance testing. Insulin requirements may need readjusting in patients taking Moducren. *Skin and sensitivity reactions:* There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuation of the drug should be considered if any such reaction is not otherwise explicable. Withdrawal should be gradual. Sensitivity reactions to Moducren may occur with or without a history of allergy or bronchial asthma. Possible exacerbation or activation of systemic lupus erythematosus reactions have been reported with thiazide diuretics. *Metabolic and endocrine:* Beta-adrenergic blocking agents may mask the signs of hyperthyroidism. Hypercalcaemia and hypophosphataemia have been reported with thiazide diuretics. Moducren should be discontinued in patients prior to testing for parathyroid function. Hyperuricaemia or acute gout may be precipitated in some patients.

Drug interactions: Moducren may potentiate other antihypertensive agents, such as reserpine or guanethidine. Its effect may be enhanced in the post-sympathectomy patient. Thiazides may increase the responsiveness to tubocurarine. Preparations containing lithium should not generally be given with diuretics because they reduce its renal clearance and add a high risk of lithium toxicity.

Children: Because the safety and efficacy of Moducren has not been established in children, it is not recommended for paediatric use.

Nursing mothers: Thiazides appear in breast milk, but it is not known whether timolol maleate or amiloride are also excreted. If the use of Moducren is deemed essential, the mother should stop nursing.

Pregnancy: Moducren is not recommended for use during pregnancy. The use of any drug in women of child-bearing age requires that the anticipated benefit be weighed against possible hazards, which include foetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

Warnings and adverse effects: Common side-effects reported are asthenia, fatigue, and bradycardia. Other effects relating to the components of Moducren are described below.

Hydrochlorothiazide and amiloride hydrochloride related effects. *Gastro-intestinal:* anorexia, nausea, vomiting, abdominal fullness or pain, flatulence, gastric irritation, cramp, constipation, diarrhoea. A few reports of gastro-intestinal bleeding associated with amiloride have been

made, although its relationship to amiloride is uncertain. Activation of probable pre-existing peptic ulcer has been reported in a few patients receiving amiloride.

Other: Rash, pruritus, transient visual disturbances, minor psychiatric disturbances such as confusion. Leucopenia, agranulocytosis, thrombocytopenia, aplastic anaemia, and haemolytic anaemia have been reported rarely following thiazide therapy. Purpura, urticaria, photosensitivity, necrotising angitis (vasculitis, cutaneous vasculitis), fever, respiratory distress, pneumonitis, and anaphylactic reactions have been reported. Blood dyscrasias have been reported rarely in patients receiving amiloride hydrochloride. Abnormalities of liver function tests thought to be related to amiloride have also been reported. Hyperuricaemia has been noted.

Thiazide therapy commonly causes headache, restlessness, jaundice (intrahepatic cholestatic jaundice), pancreatitis, xanthopsia, hyperglycaemia, glycosuria, and hyperuricaemia. One patient with hyperkalaemia and partial heart block developed complete heart block following the use of amiloride hydrochloride. Diuresis may also induce dry mouth and thirst, paraesthesiae, sialadenitis, dizziness, vertigo, weakness, muscle spasm, and orthostatic hypotension (aggravated by alcohol, barbiturates, or narcotics).

Timolol maleate related: Epigastric distress, nausea, vomiting, diarrhoea, dizziness, weakness, headache, and dyspnoea have been most commonly reported. Insomnia, increased dreaming, nightmares, congestive heart failure, severe bradycardia, bronchospasm, AV block, postural hypotension, cold extremities, Raynaud's phenomenon, fatigue, sedation, and mental depression have been reported infrequently. Hallucinations have occurred rarely.

Various rashes and pruritus have been reported in low incidence, and one case of exfoliative dermatitis has been reported.

Treatment of overdose: There is no experience of overdose with Moducen. Nevertheless, experience with its components suggests that therapy be stopped and that the patient is closely watched. If dehydration, electrolyte imbalance and hepatic coma occur, treat by the established procedures. There is no specific antidote. If ingestion is recent, emesis should be induced or gastric lavage performed. Treatment is symptomatic and supportive. If hyperkalaemia occurs, active measures should be taken to reduce the serum potassium levels. For respiratory impairment, oxygen or artificial respiration should be administered.

Severe symptomatic bradycardia: atropine sulphate, 0.25–2 mg intravenously, should be used to induce vagal blockade. If bradycardia persists, intravenous isoprenaline hydrochloride should be administered cautiously. In refractory cases, the use of a cardiac pacemaker may be considered.

Severe hypotension: a sympathomimetic pressor agent such as noradrenaline should be used. In refractory cases, the use of glucagon has been reported to be useful.

Bronchospasm: isoprenaline hydrochloride should be used. Additional therapy with aminophylline may be considered.

Acute cardiac failure: conventional therapy with digitalis, diuretics, and oxygen should be instituted immediately. In refractory cases, the use of intravenous aminophylline followed, if necessary, by glucagon has been reported useful.

Pharmaceutical precautions Store in a cool, dry place, protected from light.

Legal category POM.

Package quantities Calendar packs of 28 tablets.

Further information Similar dosage schedules and similar bioavailability rationalise the combination of hydrochlorothiazide (a saluretic), timolol maleate (a beta-adrenergic receptor blocking agent), and amiloride hydrochloride (a potassium-conserving agent) for the treatment of hypertension.

Product licence number 0025/0141.

MUMPSVAX*

Presentation Powder which, when reconstituted, contains in each dose not less than 5,000 TCID₅₀ (tissue culture infectious doses) of mumps virus vaccine expressed in terms of the assigned titre of the FDA (USA) Reference Mumps Virus. It is prepared from the Jeryl Lynn (B Level) strain, named after the patient from whom the virus was initially recovered.

Uses Mumps virus vaccine.

Mumps vaccine induces protective antibodies in essentially all non-immune recipients, provides protection against natural mumps in most cases, and has not been shown to cause significant systemic or local reactions. Evidence indicates that the mumps virus infection initiated by the vaccine is not contagious.

The vaccine is indicated for immunisation against mumps in children over 12 months of age, or adults. It is not recommended for children younger than this because they may retain maternal mumps-neutralising antibodies which may interfere with the immune response.

Recent serological evidence shows that when M-M-R* (measles, mumps, and rubella virus vaccine, live, MSD) is given simultaneously with trivalent oral polio virus vaccine, antibody responses can be expected to be comparable to those which follow administration of the vaccines at different times. From this, it follows that when Mumps vaccine is given simultaneously with either monovalent or trivalent oral polio virus vaccine, Attenuvax* (measles virus vaccine, live attenuated) and/or Meruvax* II (rubella virus vaccine, live), antibody responses can be expected to be comparable to those which follow administration of the vaccines at different times.

Note: M-M-R is not currently available in the United Kingdom.

Evidence indicates that the vaccine will not offer protection when given after exposure to natural mumps. It has been reported that immune serum globulin (human), in a dosage of 0.01–0.02 ml/lb (0.02–0.04 ml/kg), did not prevent the antibody response to the live vaccine when the two were administered simultaneously in opposite arms. However, protection afforded with this regime has not been established.

Adequate antibody levels, with continuing protection of vaccinated children exposed to mumps, have persisted for ten years without substantial decline. The pattern of antibody closely resembles that observed for natural mumps, although the antibody level is significantly lower than that following the natural infection. If this pattern continues, it will provide a basis for expectation that immunity following the vaccine will be permanent.

However, continued observation will be required to demonstrate this point.

Revaccination: Based on available evidence, there is no need to revaccinate children who were originally vaccinated when 12 months or older.

Dosage and administration To reconstitute the vaccine, all the diluent in the syringe should be injected into the vial of lyophilised vaccine, and agitated to ensure thorough mixing. The entire contents of the vial should then be drawn back into the syringe.

After suitably cleansing the immunisation site, the total volume of reconstituted vaccine should be injected subcutaneously, preferably into the outer aspect of the upper arm. Mumpsxvax must not be injected intravenously.

The dosage of vaccine is the same for all patients. *Do not give serum globulin (ISG) concurrently with Mumpsxvax.*

Contra-indications, warnings, etc

Contra-indications: Do not give Mumpsxvax to pregnant women, since the possible effects of the vaccine on foetal development are not known at this time. It is recommended that the possibility of pregnancy at the time of vaccination be ruled out, and that the possibility of pregnancy in the three months following vaccination be prevented by a medically acceptable method for pregnancy prevention.

Mumpsxvax should not be given to children less than 1 year of age.

Hypersensitivity to neomycin (each dose of reconstituted vaccine contains approximately 25 mcg of neomycin).

Malignant disease. Those with impaired immune responsiveness, whether occurring naturally or as a result of treatment with steroids, radiotherapy, cytotoxic drugs or other therapy. This contra-indication does not apply to patients who are receiving corticosteroids as replacement therapy, e.g. for Addison's disease.

Any active or suspected infection is reason for delaying vaccination.

Hypersensitivity to eggs, chicken, or chicken feathers: This vaccine is essentially devoid of potentially allergenic substances derived from host tissues (chick embryo). However, because the attenuated virus in this vaccine is propagated in cell cultures of chick embryo, there is a potential risk of hypersensitivity reactions in patients allergic to eggs, chicken, or chicken feathers. Widespread use of Mumpsxvax for over a decade has resulted in only rare, isolated reports of minor reactions attributed to allergens of this kind. Significantly, children known to be allergic to eggs, chicken, and chicken feathers experienced no reactions other than those previously seen in non-allergic children when given a vaccine similar in preparation to Mumpsxvax.

Precautions: Mumpsxvax is for subcutaneous injection; it must not be given intravenously.

Mumpsxvax may be given simultaneously with mono-valent or trivalent poliovirus vaccine, live, oral, with Attenuvax* and/or Meruvax* II.

Mumpsxvax should not be given less than one month before or after immunisation with other live virus vaccines.

Vaccination should be deferred for at least three months following blood or plasma transfusions, or administration of human immune serum globulin. If any of these substances have been used near to the time of

vaccination, a test for the presence of mumps antibody should be made at a later date.

It has been reported that live mumps virus vaccine may temporarily depress tuberculin skin sensitivity. Therefore, if a tuberculin test is to be done, it should be scheduled before or simultaneously with mumps vaccine.

A sterile syringe and Adrenaline Injection BP (1 : 1,000) should be ready for immediate use should an anaphylactoid reaction occur.

Adverse reactions: Because of the slight acidity of the vaccine (pH 6.2-6.6) patients may complain of burning and/or stinging at the injection site for a short time.

Mild fever occurs occasionally. Fever above 103°F (39.4°C) is uncommon.

Parotitis has been reported to occur in very low incidence, and orchitis rarely, in persons who were vaccinated. In most instances investigated, prior exposure to natural mumps was established. In other instances, whether or not this was due to vaccine, to prior natural mumps exposure or to other causes has not been established.

Reports of purpura and allergic reactions such as wheal and flare at the injection site, or urticaria have been extremely rare.

Very rarely, encephalitis and other nervous system reactions have occurred in recipients of the vaccine. A cause-effect relationship has not been established.

Treatment of overdosage: Nil.

Pharmaceutical precautions Prior to reconstitution, the vaccine should be stored in a refrigerator at 2-8°C (35.6-46.4°F). The vaccine should be protected from light at all times. Only the diluent supplied should be used, and the vaccine should be reconstituted just before using. It is recommended that the reconstituted vaccine should be used immediately after reconstitution.

To ensure that there is no loss of potency during shipment, the vaccine must be maintained at a temperature of 10°C (50°F) or less.

Colour: The reconstituted vaccine is yellow.

Legal category POM.

Package quantities One 0.5 ml single-dose vial of lyophilised vaccine, packed with a disposable syringe containing diluent.

Further information Mumpsxvax is grown in cell cultures of chick embryos free of avian leucosis, according to the general procedures used to prepare Enders' measles virus vaccine, live attenuated. The vaccine is tested for safety and efficacy.

No reports have been received of transmission of mumps from vaccinees to susceptible contacts.

Product licence number 0025/0072.

PNEUMOVAX* ▼

Presentation Single-dose, prefilled syringe containing, in 0.5 ml, 50 mcg of each polysaccharide type derived from capsules of the fourteen most prevalent pneumococci dissolved in isotonic saline containing 0.25% phenol.

Uses A pneumococcal vaccine affording protection against the fourteen most prevalent or invasive capsular types of pneumococci accounting for at least 80% of pneumococcal disease isolates found by ongoing surveillance (see chart).

14 pneumococcal capsular types included in Pneumovax

Nomenclature		Pneumococcal types						
US	1	2	3	4	6	8	9	
Danish	1	2	3	4	6A	8	9N	
US	12	14	19	23	25	51	56	
Danish	12F	14	19F	23F	25	7F	18C	

Pneumovax is indicated for immunisation against pneumonia and bacteraemia caused by those types of pneumococci included in the vaccine. It should be considered for all persons 2 years of age or older in whom there is an increased risk of morbidity and mortality from pneumococcal pneumonia.

However, Pneumovax may not be effective in preventing infection resulting from basilar skull fracture or from external communication with cerebrospinal fluid. Studies are under way to determine the effectiveness of the vaccine for preventing pneumococcal otitis media in infants.

Dosage and administration *Do not inject intravascularly; avoid intradermal administration.*

Administer a single 0.5 ml dose of Pneumovax subcutaneously or intramuscularly (preferably in the deltoid muscle or lateral mid-thigh) with appropriate precautions to avoid intravascular administration.

Available data suggest that revaccination should not be carried out at less than five-year intervals to minimise the frequency and severity of local reactions, especially in persons who have retained high antibody levels.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to any component of the vaccine. Adrenaline Injection BP (1 : 1,000) must be immediately available should an acute anaphylactoid reaction occur.

Do not give Pneumovax during pregnancy; the possible effects of the vaccine on foetal development are unknown.

Patients with Hodgkin's disease who have received extensive chemotherapy and/or nodal irradiation.

Warnings:

The expected serum antibody response may not be obtained in patients receiving immunosuppressive therapy.

Intradermal administration may cause severe local reactions.

Required prophylactic antibiotic therapy against pneumococcal infection should not be stopped after immunisation with Pneumovax.

Precautions: Delay the use of Pneumovax in any febrile respiratory illness or other active infection except when this delay may involve even greater risk.

Caution and appropriate care should be exercised in administering Pneumovax to individuals with severely compromised cardiac and/or pulmonary function in whom a systemic reaction would pose a significant risk.

Available data suggest that revaccination before five years may result in more frequent and severe local reactions at the site of injection.

Children under 2 years of age: Pneumovax is not recommended because antibody response to some pneumococcal capsular types may be poor.

Nursing mothers: Because it is not known whether

Pneumovax is excreted in human milk, exercise caution when giving the vaccine to nursing mothers.

Adverse reactions: Local erythema and soreness at the injection site, usually of less than 48 hours' duration, commonly occur; local induration occurs less frequently.

Low-grade fever (less than 100.9°F) occurs occasionally, usually within 24 hours of vaccination. Rarely, fever over 102°F has been reported.

Reactions of greater severity, duration, or extent are unusual.

Rarely, anaphylactoid reactions have been reported.

Pharmaceutical precautions Store at 2–8°C. The vaccine is used directly as supplied. No dilution or reconstitution is necessary. Phenol in 0.25% is present as preservative.

Pneumovax should be inspected before injection to see that it is a clear, colourless liquid without suspended particles.

All vaccine must be discarded after the expiration date.

Legal category POM.

Package quantities A single-dose, prefilled syringe.

Further information Pneumovax is a polysaccharide vaccine. The vaccine does not contain pneumococcal bacteria, but highly purified chemicals derived from the protective capsules which the bacteria produce. These are called capsular polysaccharides. It has been established that the purified capsular polysaccharides of pneumococci induce antibody production and that such antibody is effective in preventing pneumococcal disease.

Antibody levels develop by the third week following vaccination. Although the duration of protection is at present unknown, previous studies with other pneumococcal vaccines suggest that antibody protection may persist for five years. Type-specific antibody levels induced by Pneumovax decline over a 42-month period of observation, but remain significantly higher than prevaccination levels in almost all recipients who responded initially.

Invasive pneumococcal disease causes high morbidity and mortality in spite of effective antimicrobial control by antibiotics. These effects of pneumococcal disease appear due to irreversible physiological damage caused by the bacteria during the first five days following onset of illness, and irrespective of antimicrobial therapy.

Product licence number 0025/0137.

TRYPTIZOL*

Presentation Tryptizol 75, clear orange, slow-release capsules, marked 'MSD 649', containing 75 mg amitriptyline hydrochloride BP as a pelleted formulation.

Blue, film-coated tablets, marked 'MSD 23', containing 10 mg amitriptyline hydrochloride BP; yellow, film-coated tablets, marked 'MSD 45', containing 25 mg; and brown, film-coated tablets, marked 'MSD 102', containing 50 mg.

Injection, a colourless solution containing per ml 10 mg amitriptyline hydrochloride.

Syrup, a pink suspension containing, in each 5 ml, amitriptyline embonate BP equivalent to 10 mg amitriptyline.

Uses Depression (especially where sedation is required); also effective in nocturnal enuresis where organic pathology is excluded.

Dosage and administration *Depression.*

Oral therapy: Therapy should be started with a low dosage and increased gradually, according to the clinical response and any evidence of intolerance.

Adults – initial dosage: Usually 75 mg a day in divided doses. If necessary, this may be increased to a total of 150 mg a day, the additional doses being given in the late afternoon and/or at bedtime.

A small number of hospitalised patients may require as much as 300 mg a day. Appropriate care must be taken when doses of this level are used.

The sedative effect is usually rapidly apparent. The antidepressant activity may be seen within three or four days or may take up to 30 days to develop adequately.

Adults – maintenance dosage: usually 50–100 mg a day. For maintenance therapy, the total dosage may be given in a single dose preferably in the evening or at bedtime. When satisfactory improvement has been reached, dosage should be reduced to the lowest amount that will maintain relief of symptoms. Maintenance therapy should be continued for three months or longer to lessen the chances of relapse.

Elderly patients: In general, lower dosages are recommended for these patients. A daily dosage of 50 mg may be satisfactory in elderly patients who may not tolerate higher dosages. The required dosage may be administered either as divided doses or as a single dose preferably in the evening or at bedtime.

Parenteral therapy: Parenteral use of amitriptyline should be restricted to patients for whom oral therapy is inappropriate or difficult. Substitute oral therapy as soon as possible. Give 1–2 ml (10–20 mg) four times a day, intramuscularly or intravenously.

Children: Due to lack of clinical experience, Tryptizol is not recommended for the treatment of *depression* in children under 12 years of age.

Enuresis: Children aged 6–10 years may receive 10–20 mg a day, while those aged 11–16 years may need 25–50 mg a day. The recommended dosage must not be exceeded, and therefore Tryptizol 75 is not suitable for the treatment of enuresis. Treatment should not exceed three months.

This medication should be kept out of the reach of children. Tryptizol Syrup can be diluted with Syrup BP.

Because of the wide variation in the absorption and distribution of tricyclic antidepressants in body fluids, dosage should be adjusted to clinical response and not based on plasma levels. However, plasma levels may be used as a guide to toxicity or to non-compliance.

Contra-indications, warnings, etc

Contra-indications: Co-administration with monoamine oxidase inhibitors; prior sensitisation to amitriptyline; not recommended during the immediate recovery phase after myocardial infarction; arrhythmias, particularly heartblock of any degree; mania; severe liver disease; lactation; children under 6 years of age. See also 'Use in pregnancy and the nursing mother', under 'Precautions'.

Precautions: Tryptizol should be used with caution in patients with a history of epilepsy, in patients with impaired liver function and, because of its atropine-like action, in patients with a history of urinary retention, prostatic hypertrophy, narrow-angle glaucoma, or increased intra-ocular pressure. In patients with narrow-angle glaucoma even average doses may precipitate an attack of glaucoma.

Patients with cardiovascular disorders, hyperthyroid

patients, and those receiving thyroid medication or anticholinergic agents should be closely supervised and the dosage of all medications carefully adjusted.

Elderly patients are particularly liable to experience adverse reactions: especially agitation, confusion, and postural hypotension.

Tryptizol may impair alertness in some patients and activities made hazardous by diminished alertness (e.g. driving a car) should be avoided.

When Tryptizol is used for the depressive component of schizophrenia, psychotic symptoms may be aggravated. In manic-depressives, a shift towards the manic phase may occur; paranoid delusions, with or without associated hostility, may be aggravated. In such cases, a major tranquilliser should be given concurrently, or the dosage of Tryptizol reduced.

The risk of suicide remains during treatment of depressed patients and until significant remission occurs. Such patients require careful supervision.

Concurrent administration with ECT may increase the hazards of treatment, and should be limited to patients for whom it is deemed essential. If possible, Tryptizol should be discontinued several days before elective surgery because anaesthesia increases the risk of hypotension and arrhythmias.

Behavioural changes have been observed in children receiving tricyclics for the treatment of enuresis.

Use in pregnancy and the nursing mother: The safety of Tryptizol for use during pregnancy and lactation has not been established. Tryptizol is not recommended during pregnancy, especially during the first and third trimesters unless there are compelling reasons, and in these patients the benefits should be weighed against possible hazards to the foetus, child, or mother. Animal reproduction studies have been inconclusive, and clinical experience has been limited.

Drug interactions: The concurrent use of antidepressants having varying modes of action should be made only with due recognition of their possible potentiation and with a thorough knowledge of their respective pharmacologies. Monoamine oxidase inhibitors can potentiate the effects of tricyclic antidepressants such as Tryptizol, and hyperpyretic crises, severe convulsions, and fatalities have occurred. A minimum of 14 days should elapse between discontinuing an MAOI and starting Tryptizol, which should be introduced cautiously and dosage increased gradually.

Tryptizol may block the antihypertensive action of guanethidine, debrisoquine, bethanidine, and possibly clonidine. It would be advisable to review all antihypertensive therapy during treatment with tricyclic antidepressants.

Amitriptyline should not be given with sympathomimetic agents such as adrenaline, ephedrine, isoprenaline, noradrenaline, phenylephrine, and phenylpropanolamine.

Tryptizol may enhance the response to alcohol, barbiturates, and other CNS depressants. In turn, barbiturates may decrease, and methylphenidate may increase, the antidepressant action of amitriptyline.

Paralytic ileus may occur in patients taking tricyclic antidepressants in combination with drugs having an anticholinergic action.

Caution is advised if patients receive large doses of ethchlorvynol concurrently. Transient delirium has been reported in patients treated with 1 g ethchlorvynol and 75 mg to 150 mg of Tryptizol.

Warnings and adverse effects: In general, Tryptizol is

well tolerated. The side effects given below are essentially a combined list of all those of the tricyclic group of antidepressants. Some of them have not been reported with Tryptizol, but are included because of the similar pharmacologies of the group members. As the antidepressant effects of Tryptizol may not become apparent for the first 2–4 weeks of therapy, patients should be closely monitored during this period.

Cardiovascular reactions: hypotension, postural hypotension, hypertension, tachycardia, palpitations, myocardial infarction, arrhythmias, heart block, stroke. Arrhythmias and severe hypotension are likely to occur with high dosage or in deliberate overdosage.

CNS and neuromuscular: confusional states, disturbed concentration, disorientation, delusions, hallucinations, hypomania, excitement, anxiety, restlessness, insomnia, nightmares, numbness, tingling, and paraesthesiae of the extremities, peripheral neuropathy, incoordination, ataxia, tremors, convulsions, alteration of the EEG, extrapyramidal symptoms, tinnitus.

Anticholinergic: dry mouth, blurred vision, disturbance of accommodation, increased intra-ocular pressure, constipation, paralytic ileus, urinary retention, urinary tract dilatation.

Allergic: skin rash, urticaria, photosensitisation, oedema of face and tongue.

Haematological: bone-marrow depression including agranulocytosis, leucopenia, eosinophilia, purpura, thrombocytopenia.

Gastro-intestinal: nausea, epigastric distress, vomiting, anorexia, stomatitis, unpleasant taste, diarrhoea, parotid swelling, black tongue, rarely hepatitis (including altered liver function and jaundice).

Endocrine: testicular swelling, gynaecomastia; breast enlargement, galactorrhoea, increased or decreased libido, interference with sexual function, elevation or lowering of blood sugar levels, syndrome of inappropriate ADH (antidiuretic hormone) secretion.

Other reactions: dizziness, weakness, fatigue, headache, weight loss, increased perspiration, urinary frequency, mydriasis, alopecia, drowsiness, increased appetite and weight gain (may be a drug reaction or due to relief of the depression). Abrupt withdrawal after prolonged administration has caused nausea, headache and malaise. This is not indicative of addiction.

Adverse reactions such as withdrawal symptoms, respiratory depression and agitation have been reported in neonates whose mothers had taken tricyclic antidepressants in the last trimester of pregnancy.

Side-effects in enuresis: Dosages used in enuresis are low compared with those used in depression, and side-effects are therefore less frequent. The most common are drowsiness and anticholinergic effects. The only other side-effects, reported infrequently at these dosages, have been mild sweating and itching.

Treatment of overdosage: All persons suspected of having taken an overdosage should be admitted to hospital as soon as possible. Treatment is symptomatic and supportive. The stomach should be emptied as quickly as possible by emesis, followed by gastric lavage

upon arrival at hospital. Following lavage, activated charcoal may be given during the first 24–48 hours at a dosage of 20–30 g every four to six hours. An ECG should be taken and close monitoring of cardiac function instituted if there is any sign of abnormality. An open airway and an adequate fluid intake should be maintained, and body temperature regulated.

Intravenous physostigmine salicylate, 1–3 mg, has been reported to reverse the symptoms of tricyclic antidepressant poisoning. Because physostigmine is rapidly metabolised, the dosage of physostigmine should be repeated as required, particularly if life-threatening signs such as arrhythmias, convulsions, and deep coma recur or persist after the initial dose of physostigmine. Because physostigmine itself may be toxic, it is not recommended for routine use.

Standard measures should be used to manage circulatory shock and metabolic acidosis. Cardiac arrhythmias may be treated with neostigmine, pyridostigmine or propanolol. Should cardiac failure occur, use of digitalis should be considered. Close monitoring of cardiac function for not less than five days is advisable.

If convulsions occur, they should be treated with paraldehyde, diazepam or an inhalation anaesthetic. Barbiturates should not be used because Tryptizol increases their CNS-depressant action.

Dialysis is of no value because of low plasma concentrations of amitriptyline. Since overdosage is often deliberate, patients may attempt suicide by other means during the recovery phase. Deaths by deliberate or accidental overdosage have occurred with this class of medicament.

Pharmaceutical precautions Keep containers well closed; store in a cool place, protected from light. The injection and the syrup should also be protected from freezing. Tryptizol Syrup may be diluted with Syrup BP; the mixture should be used within 14 days.

Legal category POM.

Package quantities *Capsules 75 mg:* Bottles of 100.

Tablets 10 mg: Bottles of 100 and 500.

Tablets 25 mg: Bottles of 100 and 500.

Tablets 50 mg: Bottles of 100.

Injection: Vials of 10 ml.

Syrup: Bottles of 200 ml and 1,000 ml.

Further information Tryptizol is a member of the tricyclic group of antidepressants. Its mode of action in man is not known, but it is not a monoamine oxidase inhibitor (special dietary restrictions are not necessary), and it does not act primarily by stimulating the CNS. It has not produced addiction.

Product licence numbers

Capsules 75 mg 0025/0116

Tablets 10 mg 0025/0093

Tablets 25 mg 0025/0094

Tablets 50 mg 0025/0095

Injection 0025/5036

Syrup 0025/5037

* **Trade Mark**

Napp Laboratories Limited
Hill Farm Avenue
Watford
Herts WD2 7RA



AKROTHERM*

Presentation A white ointment containing; Histamine Base 0.034% w/w, Acetylcholine chloride USP 0.20% w/w, Cholesterol USP 1.00% w/w.

Uses Akrotherm exerts a local vasodilator action in the topical treatment of chilblains.

Dosage and administration Gently massage Akrotherm into the affected area three to four times a day.

Contra-indications, warnings, etc None.

Pharmaceutical precautions None.

Legal category P.

Package quantities Tube of 40 g.

Further information May be used on broken chilblains and in conjunction with systemic treatment – provides immediate relief from the itching and burning sensation.

Product licence number 0199/5011.

AUDAX* ANALGESIC EAR DROPS

Presentation Ear drops containing the Mundisal* brand of choline salicylate 20% w/v and of the penetrant ethylene oxide-polyoxypropyleneglycol condensate 1.25% w/v.

Uses For relief of pain, particularly in acute otitis media. Also of use in acute and chronic painful otitis externa and painful chronic otitis media and otalgia generally.

Dosage and administration *Infants, children and adults:* With head tilted to one side the external auditory canal is filled with Audax ear drops. The ear should be plugged with cotton wool soaked with the ear drops or a wick may be inserted if preferred. Audax ear drops should be instilled four-hourly until permanent relief of symptoms is obtained. Cleansing of the ear where necessary facilitates therapy.

Contra-indications, warnings, etc Salicylate sensitivity.

Where infection of the ear necessitates topical and/or systemic antibiotics, the Audax ear drops are designed as an adjuvant therapy.

Pharmaceutical precautions Store in a cool dry area protected from light.

Legal category P.

Package quantities Bottle containing 8 ml with separate dropper.

Further information The low surface tension of Audax ensures rapid penetration of the drops. The choline salicylate gives quick and prolonged analgesia. The pH of Audax ear drops is adjusted to approximate

closely that normally found in the external auditory meatus.

Audax ear drops contain no irritants or sensitising local anaesthetics. Audax ear drops eliminate the need to resort to oral salicylates and other systemic analgesics. In addition, Audax ear drops exert local anti-inflammatory and antipruritic effects in the ear and have their own spectrum of antimicrobial activity.

Product licence number 0337/5004.

BETADINE* AEROSOL SPRAY

Presentation Pressurised bottle containing a golden-brown solution of the Mundidone* brand of Povidone-Iodine USP 5% w/v with nitrogen as the propellant.

Uses As a skin antiseptic for treatment or prevention of infection and to aid healing in ulcers, burns, minor injuries, incisions, etc.

Dosage and administration *Adults, children and infants:* Hold the Betadine aerosol spray about 10 inches from the area to be treated; press valve firmly forwards and downwards to allow the spray to cover the desired area. Allow to dry.

Contra-indications, warnings, etc Do not spray into open eyes. In rare instances of local irritation or sensitivity discontinue treatment.

Pharmaceutical precautions Store in a cool dry place protected from light.

Legal category GSL.

Package quantities Aerosol spray of 88 ml.

Further information Betadine aerosol spray contains Povidone-Iodine, which retains the broad germicidal spectrum of iodine, but is non-stinging and non-irritating to sensitive denuded skin areas.

Betadine aerosol spray is rapidly microbicidal and quickly forms a protective film subjecting pathogens to the prompt and continued germicidal action of Povidone-Iodine.

Product licence number 0337/5022.

BETADINE* ANTISEPTIC PAINT

Presentation A golden brown, alcoholic solution containing the Mundidone* brand of Povidone-Iodine USP 10% w/v.

Uses As a general topical and quick drying antiseptic in the treatment and prevention of infection. It is ideal for Herpes simplex, Herpes zoster, grazes, abrasions, cuts and wounds, or any break in the skin which requires protection from infection.

Betadine antiseptic paint is effective in the treatment

of dermal infections caused by bacteria, fungi, yeasts, and viruses (e.g. Herpesvirus Types I and II).

Dosage and administration Apply Betadine antiseptic paint undiluted, as necessary, to affected area and allow to dry. Use twice daily, and cover with a dressing if desired.

Rinse the brush thoroughly after use.

Contra-indications, warnings, etc In rare instances of local irritation or sensitivity, discontinue treatment.

Pharmaceutical precautions Store in a cool, dry place protected from light.

Legal category P.

Package quantities Glass bottles containing 8 ml with an applicator brush.

Further information Numerous studies have established the rapid microbicidal activity of the Mupidone* brand of Povidone-Iodine contained in Betadine antiseptic paint, both in vivo and in vitro, against Gram-negative and Gram-positive bacteria, fungi, viruses and yeasts. Betadine antiseptic paint is also sporicidal.

Betadine antiseptic paint is effective in the presence of serum, blood, purulent exudate and necrotic tissue.

The applicator brush provided with Betadine antiseptic paint is for ease of application to minor wounds and infections. Rapid, prolonged and complete antiseptic cover is afforded by the use of Betadine antiseptic paint when applied topically twice daily.

Product licence number 0337/0047.

BETADINE* ANTISEPTIC SOLUTION BETADINE* ALCOHOLIC SOLUTION BETADINE* SURGICAL SCRUB

Presentation *Antiseptic Solution:* An aqueous solution containing the Mupidone* brand of Povidone-Iodine USP 10% w/v.

Alcoholic Solution: Contains the Mupidone* brand of Povidone-Iodine USP 10% w/v in an alcoholic solution.

Surgical Scrub: Contains the Mupidone* brand of Povidone-Iodine USP, 7.5% w/v with non-ionic surfactants.

All the preparations are golden-brown in colour.

Uses Degerming the skin pre-operatively and post-operatively for major and minor surgical procedures, and also in the case of the surgical scrub for pre-operative scrubbing and washing by surgeons and theatre staff.

Dosage and administration The antiseptic and alcoholic solutions should be applied full strength as often as needed. The surgical scrub should be used as a pre-operative antiseptic skin cleanser.

Contra-indications, warnings, etc A patch test should be performed in rare cases of iodine sensitivity.

Pharmaceutical precautions Store in a cool, dry place protected from light.

Legal category P.

Package quantities Containers of 500 ml and 5 litres.

Further information Numerous studies have established the rapid microbicidal activity of Povidone-Iodine contained in Betadine germicides, both in vitro and in vivo, against Gram-negative and Gram-positive bacteria,

fungi, protozoa, viruses and yeasts. Povidone-Iodine is also sporicidal.

Betadine scrub and solutions have a rapid and prolonged germicidal action and with repeat usage a cumulative germicidal effect.

Betadine scrub and solutions are active in the presence of serum, blood, purulent exudate and necrotic tissue.

They can be used for the preparation of skin and mucous membranes and for burn and wound disinfection without the risk of systemic toxicity.

Povidone-Iodine as contained in Betadine germicides is not inactivated by soap.

Product licence numbers

Antiseptic solution	0337/5901
Alcoholic solution	0337/5902
Surgical scrub	0337/5903

BETADINE* GARGLE AND MOUTH WASH

Presentation A pleasantly flavoured solution containing the Mupidone* brand of Povidone-Iodine USP 1% w/v. Amber in colour.

Uses For infected inflammatory conditions of the mouth and pharynx caused by bacterial or monilial infections, and in dental surgery.

Dosage and administration *Adults and children:* Use undiluted, or dilute with an equal volume of warm water. Gargle or rinse for at least 30 seconds. Repeat every two to four hours for as long as required.

Contra-indications, warnings, etc In rare instance of local irritation or sensitivity discontinue treatment.

Pharmaceutical precautions Store in a cool dry place protected from light.

Legal category P.

Package quantities Bottles containing 250 ml.

Further information Betadine gargle and mouth wash contains Povidone-Iodine, a complex of iodine which retains all the broad-spectrum germicidal activity of elemental iodine without its disadvantages.

The germicidal activity is maintained in the presence of blood, pus, serum and necrotic tissue.

Betadine gargle and mouth wash does not stain the skin, mucous membranes or teeth despite its powerful germicidal action.

Betadine gargle and mouth wash kills bacteria, viruses, fungi, spores and protozoa and rapidly reduces oral bacterial counts.

Product licence number 0337/0009.

BETADINE* OINTMENT

Presentation A golden-brown, water-soluble ointment containing the Mupidone* brand of Povidone-Iodine USP 10% w/w.

Uses For the treatment or prevention of infection in cuts and abrasions, minor surgical procedures and burns.

Dosage and administration *Adults, children and infants:* The affected skin should be cleaned and dried. Apply Betadine ointment liberally. May be covered with a dressing or bandage. Betadine ointment may be used as often as is required. In the treatment of burns, every

eight hours; in other treatments, apply once daily generally.

Contra-indications, warnings, etc In rare instance of local irritation or sensitivity, discontinue treatment.

Pharmaceutical precautions *Tubes:* Store in a well-closed container in a cool, dry place.

Sachets: Store in a cool dry place.

Legal category GSL.

Package quantities Sachets of 1 g. Tubes of 60 g. Jars of 500 g.

Further information Nil.

Product licence number 0337/5005.

BETADINE* SCALP AND SKIN CLEANSER

Presentation A golden-brown cleansing and sudsing surfactant solution containing the Mundidone* brand of Povidone-iodine USP 7.5% w/v.

Uses For seborrhoeic conditions of skin and scalp, acne vulgaris and other pyogenic skin conditions.

Dosage and administration *For hair and scalp:* Thoroughly wet the hair. Apply as a shampoo to the hair and scalp, rubbing well in. Allow to remain on the scalp for at least five minutes, rinse off with warm water. Reapply and work up into a rich lather before rinsing again.

For skin: Apply directly or with moistened sponge. Cleanse area thoroughly; repeat application and dry with clean or sterile towel or gauze.

Contra-indications, warnings, etc In rare instance of local irritation or sensitivity discontinue treatment.

Pharmaceutical precautions Store in a cool place protected from light.

Legal category GSL.

Package quantities Plastic squeeze bottle containing 100 ml.

Further information Betadine scalp and skin cleanser is neither a primary irritant nor a sensitiser.

It has a highly effective germicidal activity and is free from unpleasant odour.

Betadine scalp and skin cleanser is active in the presence of exfoliate debris and infected scalp lesions, does not stain the skin and does not sting the skin or the eyes. It possesses powerful deodorising properties.

Product licence number 0337/5023.

BETADINE* SHAMPOO

Presentation A golden-brown, cleansing and sudsing surfactant solution containing the Mundidone* brand of Povidone-iodine USP 4% w/v and lanolin.

Uses Seborrhoeic conditions of the scalp associated with excessive dandruff, pruritus, scaling, exudation and erythema of the scalp. Pityriasis capitis. Infected lesions of the scalp – pyoderma (recurrent furunculosis, infective folliculitis and impetigo). Cradle-cap.

Dosage and administration *For adults, children and infants:*

1. Having first wetted the hair apply two or three

capfuls of Betadine shampoo; use warm water to lather. Rinse.

2. Again apply two or three capfuls of Betadine shampoo and massage into the scalp with the tips of the fingers.

3. Work up to a golden lather using warm water.

4. Repeat treatment twice weekly until improvement is noted. Afterwards use Betadine shampoo once a week.

Contra-indications, warnings, etc In rare instance of local irritation or sensitivity, discontinue treatment.

Pharmaceutical precautions Store in a cool place protected from light.

Legal category GSL.

Package quantities Plastic squeeze bottle containing 100 ml.

Further information Betadine shampoo is neither a primary irritant nor a sensitiser.

It has a highly effective germicidal activity and is free from unpleasant odour.

Betadine shampoo is active in the presence of exfoliate debris and infected scalp lesions, does not stain the skin and does not sting the skin or the eyes. It possesses powerful deodorising properties.

Product licence number 0337/5033.

BETADINE* SKIN CLEANSER

Presentation A penetrating golden-brown, sudsing surfactant solution containing the Mundidone* brand of Povidone-iodine USP 4% w/v.

Uses Acne vulgaris of the face and neck, and other pyogenic skin conditions. As an adjuvant to systemic antibiotic therapy in treating septic lesions. For disinfection of the skin (as a liquid soap).

Dosage and administration Apply directly or with moistened sponge to the affected areas, and work up a rich lather. Allow to remain on the skin for three to five minutes, then rinse off thoroughly with warm water and dry with clean or sterile towel or gauze. For pyoderma, repeat twice a day until improvement is noted, and then once a day.

Contra-indications, warnings, etc In rare instance of local irritation or sensitivity, discontinue treatment.

Pharmaceutical precautions Store in a cool place protected from light.

Legal category GSL.

Package quantities Plastic squeeze bottle containing 100 ml.

Further information Betadine skin cleanser is neither a primary irritant nor a sensitiser.

It has a highly effective germicidal activity and is free from unpleasant odour.

Betadine skin cleanser is active in the presence of exfoliate debris and infected skin lesions, does not stain the skin and does not sting the skin or eyes. It possesses powerful deodorising properties.

Product licence number 0337/5034.

BETADINE* SKIN CLEANSER FOAM

Presentation A rich, penetrating cleansing foam,

containing the Mundidone* brand of Povidone-Iodine USP 7.5% w/v.

Uses For pyogenic and seborrhoeic skin infections particularly acne vulgaris and sycosis barbae. As an adjuvant to systemic antibiotic therapy in treating septic lesions. Ideal for disinfection of the hands and skin.

Dosage and administration Shake aerosol bottle well before use. Wet skin and with unit held upright, apply sufficient amount of Betadine skin cleanser foam, preferably with an abrasive sponge, to work up a rich, golden lather. Allow lather to remain on skin for about three minutes. Rinse thoroughly with warm water. Repeat twice a day until improvement is noted. For skin disinfection, use Betadine skin cleanser foam as a soap.

Contra-indications, warnings, etc In rare instance of local irritation or sensitivity, discontinue treatment. Contents under pressure. Do not puncture or store near heat or open flame. Never throw container into fire or incinerator.

Pharmaceutical precautions Store in a cool dry place protected from light, heat and flame.

Legal category GSL.

Package quantities Plastic-coated aerosol bottle containing 100 g.

Further information Betadine skin cleanser foam contains the broad-spectrum microbicide Povidone-Iodine. It is therefore a preparation with rapid bactericidal, fungicidal, sporicidal, protozoacidal and virucidal properties, being particularly effective against the organisms commonly associated with acne and other pyogenic skin conditions, i.e. *Staphylococcus aureus* and *Streptococcus sp.*

Betadine skin cleanser foam is non-stinging, non-staining and non-sensitising to skin and mucosa while retaining the full spectrum of activity of iodine.

The surfactant nature of the rich foam actively degreases seborrhoeic skin conditions, prevents the spread of further infection and preserves the acid mantle of the skin.

Product licence number 0337/0034.

BETADINE* VAGINAL PESSARIES BETADINE* VAGINAL GEL

Presentation As vaginal pessaries each containing the Mundidone* brand of Povidone-Iodine USP 200 mg in a water-soluble base.

As vaginal gel containing the Mundidone* brand of Povidone-Iodine USP 10% w/w.

Both preparations are golden-brown in colour.

Uses Vaginitis due to candidal, trichomonal, non-specific or mixed infections, and pre-operative preparation of the vagina.

Dosage and administration Use throughout the menstrual cycle for two to four weeks.

Pessaries: Insert with applicator night and morning. Each pessary should be wetted with water immediately prior to insertion, thus ensuring maximum dispersion of the active constituent and avoiding risk of local irritation.

Gel: Insert an applicator full of gel (5 g) every night. The regimen may be varied to combine the use of the two

vaginal preparations or in combination with the Betadine* VC kit using one in the morning and one at night.

Contra-indications, warnings, etc If irritation, redness or swelling develop, discontinue use.

Patients with a history of iodine sensitivity should not use Betadine vaginal therapies without prior investigation.

These products are spermicidal and should not be used when conception is desired.

Pharmaceutical precautions Store in a cool dry place protected from light.

Legal category GSL.

Package quantities Pessaries; 28s with applicator.

Gel; 80 g with applicator.

Further information Betadine vaginal pessaries and vaginal gel are fungicidal, trichomonacidal and bactericidal to the pathogenic organisms which cause vaginitis. They retain their powerful germicidal effect in the presence of purulent exudate, blood, serum and necrotic tissue. The treatment does not cause stinging or staining in the vagina. The preparations are water soluble and the golden-brown colouration is easily removed by washing.

Product licence numbers

Pessaries 0337/5019

Gel 0337/5020

BETADINE* VC KIT

Presentation The Betadine VC kit consists of Betadine VC concentrate (containing the Mundidone* brand of Povidone-Iodine USP 10% w/v) 250 ml, with a plastic applicator bottle and vaginal applicator.

Uses As a vaginal cleanser in the treatment of vaginitis due to candidal, trichomonal, non-specific or mixed infections, and for pre-operative disinfection of the vagina.

Dosage and administration Once a day (preferably in the morning), for a fourteen-day period, including days of the menstrual cycle.

The Betadine VC concentrate should be diluted using the measuring cap on the concentrate bottle and used according to the patient instruction leaflet provided.

May be used in combination with Betadine vaginal pessaries or vaginal gel.

Contra-indications, warnings, etc Douching is not recommended in pregnancy.

If irritation, redness or swelling develop, discontinue use. Patients with a history of iodine sensitivity should not use Betadine VC kit without prior investigation.

This product is spermicidal and should not be used when conception is desired.

Pharmaceutical precautions Store in a cool dry place protected from light.

Legal category GSL.

Package quantities Carton containing bottle of 250 ml Betadine VC concentrate, an empty applicator squeeze bottle and a plastic vaginal applicator, with patient instruction leaflet.

Further information Betadine VC kit (antiseptic vaginal cleansing kit) is fungicidal, trichomonacidal,

bactericidal and virucidal. It retains its powerful germicidal effect in the presence of purulent exudate, blood, serum and necrotic tissue.

Product licence number 0337/5021.

BRADILAN* TABLETS

Presentation Enteric and white sugar coated tablets each containing tetranicotinoylfructose (nicofuranose) 250 mg.

Uses In peripheral vascular disease including primary and secondary Raynaud's disease, intermittent claudication, night cramps, perniois and cerebrovascular disease.

In hyperlipidaemia, i.e. hypertriglyceridaemia, hypercholesterolaemia, and lipid abnormalities associated with atherosclerosis.

Dosage and administration Dosage needs to be adjusted to the individual. An average dose of 2 tablets three times a day is often sufficient, but doses of 3-4 tablets three times a day may be indicated in some patients. It is better to start therapy with 2 tablets three times a day and increase this dosage over a period of days until the effects of vasodilation are appreciated by the patient and noticed by the doctor. If minimal facial flushing is well tolerated by the patient the dosage should be maintained at this level. However, the beneficial effects of therapy are not lost by reducing the dosage slightly until flushing disappears.

Contra-indications, warnings, etc Adjust daily dosage to suit each patient individually to ambient temperature.

Patients entering an overheated room or going into a warm bed should not take Bradilan tablets immediately before doing so or they may experience increased vasodilator effects.

The vasodilator effect of Bradilan tablets is enhanced by alcoholic beverages, but their concomitant consumption is not contra-indicated.

Because of the special structure of Bradilan tablets they should not be chewed or broken, but swallowed whole.

Bradilan tablets should not be given in the 24 hours before a surgical operation.

Overdosage: Large amounts of nicotinic acid may increase blood sugar levels, increase intestinal blood flow and skin temperature. Patients with diabetes, a history of ulceration and those susceptible to hyperthermia should have any such symptoms treated.

Pharmaceutical precautions Store in a well-closed container, in a cool dry place protected from light.

Legal category P.

Package quantities 50 and 250 tablets.

Further information With Bradilan tablet therapy a clinical response is observed within days.

Correct Bradilan tablet dosage and continued therapy do not result in continued facial flushing, headache, gastric irritation and nausea which are commonly associated with nicotinic acid and its salts. Because of its sustained therapeutic activity Bradilan tablets need be given only three to four times a day.

Product licence number 0337/5006.

BROVON* INHALANT SOLUTION

Presentation A solution for inhalation containing Atropine Methonitrate BP 0.14% w/v. Adrenaline BP 0.50% w/v and Papaverine Hydrochloride BP 0.88% w/v.

Uses For relief and prevention of bronchospasm in asthma, chronic bronchitis and other respiratory diseases.

Dosage and administration Twice-daily and once-nightly use will prevent attacks. No more than two puffs should be given within thirty minutes. In acute episodes more frequent use may be necessary. In order to ensure that Brovon inhalant solution is atomised to form sufficiently small particles the Brovon Midget Inhaler must be used. By briskly pressing and releasing the rubber bulb a fine mist is produced which is inhaled through the mouth.

Contra-indications, warnings, etc Should not be prescribed with monoamine oxidase inhibitors or with sympathomimetic drugs.

Contra-indicated in patients with hypertension, thyrotoxicosis, acute coronary disease and cardiac asthma.

Overdosage: Administer alpha-adrenergic blocker by intravenous injection and a beta blocker per os. Propranolol must not be given to asthmatics because of the risk of increasing bronchoconstriction.

Pharmaceutical precautions Store in cool dry place protected from light.

Legal category P.

Package quantities Bottles containing 20 ml and 50 ml.

Further information Nil.

Product licence number 0337/5009.

CARYLDERM* GEL SHAMPOO

Presentation A pleasantly perfumed clear yellow gel shampoo containing Carbaryl 1% w/v.

Uses Pediculocide for the treatment of head and pubic lice infestations.

Dosage and administration

The source of infestation should be sought and treated.

1. Wet the hair thoroughly with warm water. Squeeze about two inches of gel shampoo into the hand and rub all over the hair, paying special attention to the roots and the scalp.

2. Apply sufficient shampoo to ensure that no part of the scalp or hair is left uncovered, and work up into a rich lather.

3. Leave for at least five minutes, rinse thoroughly with clean, warm water, and repeat procedure.

4. Comb the hair while wet with a fine-toothed metal comb to remove lice and nits (this is only necessary for cosmetic reasons since the lice and nits are dead).

5. Shampooing may be repeated after seven to nine days.

For pubic lice: Wet hair, and apply shampoo directly to the pubic hair and the hair between the legs and around the anus, and leave for at least five minutes. Cover the skin and hair completely with the shampoo. Work up lather, and then rinse thoroughly. Repeat procedure and finally remove dead crab-lice with a suitable fine-toothed

comb. The shampoo may be used again if desired a week later.

Contra-indications, warnings, etc Children under the age of six months should be treated under medical supervision.

As with all shampoos avoid contact with the eyes.

When the insecticide is used by a school nurse or other health officer in the mass treatment of large numbers of children, it is advisable that protective plastic or rubber gloves be worn.

For external use only.

Overdosage: Empty stomach contents and keep patient warm. In the event of massive ingestion atropine in doses of 1 or 2 mg may be required to counteract cholinesterase inhibition.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Tube of 40 g.

Further information Carylderm gel shampoo contains an insecticide of the carbamate group which is lethal to both lice and their eggs (nits).

It has been shown that less resistance is likely to develop to carbaryl than to some other insecticides used for human infestations. Further, Carylderm gel shampoo has a residual action on the hair.

Product licence number 0337/0044.

CARYLDERM* LOTION

Presentation A clear, colourless alcohol based lotion containing Carbaryl 0.5% w/v.

Uses Pediculocide for the treatment of head and pubic lice infestations.

Dosage and administration

The source of infestation should be sought and treated.

For head lice:

1. Sprinkle the lotion on to dry hair. Rub gently into the scalp. Care should be taken to avoid contact with the eyes.
2. Repeat until hair is thoroughly moistened.
3. Allow to dry naturally – use no heat.
4. After 12 hours, shampoo the hair.
5. Rinse, and comb the hair while wet with a fine-toothed metal comb to remove lice and nits. (This is only necessary for cosmetic reasons, since the lice and nits are dead).
6. May be repeated after seven to nine days.

For pubic lice: The lotion should be applied locally to the pubic hair and the hair between the legs and around the anus and allowed to dry naturally. The lotion may be applied again if desired a week later. The method of application, dosage, etc. are as for the head.

Contra-indications, warnings, etc Children under the age of six months should be treated under medical supervision.

When treating pubic lice, mild stinging of a transient nature may be experienced associated with the antiseptic nature of the alcoholic lotion.

When Carylderm lotion is used by a school nurse or other health officer in the mass treatment of large numbers of children, it is advisable that protective plastic or rubber gloves be worn.

For external use only.

Contains flammable alcohol. Apply and dry with care. Avoid naked flames (e.g. coal, gas or electric fire) or lighted objects (e.g. matches, cigarettes or lighters).

Do not use artificial heat (e.g. electric driers).

Dry in a warm well-ventilated room.

Overdosage: As for ethyl alcohol. Empty stomach contents and keep patient warm. In the event of massive ingestion atropine in doses of 1 or 2 mg may be required to counteract cholinesterase inhibition.

Pharmaceutical precautions Store in a cool place, protected from light.

Legal category P.

Package quantities Sprinkler-top bottle of 55 ml.

Further information An alcoholic based lotion is considered to be the most effective way of administering a high concentration of insecticide to the hair. Carylderm lotion contains an insecticide of the carbamate group, which is rapidly lethal to both lice and their eggs (nits). It has been shown that less resistance is likely to develop to carbaryl than to some other insecticides used for human infestations. Further, Carylderm lotion has a residual action on the hair.

Product licence number 0337/0038.

CHOLEBRIN* TABLETS

Presentation White tablets each containing 500 mg iocetamic acid.

Uses For oral cholecystography and cholangiography.

Dosage and administration Six tablets 12–14 hours before X-ray examination. For visualisation of the biliary ducts, a further 6 tablets should be given three hours before examination.

Contra-indications, warnings, etc The administration of Cholebrin tablets is contra-indicated in patients with advanced hepatorenal disease, severe renal impairment, and in patients known to be allergic to iocetamic acid.

Overdosage: Monitor renal function. Treat gastro-intestinal effects symptomatically.

Pharmaceutical precautions Store in a cool, dry place protected from light.

Legal category P.

Package quantities Catch covers of 6 × 500 mg tablets.

Further information Nil.

Product licence number 0337/5900.

COMPLEMENT* CONTINUS* TABLETS

Presentation Bi-convex yellow tablets, embossed 'C' on one side and  on the other. Each tablet contains 100 mg Vitamin B₆ (Pyridoxine Hydrochloride) in NAPP Laboratories' patented controlled release system.

Uses Deficiency of Vitamin B₆ (Pyridoxine Hydrochloride) caused by usage of the oral contraceptive pill.

Dosage and administration One tablet to be taken daily, or at the discretion of the physician.

Contra-indications, warnings, etc None known.

Overdosage: Ingestion of twenty or more tablets may cause headache and will alter the kinetics of levodopa. No treatment is necessary.

Pharmaceutical precautions Comploment Continus tablets should be stored in a cool place, protected from light.

Legal category P.

Package quantities PVC/foil bubble packs containing 28 tablets.

Further information 50% of women who have symptoms of pessimism, anxiety, dissatisfaction, lethargy and loss of libido associated with the taking of the oral contraceptive pill have been reported to have an absolute deficiency of vitamin B₆ (Pyridoxine hydrochloride) (*Lancet* i, 897, 1973). Comploment Continus tablets will effectively correct such pyridoxine deficiencies. The controlled release system ensures adequate supplementation of the pyridoxine from a single tablet taken daily.

Product licence number 0337/0045.

CRADOCAP* SHAMPOO

Presentation An opaque white, pleasantly perfumed shampoo, contains Cetrimide BP 10% w/w.

Uses For the treatment of Cradle Cap or Scurf Cap in babies.

Dosage and administration

1. Wet the baby's head with a little warm water.
2. Squeeze out approximately $\frac{1}{2}$ to $\frac{3}{4}$ inch of Cradocap Shampoo on to the hand and rub gently into the baby's scalp.
3. Rinse off backwards, thus avoiding any possible contact with the baby's eyes.
4. Repeat instructions 2 and 3.
5. Dry the head gently with the baby's towel.

It is suggested that the treatment is carried out at twice weekly intervals until the condition clears.

Contra-indications, warnings, etc For external use only.

Pharmaceutical precautions Store in a cool dry place.

Legal category GSL.

Package quantities 36 g tube.

Further information Cradle Cap, or Scurf Cap as it is sometimes called, is a type of dandruff which frequently occurs during the first eighteen months of life. A safe and effective remedy is required. Cradocap is such a remedy.

Product licence number 0199/5005.

DIUMIDE*-K CONTINUS* TABLETS

Presentation White and orange film-coated bi-layered tablets, bi-convex in shape embossed DK on one side and (NAPP) on the other. Each tablet contains Frusemide BP 40 mg and Potassium Chloride 600 mg (8m Eq), the

latter incorporated within the patented controlled release system.

Uses Diumide-K Continus tablets are indicated in patients requiring diuresis and concomitant Potassium supplementation.

Indications include cardiac oedema, pulmonary oedema, hepatic oedema, renal oedema and peripheral oedema of various aetiologies.

Dosage and administration The usual adult dose is one tablet daily, normally in the morning. This may be adjusted depending on the condition.

N.B. The tablets should be swallowed whole, and not chewed so as not to destroy the controlled release system constituting the Potassium Chloride layer.

Diumide-K Continus tablets are not suitable for paediatric use.

Contra-indications, warnings, etc *Contra-indications:* Diumide-K Continus tablets are contra-indicated in hyperkalaemia, precomatose states associated with liver cirrhosis, Addison's disease and concomitant administration of Potassium sparing diuretics.

Warnings: Patients with prostatic hypertrophy or impairment of micturition have an increased risk of developing acute urinary retention.

Latent diabetes may become manifest or the insulin requirements of diabetic patients may increase.

Precautions: Care should be taken in patients being concurrently administered cardiac glycosides, hypotensive agents and cephaloridine. Care should also be exercised in patients with renal insufficiency where there is a risk of hyperkalaemia. Diumide-K Continus tablets should be administered with caution during the first trimester of pregnancy.

As with all medicines, Diumide-K Continus tablets should be kept out of the reach of children.

Side-effects: Frusemide is generally well tolerated and the patented Continus tablet ensures virtual absence of gastro-intestinal side-effects often associated with Potassium administration.

In rare instance of allergic reaction treatment should be discontinued. Hyperuricaemia may occur with Frusemide therapy. Bone marrow depression has also been reported as a rare complication and therapy should be withdrawn.

Overdosage: Treatment of overdosage should be aimed at fluid replacement and correction of the resulting electrolyte imbalance.

Pharmaceutical precautions Diumide-K Continus tablets should be stored in a cool dry place protected from light.

Legal category POM.

Package quantities 50 and 250 tablets.

Further information Frusemide produces a rapid and sustained diuresis which lasts for approximately four hours following administration. The potassium chloride content is released from the patented Continus tablet over a prolonged period ensuring maximum absorption, the avoidance of 'flushing out' of the potassium by the action of the diuretic, and virtual freedom from side-effects.

Product licence number 0337/0046.

ESODERM* LOTION

Presentation A clear colourless alcohol based lotion containing Gamma benzene hexachloride BP 1% w/v Dicophane BP 1% w/v.

Uses Pesticide for the treatment of lice and scabies.

Dosage and administration

For scabies:

1. Use dampened cotton wool to apply to all parts of the body except face and scalp.
2. Rub well in and allow to dry naturally.
3. In severe cases repeat on two or three successive days.
4. Use clean underclothing and bed linen after final treatment, and bath.

For head lice:

1. Sprinkle the lotion onto dry hair. Rub gently into the scalp. Care should be taken to avoid contact with the eyes.
2. Repeat until hair is thoroughly moistened.
3. Allow to dry naturally – use no heat.
4. After 12 hours, shampoo the hair.
5. Rinse, and comb the hair while wet with a fine-toothed metal comb to remove lice and nits.
6. Should be repeated after 7–9 days.

Contra-indications, warnings, etc Children under the age of six months should be treated under medical supervision.

When Esoderm lotion is used by a school nurse or other health officer in the mass treatment of large numbers of children, it is advisable that protective plastic or rubber gloves be worn.

Contains flammable alcohol. Apply and dry with care. Avoid naked flames (e.g. coal, gas or electric fire) or lighted objects (e.g. matches, cigarettes or lighters).

Do not use artificial heat (e.g. electric dryers).

Dry in a warm well-ventilated room.

For external use only.

Overdosage: As for ethyl alcohol, empty stomach contents and keep patient warm. In the event of massive ingestion diazepam or soluble barbiturates may be administered to control convulsions. Fat and oil should be avoided and adrenaline should not be given.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities Sprinkler-top bottle of 55 ml.

Further information Gamma benzene hexachloride has a rapid action against *Sarcoptes Scabiei* and the alcoholic base aids penetration of burrows.

Product licence number 0199/5000.

ESODERM* SHAMPOO

Presentation Cream shampoo, cream in colour, containing: Gamma Benzene hexachloride BP 1% w/w, Dicophane BP 1% w/w.

Uses Pesticide for the treatment of lice infestation.

Dosage and administration

1. Soak the hair with hot water.
2. Massage 2 inches of shampoo into the scalp; leave two to three minutes.
3. Rinse with hot water.
4. Repeat (2) and work to lather.
5. Rinse thoroughly with hot water.

6. Comb hair with ordinary comb and then with a fine-toothed comb to remove all lice and nits.

7. Should be repeated after seven to nine days.

Contra-indications, warnings, etc Children under the age of six months should be treated under medical supervision.

When Esoderm shampoo is used by a school nurse or other health officer in the mass treatment of large numbers of children, it is advisable that protective plastic or rubber gloves be worn.

For external use only.

Overdosage: Empty stomach contents and keep patient warm. In the event of massive ingestion diazepam or soluble barbiturates may be administered to control convulsions. Fat and oil should be avoided and adrenaline should not be given.

Pharmaceutical precautions None.

Legal category P.

Package quantities Tube of 40 g. Jar of 300 g.

Further information Esoderm kills head lice. The content of Dicophane and gamma-hexachloride provides an effective pesticide combination.

Product licence number 0199/5001.

FERROCONTIN* CONTINUS* TABLETS

Presentation Red, film-coated, bi-convex, Continus tablets. Each tablet contains the equivalent of 100 mg Ferrous Iron in the form of Ferrous Glycine Sulphate within the patented controlled release system.

Uses Ferrocontin Continus tablets are indicated for the treatment and prophylaxis of iron deficiency anaemia.

Dosage and administration One tablet to be taken daily, or at the discretion of the physician. Ferrocontin Continus tablets should be swallowed whole and not chewed.

Contra-indications, warnings, etc As with all medicines keep out of the reach of children.

Overdosage: Inject Desferrioxamine 2 g intramuscularly. Lavage stomach with 1% sodium bicarbonate. Administer 5 g Desferrioxamine per os. Maintain fluid and electrolyte balance. The physician should be aware that Ferrous Glycine Sulphate will be released into the blood stream for a period of hours from tablets in the intestine.

Pharmaceutical precautions Store in a cool dry place protected from light.

Legal category P.

Package quantities 30 and 250 tablets.

Further information The amino acid-iron chelate Ferrous Glycine Sulphate prevents oxidation to the ferric form in the gastro-intestinal tract, thus enhancing absorption. The use of the patented controlled release system optimises the bioavailability of ferrous iron and minimises the likelihood of side-effects.

Product licence number 0337/0041.

FERROCONTIN* FOLIC CONTINUS* TABLETS

Presentation Pale orange, film-coated bi-convex Continus tablets. Each tablet contains the equivalent of

100 mg Ferrous Iron in the form of Ferrous Glycine Sulphate within the patented controlled release system and 0.5 mg Folic Acid BP.

Uses Ferrocontin Folic Continus tablets are indicated for the prophylaxis of iron and folic acid deficiencies during pregnancy.

Dosage and administration One tablet to be taken daily, or as directed by the physician. Ferrocontin Folic Continus tablets should be swallowed whole and not chewed.

Contra-indications, warnings, etc As with all medicines keep out of the reach of children.

Overdosage: Inject Desferrioxamine 2 g intramuscularly. Lavage stomach with 1% sodium bicarbonate. Administer 5 g Desferrioxamine per os. Maintain fluid and electrolyte balance. The physician should be aware that Ferrous Glycine Sulphate will be released into the blood stream for a period of hours from tablets in the intestine.

Pharmaceutical precautions Store in a cool dry place protected from light.

Legal category POM.

Package quantities 30 and 250 tablets.

Further information The amino acid-iron chelate Ferrous Glycine Sulphate prevents oxidation to the ferric form in the gastro-intestinal tract, thus enhancing absorption. The use of the patented controlled release system optimises the bioavailability of ferrous iron and minimises the likelihood of side-effects. The folic acid content of 1 tablet is unlikely to mask the presence of pernicious anaemia.

Product licence number 0337/0042.

K-CONTIN* CONTINUS* TABLETS

Presentation A pale orange, film-coated, controlled release tablet containing Potassium Chloride BP 600 mg.

Uses For potassium therapy and supplementation in patients on diuretic therapy, geriatric patients, chronic diarrhoea, prolonged use of laxatives and megaloblastic anaemia.

Dosage and administration One K-Contin Continus tablet with each diuretic tablet is the average prescribed dose, but this should be adjusted to individual patient's requirements. The range of recommended dosage is 2-5 K-Contin Continus tablets daily (approximately 16-40 mEq K⁺) or on alternate days if diuretic therapy has been so prescribed. The tablets should be swallowed whole and not chewed.

Contra-indications, warnings, etc In patients with advanced renal failure, hyperkalaemia may develop if K-Contin Continus tablets are given injudiciously.

Signs or symptoms which may indicate ulceration or obstruction of the small bowel in patients taking tablets or capsules containing potassium salts are indications for stopping the treatment with potassium preparations.

Overdosage: Empty stomach contents. Treat mild to moderate hyperkalaemia with sodium polystyrene sulphate by mouth. Severe hyperkalaemia requires electrocardiogram monitoring and calcium gluconate i.v. injection (10 to 30 ml). The physician should be aware that potassium chloride will be released into the blood stream for a period of hours from tablets in the intestine.

Pharmaceutical precautions Store in a well-closed container, in a cool dry place protected from light.

Legal category P.

Package quantities Containers of 500 and 5,000 tablets.

Further information It is well recognised that potassium chloride is the correct salt for all patients who require potassium therapy. The K-Contin Continus tablet permits gradual release of the potassium chloride into the gut physiologically and continuously for 10-12 hours. The release mechanism is dependent on the physical structure of the K-Contin Continus tablet and does not depend on the pH of the gut.

Product licence number 0337/0025.

MORHULIN* OINTMENT

Presentation A white ointment containing in a paraffin and lanolin base:

Cod liver oil BP	11.4% w/w
Zinc oxide BP	38.0% w/w

Uses Treatment of varicose ulcers, pressure sores and minor wounds.

Dosage and administration Spread thinly on gauze to cover affected area and about one inch of surrounding skin; on clean wounds dressing may remain for three days. If discharging wound, change dressing daily.

Contra-indications, warnings, etc None.

Pharmaceutical precautions None.

Legal category GSL.

Package quantities Tube of 50 g. Container of 350 g.

Further information Morhulin is non-irritating, non-sensitising with negligible odour and keeps its consistency at body temperature.

Product licence number 0199/5012.

MORSEP*

Presentation A white cream containing:

Cetrimide BP	0.5% w/w
Vitamin A	70 i.u. per g
Vitamin D ₂	10 i.u. per g

Uses A cream for the treatment of urinary ammonia dermatitis.

Dosage and administration Wash affected area and surrounding skin; gently dry; apply Morsep paying particular attention to the creases in the skin. For protection from napkin rash, repeat at each napkin change.

Contra-indications, warnings, etc None.

Pharmaceutical precautions None.

Legal category GSL.

Package quantities Tube of 40 g. Container of 300 g.

Further information Morsep's dual action relieves soreness and irritation and promotes healing.

Product licence number 0199/5014.

MST* CONTINUS* TABLETS

Presentation MST Continus tablets 10 mg are golden brown, film-coated and bi-convex. Each tablet contains 10 mg of Morphine Sulphate BP incorporated within the patented controlled release system. The tablets are marked  on one side and 10 mg on the other side.

MST Continus tablets 30 mg are dark purple, film coated and bi-convex. Each tablet contains 30 mg of Morphine Sulphate BP incorporated within the patented controlled release system. The tablets are marked  on one side and 30 mg on the other.

Uses MST Continus tablets are indicated for the prolonged relief of severe and intractable pain.

Dosage and administration MST Continus should be used twice daily. The dosage is dependent upon the severity of the pain and the patient's previous history of analgesic therapy.

A patient initially presenting with severe and intractable pain will normally be started on a dosage of one or two MST Continus tablets 10 mg twice daily. Increases in pain or tolerance to the drug will require increases in dosage using MST Continus tablets 10 mg and 30 mg alone or in combination.

A patient transferred from other oral preparations should normally receive the same total twenty four hour morphine dosage divided between the morning and evening administration.

Patients receiving MST Continus tablets in place of parenteral morphine should be given a sufficiently increased dosage to compensate for the reduction in analgesic effects associated with orally administered analgesics.

MST Continus tablets should be swallowed whole and not chewed.

Contra-indications, warnings, etc *Contra-indications:* Respiratory depression, obstructive airways disease. Concurrent administration of monoamine oxidase inhibitors or within two weeks of discontinuation of treatment with them. MST Continus tablets are not recommended for paediatric use or for use in pregnancy.

Precautions: As with all narcotics a reduction in dosage may be advisable in the elderly, in hypothyroidism, and chronic hepatic disease.

Warnings and adverse effects: Tolerance and dependence may occur. MST Continus tablets can be readily combined with the phenothiazines but it should be noted that morphine potentiates the effects of tranquillisers, anaesthetics, hypnotics and sedatives.

Nausea and vomiting may be troublesome (Vide Infra).

Pharmaceutical precautions MST Continus tablets should be stored in a cool, dry place protected from light.

Legal category POM, MDA.

Package quantities

10 mg: pack of 50 tablets.

30 mg: pack of 50 tablets.

Further information Morphine Sulphate BP is readily absorbed from the gastro-intestinal tract following oral administration. The patented controlled release system maintains plasma levels of Morphine over a period of up to twelve hours and reduces the likelihood of Morphine associated side-effects.

Product licence numbers

10 mg 0337/0055.

30 mg 0337/0059.

NITROCONTIN* CONTINUS* TABLETS

Presentation Nitrocontin Continus tablets 2.6 mg are flat, bevelled, pink, controlled release tablets containing Nitroglycerin BP 2.6 mg and embossed NC on one side and with the logo  on the other.

Nitrocontin Continus tablets 6.4 mg are flat, bevelled, pink controlled release tablets containing Nitroglycerin BP 6.4 mg and embossed  on one side and with the logo  on the other.

Uses For the prophylaxis and continued treatment of angina pectoris, whether or not associated with previous history of myocardial infarction. Nitrocontin Continus tablets are indicated in all cases in which sublingual nitroglycerin has provided temporary relief, whether these be cases of classical angina pectoris or the anginal pain subsequent to myocardial infarction.

Dosage and administration The tablets must be swallowed whole. Dosage should always be adjusted according to the response obtained by the individual patient and the severity of the anginal pain. Initially, the recommended dosage is one 2.6 mg tablet morning and evening.

If the symptoms have not been adequately controlled after a week on this regimen, the dosage should be increased to one 6.4 mg tablet morning and evening.

An increase in dosage to 6.4 mg three times daily may be found necessary in severe cases of angina pectoris which have not fully responded to the lesser recommended dosage.

Contra-indications, warnings, etc *Contra-indications:* As with all nitrites, cerebral haemorrhage and brain trauma, incipient glaucoma.

Side-effects: An infrequent side-effect of a transient nature which occurs with all nitrite administration is 'nitrite headache'. This disappears with continued treatment. Although patients develop tolerance to this symptom they do not develop tolerance to the drug. However, such side-effects are virtually absent or substantially diminished with Nitrocontin Continus tablet therapy due to the patented controlled release system.

Overdosage: Empty stomach contents. Administer oxygen if necessary. Treat methaemoglobinemia with intravenous methylene blue. Keep unconscious patients horizontal and lower head. Physicians should be aware that tablets in the intestine will release nitroglycerin for a period of hours.

Pharmaceutical precautions Store in a cool dry place protected from light.

Legal category P.

Package quantities Tablets 2.6 mg: 100 tablets.

Tablets 6.4 mg: 100 tablets.

Further information Nitroglycerin has a twofold action in relieving angina pectoris. It reduces cardiac work and dilates the coronary arteries. Thus, not only is the arterial oxygen requirement of the myocardium lessened, but the amount of oxygenated blood reaching the ischaemic heart is increased.

Nitrocontin Continus tablets provide adequate and

continuous nitroglycerin activity throughout the day and night on a simple b.d. dosage.

The need for sublingual nitroglycerin is substantially reduced as the frequency and severity of anginal attacks are decreased.

Nitrocontin Continus tablets may be co-prescribed with β -blocking agents for enhanced prophylaxis from angina. Nitrocontin Continus tablets actively prevent anginal episodes and reduce heavy dependence on multiple doses of sublingual nitroglycerin administration.

Product licence numbers

Tablets 2.6 mg 0337/5026

Tablets 6.4 mg 0337/5027

OTOSEPTIL* EAR DROPS

Presentation ear drops containing neomycin undecylate (equivalent to neomycin 0.67 mg per ml), tyrothricin (gramicidin and tyrocidin) 1.0 mg per ml, hydrocortisone 1.0 mg per ml and ethylene oxidepolyoxypropylene glycol condensate 10 mg per ml.

Uses Acute and chronic otitis externa including bacterial and fungal infections. Eczematous or seborrhoeic dermatitis of the external auditory meatus. As an adjunctive topical therapy in chronic otitis media, and post-operatively for mastoid cavities and after fenestration operations.

Dosage and administration *Adults, children and infants:* Instil 3–5 drops with the aid of the dropper supplied. A cotton-wool plug well moistened with the ear drops may be inserted if required. Repeat four times a day until relief is obtained. Alternatively, a gauze wick may be inserted and kept moist by the application of the drops four times daily.

Contra-indications, warnings, etc

Contra-indications: Infections caused by insensitive organisms and viral ear infections.

Precautions: The use of antibiotic/corticosteroid ear drops occasionally results in the overgrowth of a non-sensitive organism and signs of inflammation may be suppressed by the corticosteroid. If superinfection occurs the treatment should be stopped and appropriate treatment instituted.

Pharmaceutical precautions Store at 4°C.

Legal category POM.

Package quantities Bottles of 8 ml with separate dropper.

Further information Otoseptil ear drops are antibacterial, anti-fungal and anti-inflammatory. The anti-fungal activity is important since some 20% of cases of otitis externa are primarily of fungal or mixed fungal and bacterial aetiology.

Product licence number 0337/5025.

PHYLLOCONTIN* CONTINUS* TABLETS

Presentation Pale yellow, film-coated tablets with 'SA' on one side and  on the other. Each tablet contains aminophylline 225 mg in the patented controlled release system.

Uses For the treatment and prophylaxis of bronchospasm associated with asthma, emphysema and chronic

bronchitis. Phyllocontin Continus tablets are also indicated in the treatment of cardiac asthma and left ventricular or congestive cardiac failure.

Dosage and administration The usual daily dose is 2 tablets twice a day, taken morning and evening, following an initial week of therapy on 1 tablet twice daily.

Since patients vary in their response to Xanthines, the dosage must be titrated individually, and if maximum response is not achieved, Theophylline plasma levels should be measured. Smoking and consumption of alcohol may increase clearance of Theophylline and therefore, the dosage requirement. While the usual dose is 2 tablets twice daily, factors such as viral infections, liver disease and heart failure, may reduce clearance of Theophylline, and the dosage should be reduced if necessary. A reduction in dosage may be necessary in the elderly patient.

N.B. Tablets should be swallowed whole and not chewed.

Contra-indications, warnings, etc None.

Overdosage: Empty stomach contents. Monitor electrocardiogram and maintain fluid balance. Oral activated charcoal has been found to reduce high theophylline blood levels. In severe poisoning employ charcoal-column haemoperfusion. Treat symptoms on appearance. The physician should be aware that tablets in the intestine will continue to release aminophylline for a period of hours.

Side-effects: The risk of side-effects usually associated with aminophylline and xanthine derivatives such as nausea, gastric irritation, headache and CNS stimulation are absent or much diminished when Phyllocontin Continus tablets are given.

Pharmaceutical precautions Store in a cool, dry place protected from light.

Legal category P.

Package quantities 50 and 250 tablets.

Further information Phyllocontin Continus tablets utilise the patented controlled release mechanism, in which aminophylline is released to give an effective therapeutic blood level, lasting up to 12 hours. This release mechanism therefore minimises the unpleasant side-effects usually associated with oral doses of aminophylline, e.g. nausea and gastric irritation.

Product licence number 0337/0026.

PHYLLOCONTIN* PAEDIATRIC CONTINUS* TABLETS

Presentation Pale orange bi-convex tablets with SA/2 on one side and  on the other. Each tablet contains Aminophylline BP 100 mg in the patented controlled release system.

Uses For the treatment and prophylaxis of childhood bronchospasm associated with asthma, bronchitis and emphysema.

Dosage and administration The recommended paediatric doses are as follows:

Age 4–8 years (approx. weight 15–24 kgs or 34–53 lb): 1 tablet twice a day, taken morning and evening.

Age 8–12 years (approx. weight 24–35 kgs or 53–77 lb): 1 or 2 tablets twice a day.

Conventional oral aminophylline doses in children range from 12–20 mg/kg/24 hours. Some children with chronic asthma require and tolerate much higher doses (25–42 mg/kg/24 hours). The above dosages will therefore depend on the patient's clinical response.

For night-long prophylaxis of bronchospasm, the dosage is 1 Phyllocontin paediatric tablet on going to bed, increased to 2 tablets if necessary.

N.B. The tablets should be swallowed whole and not chewed so as not to destroy the controlled release system constituting the tablet structure.

Contra-indications, warnings, etc Should not be given concomitantly with ephedrine.

Overdosage: Empty stomach contents. Monitor electrocardiogram and maintain fluid balance. Oral activated medical charcoal has been found to reduce high theophylline blood levels. In severe poisoning employ charcoal-column haemoperfusion. Treat symptoms on appearance. The physician should be aware that tablets in the intestine will continue to release aminophylline for a period of hours.

Side-effects: The risks of side-effects usually associated with Aminophylline and Xanthine derivatives such as nausea, gastric irritation, headache and CNS stimulation are absent or much diminished when Phyllocontin Paediatric Continus tablets are given.

Pharmaceutical precautions Store in a cool, dry place protected from light.

Legal category P.

Package quantities 50 and 250 tablets.

Further information Phyllocontin Paediatric Continus tablets utilise the controlled release mechanism, in which Aminophylline is released to give an effective therapeutic blood level, lasting up to 12 hours from a single dose, thus enabling 24 hour prophylaxis on a simple b.d. dosage. The controlled release mechanism minimises the risk of unpleasant side-effects usually associated with oral doses of Aminophylline, e.g. nausea and gastric irritation. Phyllocontin Paediatric Continus tablets are ideal for night long prophylaxis of bronchospasm where Aminophylline therapy is indicated.

Product licence number 0337/0040.

PLESMET* SYRUP

Presentation Blackcurrant flavoured syrup containing the equivalent of 25 mg ferrous iron per 5 ml dose in the form of ferrous glycine sulphate.

Uses Treatment of iron deficiency anaemia in infants, adolescents and adults.

Dosage and administration *Adults:* 5–10 ml three times a day.

Children: 2–5 ml two or three times per day according to age (when necessary Plesmet syrup may be diluted with Syrup Tolu BP to make up a 5 ml dose).

Contra-indications, warnings, etc None.

Pharmaceutical precautions None.

Legal category P.

Package quantities Bottles of 100 ml and 1 litre.

Further information Chelated iron is more readily absorbed and utilised than the more conventional forms of iron. Side effects are virtually absent.

Product licence number 0191/5002

PRESSURISED BROVON* INHALER

Presentation A green, transparent, shatterproof aerosol for inhalation containing Adrenaline BP 0.50% w/v and Atropine Methonitrate BP 0.10% w/v in a freon-alcoholic propellant solution.

Uses For the relief and prevention of bronchospasm in asthma, chronic bronchitis and other respiratory diseases.

Dosage and administration Having removed the dust cap, the unit is held upright, the mouthpiece inserted between the lips, the adaptor is depressed and at the same time the patient inhales deeply. The breath is held for a moment, then the patient slowly exhales, releasing the adaptor at the same time. Each depression releases a consistently accurate measured dose of Pressurised Brovon inhalant containing adrenaline 0.25 mg and atropine 0.05 mg. Approximately 330 doses are obtained from each aerosol.

One 'puff' of Pressurised Brovon inhaler may be used four to six-hourly to prevent attacks. In an acute attack one or two puffs should suffice, repeated if necessary, not more often than every 30 minutes.

Contra-indications, warnings, etc Should not be prescribed with monoamine oxidase inhibitors or with sympathomimetic drugs.

Contra-indicated in patients with hypertension, thyrotoxicosis, acute coronary disease and cardiac asthma.

Overdosage may produce transitory tachycardia or dizziness. As with all atropine-containing preparations dryness of the mouth may occur.

It is highly inadvisable to exceed the recommended dose.

Overdosage: Administer alpha-adrenergic blocker by intravenous injection and a beta-blocker per os. Propranolol must not be given to asthmatics because of the risk of increasing broncho-constriction.

Pharmaceutical precautions Store in a cool, dry area protected from light.

Legal category POM.

Package quantities Aerosol of 17 ml.

Further information The rapid sympathomimetic action of the adrenaline and the less rapid but more prolonged parasympatholytic action of the atropine methonitrate, are both complementary and mutually enhancing in relaxing bronchospasm.

Product licence number 0337/5011.

PRESSURISED ISO-BROVON* INHALER PRESSURISED ISO-BROVON* PLUS INHALER

Presentation A green, transparent, shatterproof aerosol for inhalation containing Isoprenaline Hydrochloride USP 0.35% w/v and Atropine Methonitrate BP 0.10% w/v in a freon/alcohol propellant solution.

The PIB Plus inhaler contains Isoprenaline Hydrochloride USP 1.00% w/v and Atropine Methonitrate BP 0.10% w/v in a freon/alcoholic propellant solution.

Uses For the relief and prevention of bronchospasm in asthma, chronic bronchitis and other respiratory diseases.

Dosage and administration Having removed the dust cap the unit is held upright, the mouthpiece inserted between the lips, the adaptor is depressed and at the same time the patient inhales deeply. The breath is held for a moment, then the patient slowly exhales, releasing the adaptor at the same time. Each depression releases a consistently accurate measured dose of PIB inhalant. Approximately 330 doses are obtained from each aerosol.

The PIB inhalers may be used four- to six-hourly to prevent attacks. In an acute attack one or two 'puffs' should suffice, repeated if necessary, not more often than every 30 minutes.

Contra-indications, warnings, etc Should not be prescribed with monoamine oxidase inhibitors or with sympathomimetic drugs.

Overdosage may produce transitory tachycardia or dizziness. As with all atropine-containing preparations dryness of the mouth may occur.

Contra-indicated in patients with hypertension, thyrotoxicosis, acute coronary disease and cardiac asthma.

It is highly inadvisable to exceed the recommended dose.

Overdosage: Administer alpha adrenergic blocker by intravenous injection and a beta blocker per os. Propranolol must not be given to asthmatics because of the risk of increasing bronchoconstriction.

Pharmaceutical precautions Store in a cool dry place protected from light.

Legal category POM.

Package quantities Aerosol of 17 ml.

Further information Nil.

Product licence numbers

PIB 0337/5012

PIB Plus 0337/5010

PRIODERM* CREAM SHAMPOO

Presentation A light-orange pearlescent cream shampoo containing malathion 1.0% w/w.

Uses Pesticide for the treatment of head and pubic lice.

Dosage and administration The source of infestation should be sought and treated.

For head lice: Wet hair thoroughly with warm water, squeeze about 2 inches of the cream shampoo into the hand and rub all over the hair, paying special attention to the roots and the scalp. Apply sufficient shampoo to ensure no part of the scalp or hair is left uncovered and work into a lather.

Leave for four or five minutes, rinse thoroughly with clean water, and repeat the procedure. Comb the hair while wet with a fine-toothed metal comb to remove lice and nits. (This is only necessary for cosmetic reasons since the lice and nits are dead.) May be repeated after seven to nine days.

For pubic lice: Wet area, and apply shampoo directly to the pubic hair and the hair between the legs and around the anus, and leave for at least five minutes. Cover the skin and hair completely with the shampoo.

Work up a lather, and then rinse thoroughly. Repeat

procedure, and finally remove dead crab-lice with a suitable fine-toothed comb.

Contra-indications, warnings, etc Children under the age of 6 months should be treated under medical supervision.

As with all shampoos, avoid contact with the eyes. When Prioderm cream shampoo is used by a school nurse or other health officer in the mass treatment of large numbers of children, it is advisable that gloves be worn.

For external use only.

Overdosage: Empty stomach contents and keep patient warm. In the event of massive ingestion atropine and pralidoxime may be required to counteract cholinesterase inhibition.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Tube of 40 g.

Further information Prioderm cream shampoo is lethal to both lice and their eggs.

Product licence number 0337/0036.

PRIODERM* LOTION

Presentation A clear colourless alcohol based lotion containing Malathion 0.5 w/v.

Uses A pesticide for the treatment of head lice, pubic lice and scabies.

Dosage and administration The source of infestation should be sought and treated.

For head lice:

1. Sprinkle the lotion on the hair. Rub gently into the scalp. Care should be taken to avoid the eyes.
2. Repeat until the scalp is thoroughly moistened.
3. Allow to dry naturally – use no heat.
4. After 12 hours shampoo the hair.
5. Rinse and comb the hair while wet with a fine-toothed metal comb to remove lice and nits (this is only necessary for cosmetic reasons, since the lice and nits are dead).
6. May be repeated after seven to nine days.

For pubic lice: The lotion should be applied locally to the pubic hair and the hair between the legs and around the anus. The method of application, dosage etc. are as for the head.

For scabies:

1. Use dampened cotton wool to apply to all parts of the body except face and scalp.
2. Rub well in and allow to dry naturally.
3. Use clean bed linen and underclothes after final treatment. Do not bathe until twelve hours after treatment.

Contra-indications, warnings, etc Contains flammable alcohol. Apply and dry with care. Avoid naked flames (e.g. coal, gas or electric fire) or lighted objects (e.g. matches, cigarettes or lighters).

Do not use artificial heat (e.g. electric dryers).

Dry in a warm well-ventilated room.

Children under the age of 6 months should be treated under medical supervision.

When treating pubic lice, mild stinging of a transient nature may be experienced associated with the antiseptic nature of the alcoholic lotion.

When Prioderm lotion is used by a school nurse or other health officer in the mass treatment of large numbers of children, it is advisable that protective plastic or rubber gloves be worn.

For external use only.

Overdosage: As for ethyl alcohol, empty stomach contents and keep patient warm. In the event of massive ingestion atropine and pralidoxime may be required to counteract cholinesterase inhibition.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities Sprinkler-top bottle of 55 ml.

Further information Prioderm lotion is rapidly lethal to both the lice and eggs and affords several weeks' protection.

The volatile alcoholic base evaporates to dryness within one hour leaving a high concentration of malathion on the hair.

Product licence number 0199/5002.

SEDONAN* EAR DROPS

Presentation Eardrops containing phenazone BPC 5% w/w and chlorbutol 1% w/w in anhydrous glycerin.

Uses For the relief of pain due to acute and chronic otitis media, otitis externa (acute and chronic), furuncles, boils and inflammation of the external auditory canal.

Dosage and administration Instil 4–5 drops with the aid of the dropper into the external auditory canal, and plug with cotton wool. Repeat as required. It is not necessary to warm the drops.

Contra-indications, warnings, etc The action of Sedonan ear drops is purely analgesic and where middle ear infection is present, it is a useful adjuvant to antibiotic therapy.

Pharmaceutical precautions Store in a cool dry place protected from light.

Legal category P.

Package quantities Bottle containing 8 ml with separate dropper.

Further information Nil.

Product licence number 0337/5008.

TEEJEL* GEL (MOORE'S*)

Presentation A colourless, analgesic, antimicrobial gel for topical application containing the Mundisal* brand of choline salicylate 8.7% w/w and cetyltrimethylbenzylammonium chloride 0.01% w/w in a vehicle formulated to enhance the therapeutic effect.

Uses Relief of pain and infection in and around the mouth in oral ulcers, including aphthous, traumatic and herpetic. Infant teething and denture chafing. Painful stomatitis, gingivitis and glossitis.

Dosage and administration *Adults:* Using a clean finger massage approximately half an inch of Teejel gel onto the tender, painful area. The gel may be applied every three to four hours as required.

Children: (from 4 months to 2 years): Using a clean finger, massage approximately a quarter of an inch of the Teejel gel onto the affected area. The gel may be applied every three to four hours as required.

Contra-indications, warnings, etc Contra-indicated in salicylate sensitivity.

Pharmaceutical precautions Store in a cool, dry place.

Legal category GSL.

Package quantities Sealed tubes containing 10 g.

Further information Nil.

Product licence number 0337/5016.

TRILISATE* TABLETS

Presentation Pale orange, capsule shaped, scored tablets containing 500 mg salicylate as Choline Magnesium Trisalicylate. The tablets embossed 'NAPP 500' on one side and 'TRILISATE' on the reverse.

Uses Trilise tablets are indicated for relief of the signs and symptoms of rheumatoid arthritis, osteoarthritis and other arthroses.

Dosage and administration Two tablets twice a day for osteoarthritis and mild to moderate arthroses. Three tablets twice a day for rheumatoid arthritis and the more severe arthroses.

Contra-indications, warnings, etc *Contra-indications:* Hypersensitivity to aspirin. Active peptic ulceration. Haemophilia.

Precautions: Concurrent administration with other analgesics containing aspirin. As with other salicylate, Trilise tablets should be used with caution in patients with chronic renal insufficiency, or with erosive gastritis or peptic ulcer.

Trilise tablets should be used with caution in pregnancy.

Warnings and adverse effects: May induce gastrointestinal haemorrhage. Reports indicate that when salicylates are given with steroids, the butazones or alcohol, the risk of gastrointestinal ulceration is increased.

Trilise tablets are not recommended for children under twelve years of age. As with all medicines, Trilise tablets should be kept out of reach of children.

Overdosage: Empty stomach contents and lavage stomach with 5% sodium bicarbonate solution. Severe overdosage should be treated by diuresis induced by intravenous saline with sodium bicarbonate, or dextrose solution. Electrolyte levels and acid base balance should be monitored and corrected as necessary.

Pharmaceutical precautions Trilise tablets should be stored in a cool, dry place, protected from light.

Legal category P.

Package quantities Containers of 60 tablets.

Further information When Trilise tablets are administered, the salicylate is absorbed rapidly and reaches peak blood levels within two hours. At recommended doses, the therapeutic range of 5 to 30 mg/100 ml is achieved, and a steady state condition is normally reached after 4–5 doses.

Trilise tablets do not cause any significant faecal blood loss nor do they affect platelet aggregation.

Trilistate tablets do not cause any observable stomach mucosal irritation as determined by endoscopic examination.

Product licence number 0337/0053.

XERUMENEX* EAR DROPS

Presentation Ear drops containing triethanolamine polypeptide oleate condensate 10% w/w.

Uses Routine removal of excessive or impacted wax. Removal of wax to facilitate inspection of the tympanum or audiometry.

Dosage and administration With head tilted to the side at 45° angle fill ear canal with drops. Insert cotton wool plug soaked in Xerumenex and allow the drops to remain in the ear for 15–30 minutes. The drops should not be allowed to remain in the ear longer. Then gently flush or wash the ear with lukewarm water, using a soft rubber syringe and avoiding excessive pressure. If a second application is necessary, in unusually hard impactions, the procedure may be repeated.

Contra-indications, warnings, etc Use with care in presence of perforated ear drum.

Patients using Xerumenex at home should be instructed never to attempt to remove wax themselves by the insertion of objects such as matchsticks and hairpins, nor to leave the drops in for longer than 15–30 minutes.

On rare occasions patients who misuse the drops and leave them in longer than advised develop a localised skin reaction.

Pharmaceutical precautions Store in a cool, dry place protected from light.

Legal category P.

Package quantities Bottle of 8 ml with separate dropper.

Further information Nil.

Product licence number 0337/5007.

X-PREP* LIQUID

Presentation A chocolate-flavoured brown liquid purgative containing purified, standardised extract of senna fruit equivalent to 142 mg Sennosides A and B in each 71 ml dose.

Uses A single-dose pre-radiographic purgative given the day prior to radiographic examination, particularly in gastro-intestinal and urological procedures.

Dosage and administration *Adults:* The contents of a complete bottle, 71 ml should be taken between 2 and 4 pm on the day prior to X-ray examination. This should be followed by at least a tumbler full of water.

Children (under 14 years) and frail underweight patients: The dosage is 1 ml per kg body weight taken between 2 and 4 pm on the day before the examination. The dosage may be split into equal volumes with one hour between each administration. Each administration should be followed by a tumbler full of water. Patients should be advised to expect a strong, thorough bowel action to begin approximately six to eight hours later.

Contra-indications, warnings, etc Mild to severe griping and some nausea occur occasionally, as with all purgatives; however, these are generally less of a problem with X-Prep liquid.

A light, bland, fat-free meal should precede administration. No solid food should be taken after administration and nothing at all after 10 pm on the day prior to X-ray examination.

In diabetic patients, the doctor should be aware of the sugar content of X-Prep liquid (46.86 g per 71 ml dose).

The usual clinical contra-indications for purgatives apply to X-Prep liquid.

Pharmaceutical precautions Store in a cool dry place protected from light.

Legal category P.

Package quantities Bottles containing 71 ml.

Further information Nil.

Product licence number 0337/5017.

**Trade Mark*

ALBUCID* EYE DROPS
ALBUCID* EYE OINTMENT

Presentation Albucid Eye Drops contain 10%, 20% and 30% sulphacetamide sodium pH adjusted. Sodium pentachlorophenate, 0.01%, is included as a preservative.

Albucid Eye Ointment contains 2½% and 6% sulphacetamide sodium pH adjusted in a greasy base and 10% sulphacetamide sodium pH adjusted in a water-miscible base.

Uses *Albucid Eye Drops: Albucid Eye Drops 10%:* Mild infections of the conjunctiva and eyelids.

Industrial eye injuries. Prophylaxis against infection.

Albucid Eye Drops 20%: Conjunctivitis and ophthalmia neonatorum.

Albucid Eye Drops 30%: Severe conjunctivitis. Corneal ulceration including dendritic ulceration. Trachoma.

Albucid Eye Ointment: Albucid Eye Ointment 2½%: Mild infections of the conjunctiva and eyelids. Industrial eye injuries. Prophylaxis against infection.

Albucid Eye Ointment 6%: Conjunctivitis. Trachoma. Corneal ulceration including dendritic ulceration.

Albucid Eye Ointment 10%: Blepharitis and styes.

Dosage and administration *Albucid Eye Drops:* Adults and children: 2–4 drops two to six hourly.

Albucid Eye Ointment: Adults and children: 2½% and 6% at night. 10% apply to lids two to four times daily.

Contra-indications, warnings, etc Known sensitivity to sulphonamides.

Side-effects: Some transient irritation may occur, especially with the higher concentrations.

Pharmaceutical precautions Store at room temperature. Do not freeze.

Legal category POM.

Package quantities *Albucid Eye Drops (all strengths):* Opaque white polythene bottles with coloured caps, containing 10 ml sterile solution. Colour coding of caps:

10% drops – green

20% drops – brown

30% drops – red

Albucid Eye Ointment (all strengths): 4 g tube sterile.

Further information Nil.

Product licence numbers

Albucid Eye Drops 10% 0188/5912

20% 0188/5911

30% 0188/5910

Albucid Eye Ointment 2½% 0188/5915

6% 0188/5914

10% 0188/5916

ALGESAL*

Presentation Off-white, lavender-scented cream containing diethylamine salicylate 10% w/w in a vanishing cream base.

Uses Analgesic balm for use in neuralgia, fibrositis, lumbago, sciatica. Pain in muscles, joints and soft tissues due to rheumatism, injury and over-use.

Dosage and administration Algesal should be massaged over the whole of the affected area until the cream has been fully absorbed and the skin is dry. This may be repeated several times a day as often as the pain demands. If the skin is too tender for massage in conditions such as cellulitis, Algesal may be applied as a liberal dressing on lint or gauze.

Contra-indications, warnings, etc Algesal should not be used if the surface of the skin is broken.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Collapsible tubes of 40 g.

Further information Nil.

Product licence number 1752/5000.

ASMAPAX* TABLETS

Presentation Buff-coloured round, bevelled tablet with 'Asmapax' and 'N' on one side and bisecting line on the obverse. Each tablet contains:

Ephedrine resinate (equivalent to	
Ephedrine Hydrochloride BP 50 mg)	123 mg
Theophylline Hydrate BP	65 mg

Uses Prolonged action bronchodilator.

Relief of bronchospasm in chronic bronchitis asthma and similar disorders.

Dosage and administration *Adults:* 1–2 tablets two or three times a day.

Children 5–12 years: ½ tablet two or three times a day, or as directed.

Contra-indications, warnings, etc A known sensitivity to ephedrine is the only absolute contra-indication, but Asmapax should be used with caution in patients with cardiac conditions, hypertension, hyperthyroidism or prostatic enlargement. Like all sympathomimetic amines, ephedrine should not be used in conjunction with monoamine oxidase inhibitors.

The recognised central stimulatory effects and occasional urinary retention caused by ephedrine are rare, due to the sustained release that resination of ephedrine produces.

In cases of overdosage, gastric lavage should be undertaken, followed by mild sedation.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Containers of 30 and 250 tablets.

Further information Nil.

Product licence number 0188/5920.

CLARADIN*

Presentation Round white bevelled edge tablets with a breakline. Each tablet contains aspirin 300 mg in an effervescent base.

Uses Analgesic and antipyretic at recommended dosage. For conditions where a truly soluble aspirin tablet will provide the most effective and acceptable treatment, i.e. relief of mild to moderate pain and/or reduction of fever associated with upper respiratory tract infections and painful or febrile disorders, such as influenza, pyrexia, neuralgia, rheumatic pain, dysmenorrhoea, migraine pain.

Dosage and administration *Adults:* 2–3 tablets every four hours. Do not exceed 13 tablets in 24 hours unless so directed.

Children: 4–6 years: $\frac{1}{2}$ tablet every four hours.

6–12 years: 1 tablet every four hours. Do not exceed 4 tablets (4–6 years) or 8 tablets (6–12 years) in 24 hours unless directed.

Discard remainder of tablet which will deteriorate once removed from foil.

Claradin Tablets should be allowed to dissolve completely in half a glass of water before administration.

Contra-indications, warnings, etc

Contra-indications: Active peptic ulceration. Haemophilia. Hypersensitivity.

Use in pregnancy: There is clinical or epidemiological evidence of safety in human pregnancy.

Precautions: Aspirin may prolong labour and contribute to maternal and neonatal bleeding, and is best avoided at term. May enhance the effects of anti-coagulants. May inhibit action of uricosurics. May precipitate bronchospasm. May induce attacks of asthma in susceptible subjects.

Warnings and adverse effects: Hypersensitivity to asthma. May induce gastro-intestinal haemorrhage, occasionally major.

Side-effects: Reports of side-effects are infrequent.

Overdosage: The conventional treatment of salicylate overdosage should be employed. Gastric lavage, forced alkaline diuresis and supportive therapy.

Pharmaceutical precautions Store at room temperature in a dry place and do not remove tablets from the foil until required.

Legal category P.

Package quantities Claradin Tablets are available in cartons of 100 tablets (10 strips of 10 tablets). The tablets are packed in moisture-proof aluminium foil.

Further information Claradin Tablets present aspirin in an effervescent form which dissolves completely in water giving a clear solution with a slight citrus flavour. Claradin has a sodium ion content of 7.1 mEq per tablet.

Product licence number 0188/0010.

CORTUCID* EYE DROP CREAM

Presentation Cortucid is a bland, fluid cream containing sulphacetamide sodium pH adjusted 10.0% w/w, hydrocortisone acetate 0.5% w/w in a water miscible cream base.

Uses Cortucid gives prompt relief of inflammatory conditions of the eye, whilst protecting the eye against the increased hazard of infection resulting from the use of a corticosteroid.

Cortucid is for the treatment of inflammatory eye conditions of either bacterial or allergic origin.

Dosage and administration It is suggested that the cream should be dropped into the eye every three to six hours until the condition improves (about two days). Thereafter the number of applications per day may be reduced, but treatment should be continued for at least two days after the condition has subsided.

Contra-indications, warnings, etc Cortucid should not be used in patients with ocular tuberculosis, herpes ophthalmicus, corneal ulceration, trachoma or glaucoma.

Cortucid is contra-indicated also in patients exhibiting true sensitivity to one of the ingredients.

Precautions: Topical administration of any corticosteroid to pregnant animals can cause abnormalities of foetal development. The relevance of this finding in human beings has not been established, however, topical steroids should not be used extensively in pregnancy i.e. in large amounts or for prolonged periods.

In infants, long term continuous topical therapy should be avoided. Adrenal suppression can occur even without occlusion.

Pharmaceutical precautions Store in a cool, dry place.

Legal category POM.

Package quantities Cortucid is packed in tubes containing 3 g.

Further information Inflammation of the eye, if allowed to persist, may result in the formation of vision-impairing scar tissue. Cortucid is formulated with hydrocortisone to safely suppress the inflammation and with sodium sulphacetamide, long considered to be the most suitable bacteriostat for local application in the eye.

Product licence number 0188/0010.

GENTICIN* CREAM GENTICIN* OINTMENT

Presentation Gentacin Cream is a white, smooth cream which contains gentamicin sulphate $\equiv$ 0.3% w/w gentamicin base (3,000 units per 1 g) in a water-miscible base.

Gentacin Ointment is a colourless, opaque ointment which contains gentamicin sulphate $\equiv$ 0.3% w/w gentamicin base (3,000 units per 1 g) in a greasy base.

Uses The unique broad spectrum of activity of Gentacin Cream and Ointment makes them ideally suitable for the topical treatment of all bacterial skin conditions.

Gentacin Cream and Ointment are indicated particularly in infected wounds, impetigo, varicose ulcers, Decubitus ulcers, Sycosis barbae, folliculitis, burns.

Dosage and administration Gentacin Cream and Ointment are intended for topical use only and should be

applied three to four times daily to the infected area, covering with a gauze dressing if necessary. Cream preparations are recommended for moist lesions and ointment for dry conditions.

Contra-indications, warnings, etc There are no specific contra-indications except in cases of true sensitivity to one of the ingredients.

Pharmaceutical precautions Store at room temperature. Do not freeze.

In order to preserve the therapeutic activity of these products they should not be diluted.

Legal category POM.

Package quantities Gentacin Cream and Ointment are available in 15 g and 100 g tubes.

Further information The unique range and degree of antibacterial activity of Gentacin coupled with freedom from troublesome side effects make it the antibiotic of choice for bacterial skin conditions, particularly where the pathogens involved or their sensitivity to antibiotics are unknown.

Product licence numbers

Gentacin Cream 0188/5926

Gentacin Ointment 0188/5927

GENTACIN* EYE/EAR DROPS

Presentation Gentamicin sulphate $\equiv$ 0.3% w/v gentamicin base in sterile aqueous isotonic solution. 10 ml opaque white polythene bottles with white plastic caps. Benzalkonium chloride and borax are included as preservatives.

Uses Gentacin (gentamicin) is a proven bactericidal antibiotic active against an extremely broad spectrum of Gram-positive and Gram-negative bacteria. Gentacin Eye/Ear Drops are therefore particularly useful in all external bacterial infections of the eye, where the bacterial organisms are often very varied.

In particular Gentacin Eye/Ear Drops are indicated in conjunctivitis, blepharitis, styes, corneal ulcers, prophylaxis in trauma.

Gentacin Eye/Ear Drops have also been used extensively in infected ear conditions.

Dosage and administration *For adults and children:*

Eyes: 1–3 drops instilled in affected eye three to four times a day or as required.

Ears: The area should be cleaned and 2–4 drops instilled three to four times a day and at night. In middle ear infections the cavity may be filled with drops.

Contra-indications, warnings, etc No special precautions are indicated.

Pharmaceutical precautions Store at room temperature. Do not freeze.

Legal category POM.

Package quantities Gentacin Eye/Ear Drops are available in opaque white polythene bottles with white plastic caps containing gentamicin sulphate $\equiv$ 0.3% w/v gentamicin base (3,000 units/ml).

Further information Gentisone HC Ear Drops are also available where a mild steroid (hydrocortisone acetate 1.0% w/v) is required in addition to Gentacin

(gentamicin sulphate 0.3% w/v) to treat infections complicated by an inflammatory condition such as often occurs in the outer ear.

Product licence number 0188/5007.

GENTACIN* EYE OINTMENT ▼

Presentation Gentacin Eye Ointment is a sterile, colourless, opaque ointment which contains gentamicin sulphate $\equiv$ 0.3% w/w gentamicin base (3,000 units per 1 g) in a greasy base.

Methylhydroxybenzoate and propylhydroxybenzoate are included as preservatives.

Uses Gentacin (gentamicin) is a proven bactericidal antibiotic active against an extremely broad spectrum of Gram-positive and Gram-negative bacteria. Gentacin Eye Ointment is therefore particularly useful in all external bacterial infections of the eye, where the bacterial organisms are often very varied.

In particular Gentacin Eye Ointment is indicated in conjunctivitis, blepharitis, styes, corneal ulcers, prophylaxis in trauma.

Dosage and administration *For adults and children:*

Gentacin Eye Ointment should be applied three to four times daily to the infected area.

Contra-indications, warnings, etc There are no specific contra-indications except in cases of true sensitivity to one of the ingredients.

Pharmaceutical precautions Store at room temperature. In order to preserve the therapeutic activity of Gentacin Eye Ointment it should not be diluted.

Legal category POM.

Package quantities Gentacin Eye Ointment is available in 3g tubes.

Further information The unique range and degree of antibacterial activity of Gentacin coupled with freedom from troublesome side effects make it the antibiotic of choice for bacterial eye conditions particularly where the pathogens involved or their sensitivity to antibiotics are unknown.

Product licence number 0188/0057.

GENTACIN* HC CREAM GENTACIN* HC OINTMENT

Presentation Gentacin HC cream is a white, smooth cream which contains hydrocortisone acetate 1.0% w/w, gentamicin sulphate $\equiv$ 0.3% w/w gentamicin base (3,000 units per 1 g) in a water-miscible base.

Gentacin HC Ointment is a colourless, opaque ointment which contains hydrocortisone acetate 1.0% w/w, gentamicin sulphate $\equiv$ 0.3% gentamicin base (3,000 units per 1 g) in a greasy base.

Uses Gentacin has been combined with 1.0% w/w hydrocortisone for the treatment of those inflammatory skin conditions where secondary bacterial infections may be involved.

Gentacin HC Cream and Ointment are indicated particularly in infective eczemas (infantile, atopic, allergic, seborrhoeic, etc), infective contact dermatitis, infected pemphigus, otitis externa, infected pruritus.

Dosage and administration Genticin HC Cream and Ointment are intended for topical use only and should be applied three to four times daily to the infected area, covering with a gauze dressing if necessary. Cream preparations are recommended for moist lesions and ointment for dry conditions.

Contra-indications, warnings, etc There are no specific contra-indications except in cases of true sensitivity to one of the ingredients.

Precautions: Topical administration of any corticosteroid to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established, however, topical steroids should not be used extensively in pregnancy i.e. in large amounts or for prolonged periods.

In infants long term continuous topical therapy should be avoided. Adrenal suppression can occur even without occlusion.

Steroids may delay the healing of leg ulcers or pressure sores.

Pharmaceutical precautions Store at room temperature. Do not freeze.

In order to preserve the therapeutic activity of these products they should not be diluted.

Legal category POM.

Package quantities Genticin HC Cream and Ointment are available in tubes of 15 g.

Further information The unique range and degree of antibacterial activity of Genticin coupled with freedom from troublesome side-effects make it the antibiotic of choice for bacterial skin conditions, particularly where the pathogens involved or their sensitivity to antibiotics are unknown.

Product licence numbers

Genticin HC Cream	0188/5922
Genticin HC Ointment	0188/5928

GENTICIN* INJECTABLE GENTICIN* PAEDIATRIC INJECTION

Presentation *Genticin Injectable:* Each 2 ml multidose vial and snap-off ampoule contains a 2 ml solution of gentamicin sulphate $\equiv$ 80 mg gentamicin base, with preservatives.

Genticin Paediatric Injection: Each 2 ml multidose vial contains a 2 ml solution of gentamicin sulphate $\equiv$ 20 mg gentamicin base, with preservatives.

Uses Genticin (gentamicin) is a proven bactericidal antibiotic active against an extremely broad spectrum of Gram-positive and Gram-negative pathogens including *Escherichia coli*, *Klebsiella*, *Proteus*, *Pseudomonas aeruginosa* and antibiotic-resistant strains of *Staph. aureus*. Genticin is often active against strains resistant to streptomycin, kanamycin and other unrelated antibiotics.

Indications for the use of Genticin are bacteraemia, septicaemia, urinary-tract infections, severe chest infections, severe neonatal infections and other systemic infections due to susceptible bacteria.

Dosage and administration Genticin is normally administered intramuscularly, but may be given intravenously if required.

If intravenous administration is necessary the normal intramuscular dose should be given as a bolus injection

into the tubing of the giving set or directly into the venous system over a period of two to three minutes. Genticin should not be given as a slow infusion or mixed with other drugs before use (see technical literature and below for incompatibilities).

With either intramuscular or intravenous administration the following dosage applies:

Adults: 60 kg and over: 80 mg eight-hourly.

Less than 60 kg: 60 mg eight-hourly.

Urinary-tract infections: As above.

Alternatively, if renal function is not impaired, 160 mg once daily may be used.

In life-threatening infections the frequency of dosage may need to be increased to six-hourly and the quantity of each dose may also be increased at the discretion of the clinician up to a total dosage of 5 mg/kg in 24 hours. In such cases it is advisable to monitor gentamicin serum levels.

Children: Genticin Paediatric Injection is one quarter the strength of Genticin Injectable (see above).

In children and in neonates, it can be expected that serum levels will be lower than those found in adults at equivalent dosage per body weight.

The recommended paediatric dosage is therefore as follows:

Up to 12 years: 6.0 mg/kg in 24 hours in 3 equally divided doses (i.e. 2.0 mg/kg eight-hourly).

In infants up to two weeks this dosage should be given in 2 equally divided doses (i.e. 3.0 mg/kg 12-hourly).

Serum levels should preferably be monitored daily.

In neonates, infants and children, subsequent dosage will often need to be increased to achieve therapeutic serum levels. Peak levels occur about one hour after intramuscular injection and should reach 4 mcg/ml, but not exceed 10 mcg/ml.

Contra-indications, warnings, etc There is no absolute contra-indication other than sensitivity to one of the ingredients.

Since those toxic symptoms that can be elicited are usually reversible, and since the conditions predisposing towards excess serum levels are well defined, it is considered that gentamicin is a relatively safe antibiotic for systemic therapy. As with all aminoglycosides, at critical levels gentamicin exhibits toxicity. With gentamicin the vestibular mechanism may be affected when serum levels of 10 μ g/ml are exceeded. This is usually reversible if observed promptly and the dose adjusted. In the patient with normal renal function it is virtually impossible to achieve these levels at standard dosage. Where renal function is impaired through disease or old age the frequency, but not the amount, of each dose should be reduced according to the degree of impairment. Gentamicin is excreted by simple glomerular filtration, and dosage frequency may be predicted by assessing creatinine clearance rates or blood urea and reducing the frequency accordingly. The following table may be useful when treating adults.

It is also advisable to check serum levels to confirm that peak (one hour) levels do not exceed 10 μ g/ml.

Genticin Injectable should not be used in pregnancy except in life-threatening situations.

Pharmaceutical precautions Genticin is a remarkably stable antibiotic and does not require to be kept under refrigerated conditions. In general we would not advise mixing Genticin Injectable with any other drug prior to administration.

<i>Blood urea (mg/100 ml)</i>	<i>Creatinine clearance (GFR) (ml/min)</i>	<i>Dose and frequency of administration</i>
< 40	> 70	80 mg† 8-hourly
40–100	30–70	80 mg† 12-hourly
100–200	10–30	80 mg† daily
> 200	5–10	80 mg† every 48 hours
Twice-weekly intermittent haemodialysis	< 5	80 mg† after dialysis

† 60 mg if body weight < 60 kg.

In particular the following are incompatible in mixed solution with Gentamicin Injectable: penicillins, cephalosporins, Erythromycin, Lipiphysan, heparins, †sodium bicarbonate.

Dilution in the body will obviate the danger of physical and chemical incompatibility and enable Gentamicin Injectable to be given concurrently with the drugs listed above either as a bolus injection into the drip tubing, with adequate flushing, or at separate sites. However, in the case of carbenicillin and gentamicin they should only be given at separate sites.

There is evidence that any potential nephrotoxicity of cephalosporins may be increased in the presence of gentamicin and we would recommend monitoring of kidney function if this combination is used. (For further information on mixed antibiotic therapy see section on 'Further information'.)

Neuromuscular blockade and respiratory paralysis have occasionally been reported from administration of aminoglycosides to patients who have received curare-type muscle relaxants during anaesthesia.

Legal category POM.

Package quantities *Gentamicin Injectable*: Ampoules and vials are packed in boxes of 5, 25 and 100 in trays of 5.

Gentamicin Paediatric Injection: Vials are packed in boxes of 5.

Further information Gentamicin has been shown to have a uniquely broad spectrum of activity and its use is recommended in bacterial infections where urgent, effective and, often, blind chemotherapy is called for. For combined antibiotic therapy with Gentamicin Injectable and Gentamicin Paediatric Injection the following rules of thumb may apply:

1. Gentamicin Injectable (or Gentamicin Paediatric Injection) act synergistically with penicillins and this combination is particularly useful against enterococci.

2. Gentamicin Injectable (or Gentamicin Paediatric Injection) and bacteriostatic antibiotics may give an antagonistic interaction (e.g. as with chloramphenicol). In the specific case of clindamycin and lincomycin the disadvantage of antagonism may be outweighed by the addition of activity against anaerobic organisms.

Product licence numbers

Gentamicin Injectable 0188/5909
Gentamicin Paediatric Injection 0188/5905

†Carbon dioxide may be liberated on addition of the two solutions. Normally this will dissolve in the solution, but under some circumstances small bubbles may form.

GENTICIN* INTRATHECAL

Presentation Gentamicin Intrathecal 2 ml snap-off ampoule. Each 1 ml contains Gentamicin Sulphate BP 1.0 mg gentamicin base (1,000 units) and Sodium Chloride Ph. Eur. (8.5 mg) to render the solution isotonic.

Uses Gentamicin (gentamicin) is a proven bactericidal antibiotic active against an extremely broad spectrum of Gram-positive and Gram-negative pathogens, including *E. coli*, *H. influenzae*, *Proteus*, *Pseudomonas*, *Neisseria meningitidis* and staphylococci which are the pathogens often associated with infection of the CSF.

Gentamicin Intrathecal is recommended for bacterial meningitis and ventriculitis.

Although gentamicin crosses the blood brain barrier it has been shown as with other antibiotics that parenteral therapy should be supported with intrathecal or intraventricular administration.

Dosage and administration The recommended daily dose is 1 mg gentamicin base intrathecally or intraventricularly plus 2.4 mg/kg/day intramuscularly in three equally divided doses at eight-hourly intervals in adult patients.

In children the supportive intramuscular dosage is: Up to 12 years: 6.0 mg/kg in 24 hours in three equally divided doses (i.e. 2.0 mg/kg eight hourly).

In infants up to two weeks this dosage should be given in two equally divided doses (i.e. 3.0 mg/kg 12 hourly).

The intraventricular/intrathecal dose may need to be increased at the discretion of the Clinician to obtain adequate CSF levels which can be controlled by assay, particularly if a severe degree of hydrocephalus is present. Treatment should continue until the CSF is shown to be bacteriologically clear.

Contra-indications, warnings, etc There are no absolute contra-indications.

Where renal function is impaired the frequency of dosage by *Systemic* routes should be reduced to avoid serum levels in excess of 10 mcg/ml.

In patients with normal renal function it is virtually impossible to achieve these levels with the standard dosage, but with gentamicin the vestibular mechanism may be affected when these levels are exceeded. This is usually reversible if observed in time and the dose adjusted.

Pharmaceutical precautions Gentamicin is a remarkably stable antibiotic and does not require to be kept under refrigerated conditions. In general we would not advise mixing Gentamicin Intrathecal with any other antibiotic prior to administration.

Legal category POM.

Package quantities Gentamicin Intrathecal is made available in boxes of 5.

Further information Shelf-life – four years.

Product licence number 0188/0004.

GENTICIN* PURE POWDER

Approved name: Gentamicin sulphate

Presentation Gentamicin Pure Powder is a non-sterile, hygroscopic powder. The weight of powder in each pack will vary according to potency, but will be approximately 1.8 g gentamicin sulphate to 1.0 g gentamicin base (1 million units).

Uses Genticin Pure Powder is supplied for the preparation of preservative-free solutions of gentamicin for intrathecal and intraventricular administration in meningitis and ventriculitis.

Dosage and administration The suggested daily dosage for all ages is 1 mg gentamicin base intraventricularly or intrathecally plus the recommended intramuscular dose of Genticin Injectable or Genticin Paediatric Injection. The intraventricular/intrathecally dose may need to be increased at the discretion of the clinician to obtain adequate CSF levels which can be controlled by assay, particularly if a severe degree of hydrocephalus is present.

Contra-indications, warnings, etc Where renal function is impaired the frequency of dosage by the systemic route should be reduced to avoid serum levels in excess of 10 mcg/ml. In the patient with normal renal function it is virtually impossible to achieve these levels with the standard dosage, but with gentamicin the vestibular mechanism may be affected when these levels are exceeded. This is usually reversible if observed in time and the dose adjusted.

Pharmaceutical precautions Genticin Pure Powder should be stored at room temperature and has a shelf-life of two years in *unopened* vials.

Care should be taken after the container has been opened to replace the stopper immediately.

Genticin Pure Powder may be dissolved in water or in normal saline for injection purposes in order to obtain a preservative-free solution. This should be sterilised before use, preferably by membrane filtration.

Legal category POM.

Package quantities Genticin Pure Powder is available in airtight, moisture-proof containers containing 1 g of gentamicin base.

Further information The package leaflet contained in every pack gives a suggested method for the preparation of intrathecal injection based on 1 mg of gentamicin base per 1 ml.

Product licence number 0188/5906.

GENTISONE* HC EAR DROPS

Presentation Gentamicin sulphate $\equiv$ 0.3% w/v gentamicin base plus 1.0% w/v hydrocortisone acetate as a sterile aqueous suspension in 10 ml opaque white polythene bottles with orange plastic caps. Borax and benzalkonium chloride are included as preservatives.

Uses Genticin (gentamicin) is a proven bactericidal antibiotic active against an extremely broad spectrum of Gram-positive and Gram-negative bacteria. Gentisone HC Ear Drops are therefore particularly useful in combating bacterial infections of the ear where the offending organisms are often varied and difficult to identify.

Gentisone HC Ear Drops are indicated in otitis externa, chronic suppurative otitis media, prophylaxis in trauma and pre- and post-operatively in surgery to the ear including infected mastoidectomy cavities.

Dosage and administration The area should be cleaned and 2–4 drops instilled three to four times a day and at night. In middle ear infections the cavity may be filled with drops.

Contra-indications, warnings, etc

There are no specific contra-indications except in cases of true sensitivity to one of the ingredients.

Precautions: Topical administration of any corticosteroid to pregnant animals can cause abnormalities of foetal development. The relevance of this finding in human beings has not been established, however, topical steroids should not be used extensively in pregnancy i.e. in large amounts or for prolonged periods.

In infants long term continuous topical therapy should be avoided. Adrenal suppression can occur even without occlusion.

Pharmaceutical precautions Store at room temperature. Do not freeze.

Legal category POM.

Package quantities Gentisone HC Ear Drops are available in 10 ml opaque white polythene bottles with orange plastic caps containing gentamicin sulphate $\equiv$ 0.3% w/v gentamicin base (3,000 units/ml) and 1.0% w/v hydrocortisone acetate.

Further information Genticin Eye/Ear Drops are also available where a plain antibiotic solution is required for topical application, for example, in the treatment of simple infections of the eye and ear.

Product licence number 0188/5925.

MICROPAQUE* D.C.

Presentation A low viscosity white suspension containing 100 % w/v of barium sulphate with a bland taste and particularly suited to the Double Contrast Technique.

Uses Radiological investigations of the gastro-intestinal tract.

Dosage and administration The volume of Micropaque D.C. used will depend on the patient, the procedure and technique involved. The following dosages represent a basic guide to the quantities suitable for routine examinations:

Barium Swallow.	40–60 ml undiluted
Double Contrast Stomach And Duodenum Examination	100–150 ml undiluted
Follow through Small Bowel Examination	150–250 ml undiluted
Barium Enema	250–500 ml diluted with 500–1000 ml water.

Contra-indications, warnings, etc Perforation of any region of the gastro-intestinal tract. Intestinal obstruction. Pyloric stenosis might be considered as contra-indications to the use of barium sulphate. Administration of a barium enema should proceed with particular care in patients with existing intestinal disease, in children, the elderly or the debilitated.

In choosing the route of administration, the possibility of actual or incipient bowel obstruction should be borne in mind.

Pharmaceutical precautions Shake well before use. Store at room temperature. Do not freeze. A light brown supernatant layer may appear and is quite normal. It will disappear when the bottle is shaken.

Legal category P.

Package quantities 300 ml plastic bottle containing 250 ml suspension and 50 ml 'shake space'. 15 bottles in each pack.

Further information Micropaque D.C., having a high density combined with a low viscosity, has been formulated to demonstrate particularly fine definition in conjunction with a suitable effervescent distending agent for Double Contrast Technique in the gastro-intestinal tract.

Product licence number 0838/0002.

MICROPAQUE* HD ▼

Presentation A fine white powder containing 96% w/w barium sulphate. It has a bland taste of vanilla.

Uses Double contrast radiological investigations of the gastrointestinal tract.

Dosage and administration Micropaque HD Powder must be reconstituted before use by adding water. 150 ml of a suspension containing 200% w/v barium sulphate is obtained by adding 83 ml water to 312 g of powder followed by vigorous shaking. Optimum dispersion is obtained by shaking for approximately one minute.

Although the volume of suspension used will depend on the patient, the procedure and technique involved, the following dosages of Micropaque HD represent a basic guide to the quantities suitable for routine examinations of the upper gastrointestinal tract.

Barium swallow	40–60 ml
Double contrast stomach and duodenum examination	100–150 ml
Follow-through examination of the small bowel	150–250 ml

Contra-indications, warnings, etc Perforation of any region of the gastrointestinal tract. Intestinal obstruction. Pyloric stenosis might be considered as a contra-indication to the use of barium sulphate. Administration of a barium enema should proceed with particular care in patients with existing intestinal disease, in children, the elderly or the debilitated.

Pharmaceutical precautions Store at room temperature in a dry place. Micropaque HD should be used as soon as possible after reconstitution and in any event within two hours of adding water.

Legal category P.

Package quantities 500 ml polypropylene beaker containing 312 g barium sulphate (96% w/w). 20 beakers in each pack.

Further information Micropaque HD produces a high density, low viscosity suspension on reconstitution that is especially designed for double contrast examinations of the upper gastrointestinal tract. It should be used in conjunction with a compatible gas producing agent such as Nicholas Co₂ Granules.

Product licence number 0188/0055.

MICROPAQUE* STANDARD

Presentation A creamy-white suspension containing 100% w/v of barium sulphate with a bland characteristic taste of butterscotch-vanilla.

Uses Radiological investigations of the gastro-intestinal tract.

Dosage and administration *Adults: Oesophagus:* Use undiluted Micropaque standard orally as required. For prolonged adhesion use Microtrast Oesophageal Paste.

Stomach and duodenum: To demonstrate the mucosal pattern use up to 50 ml of undiluted Micropaque standard orally, follow this with a further 100 ml of Micropaque standard diluted with 100 ml of water for demonstration of stomach distension and emptying function. If this biphasic technique is not used, 150 ml of Micropaque Standard diluted with 50 ml of water may be given.

Small intestine: Use 100 ml of Micropaque Standard diluted with 150 ml of water or follow through from stomach examination.

Colon: For examination by barium enema using the filled colon technique, use 1 volume of Micropaque standard to 2 volumes of water made up to the required quantity. For double contrast studies use 1–2 volumes of Micropaque standard to 1 volume of water. 400 ml total volume is usually sufficient. An important pre-requisite is a thorough cleansing preparation of the colon and an examination time of preferably not greater than 15 minutes.

Children: No children's dosage recommended as such investigations in children are rare and specialised. The dosage will therefore be tailored by the radiologist to suit the special requirements in each case.

Contra-indications, warnings, etc Perforation of any region of the gastro-intestinal tract. Intestinal obstruction. Paralytic ileus or pyloric stenosis might be considered as contra-indications to the use of barium sulphate preparations. Administration of a barium enema should proceed with particular care in patients with existing intestinal disease in children, the elderly or the debilitated. In choosing the route of administration, the possibility of actual or incipient bowel obstruction should be borne in mind.

Pharmaceutical precautions Shake before use.

Store at room temperature. Do not freeze. A light brown supernatant layer may appear and is quite normal. It will disappear when the bottle is shaken.

Legal category P.

Package quantities 250 ml plastic bottle, 2 litre plastic bottle.

Further information Nil.

Product licence number 0838/5903

MICROPAQUE* POWDER

Presentation A cream-coloured, free-flowing fine powder, which, when reconstituted with water, has a pleasant bland characteristic butterscotch/vanilla flavour. The powder contains 92% w/w barium sulphate.

Uses Radiological investigations of the gastro-intestinal tract.

Dosage and administration *Standard mix. Method of preparation:*

1. Measurement of volume. To 8 volumes of powder add 7 volumes of water, e.g. to 800 ml of powder add 700 ml of water to make 1 litre of liquid dispersion.

2. Measurement by weight. Add to 1 kg of powder sufficient water to make up to 1 litre of liquid dispersion. Water should always be added to the powder with slow stirring.

Adults: Oesophagus: Use undiluted Micropaque orally as required. For prolonged adhesion use Microtrast Oesophageal Paste.

Stomach and duodenum: To demonstrate the mucosal pattern use up to 50 ml of undiluted Micropaque orally. Follow this with a further 100 ml of Micropaque diluted with 100 ml of water for demonstration of stomach distension and emptying function. If this biphasic technique is not used, 150 ml of Micropaque Liquid diluted with 50 ml of water may be given.

Small intestine: Use 100 ml of Micropaque diluted with 150 ml of water or follow through from stomach examination.

Colon: For examination by barium enema using the filled colon technique use 1 volume of Micropaque to 2 volumes of water made up to the required quantity. For double contrast studies use 1–2 volumes of Micropaque to 1 volume of water. 400 ml total volume is usually sufficient. An important prerequisite is a thorough cleansing of the colon and an examination time of preferably not greater than 15 minutes.

Children: No children's dosage is recommended as such investigations in children are rare and specialised. The dosage will therefore be tailored by the radiologist to suit the special requirements in each case.

Contra-indications, warnings, etc Perforation of any region of the gastro-intestinal tract. Intestinal obstruction. Paralytic ileus or pyloric stenosis might be considered as contra-indications to the use of barium sulphate preparations. Administration of a barium enema should proceed with particular care in patients with existing intestinal disease, in children, the elderly or the debilitated. In choosing the route of administration, the possibility of actual or incipient bowel obstruction should be borne in mind.

Pharmaceutical precautions Store at room temperature in a dry place.

Legal category P.

Package quantities 3.5 kg plastic containers.

Further information Nil.

Product licence number 0838/5904.

MICROTRAST*

Presentation An off-white, viscous paste with a faint colour of vanilla and a bland, pleasant and characteristic faintly butterscotch/vanilla flavour. Contains 70% w/w barium sulphate.

Uses Radiographic study of the mucosal outline and pattern of the entire oesophagus, swallowing mechanism, oesophageal peristalsis, heart size and configuration.

Dosage and administration **Adults:** A large teaspoonful (10 g) to a tablespoonful (45 g) as required, orally.

Children: No children's dosage recommended as such investigations in children are rare and specialised. The dosage will therefore be tailored by the radiologist to suit the special requirements in each case.

Contra-indications, warnings, etc Perforation of any region of the gastro-intestinal tract. Paralytic ileus or pyloric stenosis might be considered as contra-indications to the use of barium sulphate preparations. Administration of a barium enema should proceed with particular care in patients with existing intestinal disease, in children, the elderly or the debilitated. In choosing the route of administration, the possibility of actual or incipient bowel obstruction should be borne in mind.

Pharmaceutical precautions Store at room temperature. Do not freeze.

Legal category P.

Package quantities 800 g in a plastic tube.

Further information Nil.

Product licence number 0838/5902.

NEO-MERCAZOLE* TABLETS

Presentation Round, shallow convex, pink, compression-coated tablet containing a white core. Impressed with 'B.S.' on one side and a bisecting line on the obverse. Each tablet contains Carbimazole BP 5 mg.

Uses Anti-thyroid agent. Neo-Mercazole is indicated in all conditions where reduction of thyroid synthesis is required.

1. Thyrotoxicosis (as the sole treatment).
2. Preparation prior to thyroidectomy (selected patients).
3. In combination with radioactive iodine ablative therapy.

Dosage and administration **Adults:** The usual initial total daily dose is 30 mg, but this may be increased to 40–60 mg daily in divided doses, in severe cases. Once control is achieved, dosage is gradually reduced to the lowest maintenance level, compatible with adequate control.

Children: The usual daily dosage is 15 mg or as directed by the physician.

Contra-indications, warnings, etc If reactions to neo-Mercazole are to be encountered, they normally occur within the first eight weeks of starting treatment. The most common minor side-effects are nausea, headache, arthralgia, mild gastric distress and skin rashes. Occasional hair loss has been reported. These side-effects are usually self-limiting and may not require withdrawal of the drug.

Bone-marrow depression has been reported, but these serious side-effects are rare and do not appear to be time or dose related. Routine blood tests are not necessary and, because of the nature of the disorder, are impractical, but it is imperative that patients be warned about the onset of sore throats or other manifestations which might suggest the early development of bone-marrow depression.

It is important that the drug is stopped and the physician concerned contacted immediately. There is some evidence that early withdrawal of the drug will lead to complete recovery.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Containers of 100 and 500 tablets.

Further information *Dosage and precautions in pregnancy:* The dose of Neo-Mercazole must be regulated by the patient's clinical condition. It is most important to appreciate that the basic metabolic rate is raised during pregnancy (the rise averages 25% above normal and occurs mainly in the second half of pregnancy) and that the dosage must be adjusted accordingly.

The smallest dose compatible with rendering the patient symptom-free should be employed and during the last three months should, if possible, not exceed 15 mg daily.

If the patient's condition is satisfactory, Neo-Mercazole should be discontinued three to four weeks before delivery. Neo-Mercazole is secreted in breast milk, and if treatment is continued during lactation, the patient should not be allowed to breast feed her baby.

Product licence number 0188/5907.

NEUTRADONNA* POWDER

Presentation White/off white powder. Each 1 g of powder contains aluminium sodium silicate 989.6 mg with belladonna alkaloids (calculated as hyoscyamine) 0.075 mg.

Uses Neutradonna is recommended for use in gastro-intestinal disorders, including peptic ulcer, hiatus hernia, pregnancy dyspepsia and other hyperacidic dyspepsias. Aluminium sodium silicate has a rapid but prolonged antacid action, and belladonna relaxes spasm of the gastro-intestinal tract and also reduces acid secretion by the stomach.

Dosage and administration *Adults:* 1 or 2 level 5 ml spoonfuls up to four times a day after meals. The powder should be taken stirred into a little milk or water. The last dose of Neutradonna each day should be taken at bedtime.

Children: 2-6 years: $\frac{1}{2}$ level 5 ml spoonful up to four times a day.

6-12 years: $\frac{1}{2}$ -1 level 5 ml spoonful up to four times a day.

Contra-indication, warnings, etc Glaucoma. Neutradonna should be prescribed with caution for patients having prostatic enlargement, or known sensitivity to Belladonna.

Side-effects: Dryness of the mouth and blurring of vision may occur on large doses due to the belladonna content of Neutradonna.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Containers of 25 g and 100 g powder.

Further information Nil.

Product licence number 0188/5908.

NEUTRADONNA* TABLETS

Presentation White circular bevelled tablets containing aluminium sodium silicate 650 mg, belladonna alkaloids (calculated as hyoscyamine) 0.048 mg.

Uses Neutradonna is recommended for use in gastro-intestinal disorders, including peptic ulcer, hiatus hernia,

pregnancy dyspepsia and other hyperacidic dyspepsias. Aluminium sodium silicate has a rapid but prolonged antacid action, and belladonna relaxes spasm of the gastro-intestinal tract and also reduces acid secretion by the stomach.

Dosage and administration *Adults:* 2-3 tablets up to four times a day. The tablets should preferably be chewed. The last dose of Neutradonna each day should be taken at bedtime.

Children: 2-6 years: $\frac{1}{2}$ -1 tablet up to four times a day.

6-12 years: 1-1 $\frac{1}{2}$ tablets up to four times a day.

Contra-indications, warnings, etc Glaucoma. Neutradonna should be prescribed with caution for patients having prostatic enlargement, or known sensitivity to Belladonna.

Side-effects: Dryness of the mouth and blurring of vision may occur on large doses due to the belladonna content of Neutradonna.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Box of 120 tablets (10 cartons of 12).

Further information Nil.

Product licence number 0188/5913.

PALAPRIN* FORTE TABLETS

Presentation Oval pale orange tablets. Embossed 'PALAPRIN FORTE' on one face and the reverse is scored and bears two oval symbols enclosing the letters 'BS'.

Each tablet contains aloxiprin 600 mg.

Uses Analgesic/anti-inflammatory agent in rheumatoid arthritis, osteoarthritis, various forms of spondylitis and other 'rheumatic' conditions where high dosage salicylate therapy is required.

Use in Pregnancy: There is clinical and epidemiological evidence of safety in human pregnancy.

Dosage and administration *Adults:* Usual dose 300-1200 mg.

Maximum 4.8 g daily in divided doses, i.e. one tablet per stone (6 kg) daily in divided doses. In acute rheumatic conditions up to 9.6 g daily in divided doses.

Dosage should be carefully controlled, and in conditions where high-dosage therapy is used, i.e. Still's disease, plasma salicylate levels should be monitored in accordance with the physician's requirements.

The tablets should preferably be dispersed in water before administration, but can be chewed, sucked or swallowed whole with a draught of water if required.

Contra-indications, warnings, etc

Contra-indications: True hypersensitivity to salicylates.

As with any form of salicylate, concurrent administration with anticoagulant therapy can lead to an alteration in prothrombin time which will necessitate a dosage adjustment based on laboratory studies. Active peptic ulceration; haemophilia.

Precautions: Aloxiprin may prolong labour and contribute to maternal and neonatal bleeding and is best avoided at term. May enhance effects of anti-coagulants. May inhibit action of uricosurics. May precipitate broncho-

spasm. May induce attacks of asthma in susceptible subjects.

Warnings and Adverse Effects: Hypersensitivity and asthma. May induce gastro-intestinal haemorrhage, occasionally major. May cause constipation and tinnitus.

Overdosage: The conventional treatment of salicylate overdosage should be employed – gastric lavage, forced alkaline diuresis and supportive therapy.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Containers of 250.

Further information The body-weight dosage regime has been recommended to ensure salicylate blood levels which will give anti-inflammatory, as well as analgesic, effect. Should this dosage produce tinnitus a downward adjustment of dose should be made until symptom disappears.

Aloxiaprin 600 mg is equivalent to acetylsalicylic acid 500 mg, but the salicylate is released largely in the alkaline medium of the small intestine, thereby reducing the likelihood of salicylate-induced dyspepsia.

Product licence number 0188/0038.

POLYCROL* GEL

Presentation A white peppermint-flavoured suspension containing in each 5 ml:

Activated methylpolysiloxane	25 mg
Magnesium hydroxide	100 mg
Aluminium hydroxide gel	4.75 ml

Uses Polycrol is recommended for use in gastro-intestinal disorders, including dyspepsia, peptic ulcer oesophagitis, hiatus hernia, post-operational abdominal pains. Polycrol rapidly relieves acid pain disperses gastric foam and assists eructation of gas and air.

The de-foaming action accelerates penetration of antacids throughout the gastric contents, thus protecting the gastric mucosa from the effects of excess acid.

Dosage and administration *Adults:* One or two 5 ml spoonfuls of gel three times a day after meals or as directed.

Children: 1–5 years: Half 5 ml spoonful three times a day.

6–12 years: One 5 ml spoonful three times a day. Or as directed.

Contra-indications, warnings, etc There are no known contra-indications to the use of Polycrol.

Side-effects: Nausea rarely encountered.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Bottles containing 300 ml of gel.

Further information Polycrol contains a balanced mixture of antacids (aluminium and magnesium hydroxides) together with a potent surface-active compound (methylpolysiloxane).

The antacids are balanced to avoid any bowel reaction and with Polycrol neither constipation nor diarrhoea will occur.

Product licence number 0188/5930.

POLYCROL* TABLETS

Presentation Circular, flat-faced tablet consisting of two layers, one green, the other white. Each tablet contains:

Activated methylpolysiloxane	25 mg
Aluminium hydroxide/magnesium carbonate co-dried gel	275 mg
Magnesium hydroxide	100 mg

Uses Polycrol is recommended for use in gastro-intestinal disorders, including dyspepsia, peptic ulcer, duodenitis, gastritis, flatulent dyspepsia, aerophagy, oesophagitis, hiatus hernia, post-operational abdominal pains. Polycrol rapidly relieves acid pain, disperses gastric foam and assists eructation of gas and air.

The de-foaming action accelerates penetration of antacids throughout the gastric contents, thus protecting the mucosa from the effects of excess acid.

Dosage and administration *Adults:* 1 or 2 tablets to be chewed two to three times a day after meals or as directed.

Children: 1–5 years: $\frac{1}{2}$ tablet to be chewed two to three times a day.

6–12 years: 1 tablet to be chewed two to three times a day.

Contra-indications, warnings, etc There are no known contra-indications to the use of Polycrol.

Side-effects: Nausea is rarely encountered.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Box of 200 tablets (10 cartons of 20 tablets).

Further information Polycrol contains a balanced mixture of antacids (aluminium and magnesium hydroxides) together with a potent surface-active compound (methylpolysiloxane).

The antacids are balanced to avoid any bowel reaction and with Polycrol neither constipation nor diarrhoea will occur.

Product licence number 0188/5919.

POLYCROL* FORTE GEL

Presentation A white, viscous, peppermint-flavoured gel. Each 5 ml contains:

Activated methylpolysiloxane	125 mg
Magnesium hydroxide	100 mg
Aluminium hydroxide gel	4.75 ml

Uses For antacid/deflatulent therapy in conditions such as: dyspepsia of functional or organic origin, heartburn, hiatus hernia, flatulence and abdominal distension, oesophagitis, gastritis, symptomatic treatment of peptic ulcer and other indications where flatulence/hyperacidity may be present.

Dosage and administration *Adults:* One to two 5 ml spoonfuls between meals and at bedtime or as directed.

Children: Under 5 years: Half 5 ml spoonful with food as required up to 6 doses per day.

5–12 years: One 5 ml spoonful as required up to 6 doses per day.

Contra-indications, warnings, etc

Contra-indications: There are no known contra-indications to the use of Polycrol.

Side-effects: Nausea is rarely encountered.

Pharmaceutical precautions Keep bottle well closed.

Legal category P.

Package quantities 300 ml plastic bottle.

Further information Nil.

Product licence number 0188/5929.

POLYCROL* FORTE TABLETS

Presentation White, circular, bi-convex tablets embossed 'N' on both faces. Each tablet contains:

Activated methylpolysiloxane	250 mg
Magnesium hydroxide	100 mg
Aluminium hydroxide/magnesium carbonate co-dried gel	275 mg

Uses For antacid/deflatulent therapy in conditions such as: dyspepsia of functional or organic origin, heartburn, hiatus hernia, flatulence and abdominal distension, oesophagitis, gastritis, symptomatic treatment of peptic ulcer and other indications where flatulence/hyperacidity may be present.

Dosage and administration One to two tablets between meals and at bedtime or as directed. The tablets should be chewed or sucked.

Not intended for administration to children.

Contra-indications, warnings, etc

Contra-indications: There are no known contra-indications to the use of Polycrol.

Side-effects: Nausea is rarely encountered.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Containers of 100 tablets.

Further information Nil.

Product licence number 0188/5918.

VASCARDIN* TABLETS

Presentation White, bi-convex tablets, embossed with letter 'N' on one face and a break line on the other. Each tablet contains sorbide nitrate 10 mg.

Uses Angina pectoris – reduction of frequency and severity of attacks. Reduction of cardiac workload and oxygen consumption. Used alone or in combination with beta-blockade in certain patients.

Congestive cardiac failure, as adjunctive therapy.

Dosage and administration Oral: *for prophylaxis:* 1 tablet (10 mg) initially, 2–3 times daily rising as necessary up to 140 mg/day in divided doses.

Dosage should be increased gradually to minimise the possibility of nitrate headache and achieve tolerance. If the headache does occur, it can be relieved by simple analgesics.

Congestive cardiac failure: 10–30 mg 4 times daily as adjunctive therapy to other standard drugs (cardiac glycosides and diuretics).

Sub-lingual: 1 tablet, at the onset of acute anginal attacks, repeat if necessary.

Contra-indications, warnings, etc Use with caution in patients with glaucoma. If used concurrently with anticoagulant therapy, aspirin or other salicylates should not be taken. The product should not be used during pregnancy unless considered essential by the physician.

This product should not be used in patients with severe anaemia, head trauma or cerebral haemorrhage, nor in patients with known sensitivity to the nitrates.

Side-effects: During the first few days' treatment some patients may experience nitrate headache (see under 'Dosage and administration').

Pharmaceutical precautions Store in a dry place. Replace cap firmly after use.

Legal category P.

Package quantities Containers of 100 tablets.

Further information Nil.

Product licence number 0188/5931.

*Trade Mark

Nordisk-UK
Highview House
Tattenham Crescent
Epsom Downs
Surrey KT18 5QJ



VELOSULIN*

Neutral Insulin Injection BP, highly purified pork.

Presentation Velosulin is a neutral solution that is available in 10 ml vials containing 40 iu/ml, 80 iu/ml and 100 iu/ml.

Uses Velosulin is for use in the treatment of insulin-dependent diabetics. It has a rapid onset and a short duration of action. It is particularly suitable in the treatment of diabetic coma and pre-coma. It may be mixed with Insulatard (NPH), Mixtard 30/70 or Inlitar 50/50 in all proportions without changing the characteristic effect of any of the types of insulin.

Velosulin has been manufactured from highly purified pork insulin.

The minimal antigenic properties of this insulin quality make it recommendable in the treatment of new insulin-demanding cases of diabetes, in the treatment of lipotrophy, insulin allergy and insulin resistance; also in the treatment of patients needing supportive insulin therapy, e.g. during pregnancy or operation.

Dosage and administration Velosulin may be given by subcutaneous, intramuscular or intravenous injection. The dosage is determined by the physician. Velosulin has a duration of action of some $\frac{1}{2}$ to 8 hours, having its maximum effect between 1 and 3 hours after injection.

Contra-indications, warnings, etc Insulin is contra-indicated in hypoglycaemia. In the event of an overdose, glucose should be given either orally or intravenously. Glucagon may also be administered.

Diabetics previously treated with insulin of beef or mixed beef/pork origin may require to have their dosage adjusted downwards if changed to Velosulin.

Pharmaceutical precautions Velosulin should be stored between 2 and 8 degrees centigrade, protected from sunlight. Insulin which has been frozen should not be used.

Legal category P.

Package quantities 10 ml vials of 40 iu/ml.
10 ml vials of 80 iu/ml.
10 ml vials of 100 iu/ml.

Further information Nil.

Product licence numbers

3132/0010 (40 iu/ml)
3132/0011 (80 iu/ml)
3132/0019 (100 iu/ml)

INSULATARD*

Isophane Insulin Injection (NPH) BP, highly purified pork.

Presentation Insulatard is a neutral suspension of highly purified microcrystalline pork insulin that is available in 10 ml vials containing 40 iu/ml, 80 iu/ml and 100 iu/ml.

Uses Insulatard is for use in the treatment of diabetics. It is given once or twice a day according to the needs of the patient. It may be mixed with Velosulin, Mixtard 30/70, or Inlitar 50/50 in all proportions without changing the characteristic effect of any of the types of insulin.

Insulatard has been manufactured from highly purified pork insulin.

The minimal antigenic properties of this insulin quality make it recommendable in the treatment of new insulin-demanding cases of diabetes, in the treatment of lipotrophy, insulin allergy and insulin resistance; also in the treatment of patients needing supportive insulin therapy, e.g. during pregnancy or operation.

Dosage and administration Insulatard may be given by subcutaneous or intramuscular injection. The dosage is determined by the physician. Insulatard has a duration of action of some $1\frac{1}{2}$ to 24 hours, having its maximum effect between 4 and 12 hours after injection.

Contra-indications, warnings, etc Insulin is contra-indicated in hypoglycaemia. In the event of an overdose, glucose should be given either orally or intravenously. Glucagon may also be administered.

Diabetics previously treated with insulin of beef or mixed beef/pork origin may require to have their dosage adjusted downwards if changed to Insulatard.

Pharmaceutical precautions Insulatard should be stored between 2 and 8 degrees centigrade, protected from sunlight. Insulin which has been frozen should not be used.

Legal category P.

Package quantities 10 ml vials of 40 iu/ml.
10 ml vials of 80 iu/ml.
10 ml vials of 100 iu/ml.

Further information Nil.

Product licence numbers

3132/0001 (40 iu/ml)
3132/0002 (80 iu/ml)
3132/0018 (100 iu/ml)

MIXTARD* 30/70 INITARD* 50/50

Presentation *Mixtard 30/70* is a neutral suspension of highly purified pork insulin comprising 30% Neutral Insulin Injection BP in solution and 70% Isophane Insulin Injection BP in microcrystalline form. Available in 10 ml vials containing 40 iu/ml (12 iu Neutral Insulin + 28 iu Isophane Insulin) 80 iu/ml (24 iu Neutral Insulin + 56 iu Isophane Insulin) and 100 iu/ml (30 iu Neutral Insulin + 70 iu Isophane Insulin).

Initard 50/50 is a neutral suspension of highly purified pork insulin comprising 50% Neutral Insulin Injection BP in solution and 50% Isophane Insulin Injection BP in microcrystalline form. Available in 10 ml vials containing 40 iu/ml (20 iu Neutral Insulin + 20 iu Isophane Insulin) 80 iu/ml (40 iu Neutral Insulin + 40 iu Isophane Insulin) and 100 iu/ml (50 iu Neutral Insulin + 50 iu Isophane Insulin).

Uses Treatment of insulin-dependent diabetics.

Mixtard 30/70 may be used once or twice daily, depending on the needs of the patient.

Initard 50/50 may be used once or twice daily, depending on the needs of the patient. It has a more intense initial effect than *Mixtard 30/70*.

Velosulin or *Insulatard* may be added to *Mixtard 30/70* or *Initard 50/50* in all proportions without changing the characteristic effect of any of the types of insulin.

The minimal antigenic properties of this insulin quality make it recommendable in the treatment of new insulin-demanding cases of diabetes, in the treatment of lipoatrophy, insulin allergy and insulin resistance. Also in the treatment of patients needing supportive insulin therapy, e.g. during pregnancy or operation.

Dosage and administration The dosage of *Mixtard 30/70* and *Initard 50/50* to be determined by the physician.

Mixtard 30/70 when injected subcutaneously has a duration of action of some $\frac{1}{2}$ to 24 hours, having its maximum effect between 4 and 8 hours. It may also be given by intramuscular injection, in which case the duration of action will be somewhat shorter.

Initard 50/50 when injected subcutaneously has a duration of action of some $\frac{1}{2}$ to 24 hours, having its maximum effect between 4 and 8 hours. It may also be given by intramuscular injection, in which case the duration of action will be somewhat shorter.

Initard 50/50 has a stronger initial effect than *Mixtard 30/70*.

Suspensions of *Mixtard 30/70* and *Initard 50/50* should be shaken gently before use.

Contra-indications, warnings, etc Insulin is contra-indicated in hypoglycaemia. In the event of overdosage, glucose should be given either orally or intravenously. Glucagon may also be administered. *Mixtard 30/70* or *Initard 50/50* suspensions should not be given intravenously.

Patients previously treated with other commercially available insulins of beef or mixed beef/pork origin may require to have their dosage reduced when transferred to *Mixtard 30/70* or *Initard 50/50*. The dosage reduction may be immediate, or occur over a period of weeks or months.

Pharmaceutical precautions *Mixtard 30/70* and *Initard 50/50* should be stored between 2 and 8 degrees centigrade, protected from sunlight. Insulin which has been frozen should not be used.

Legal category P.

Package quantities 10 ml vials of 40 iu/ml.
10 ml vials of 80 iu/ml.
10 ml vials of 100 iu/ml.

Further information Nil.

Product licence numbers

<i>Initard 50/50</i> (40 iu/ml)	3132/0012
(80 iu/ml)	3132/0013
(100 iu/ml)	3132/0020
<i>Mixtard 30/70</i> (40 iu/ml)	3132/0014
(80 iu/ml)	3132/0015
(100 iu/ml)	3132/0021

*Trade Mark

Norgine Limited

59-62 High Holborn
London WC1V 6EB



ALCOS-ANAL* OINTMENT

Presentation White ointment. Active ingredients:

Sodium oleate	10%
Hydroxypolyethoxydodecane	2%
Chlorothymol	0.1%

Uses Symptomatic relief of haemorrhoids and pruritus ani.

Dosage and administration Ease off cap of applicator and screw applicator on to tube. An applicator full of ointment should then be squeezed into the anal canal. Some ointment will remain in the applicator. To avoid wastage, the applicator should be left on the tube, wiped clean and the cap replaced.

External haemorrhoids should be massaged with the ointment in the usual way, night and morning and after every bowel action.

In addition, the usual precautions of strict cleanliness, avoidance of straining, and a bulky diet or a mild laxative to ensure soft stools, are essential.

Treatment should be carried out for at least six weeks, even though relief may be felt after only a few days. Treatment should be discontinued only when advised by the doctor.

Contra-indications, warnings, etc None reported. In a small number of cases the initial application may produce a burning sensation. The patient should persevere with the treatment as this feeling usually diminishes within two or three days.

Pharmaceutical precautions Store in a cool dry place.

Legal category P.

Package quantities Tube of 20 g packed in a carton with capped applicator.

Further information Nil.

Product licence number 0322/0032.

ALCOS-ANAL* SUPPOSITORIES

Presentation White, hard torpedo-shaped suppository. Active ingredients:

Sodium oleate	200 mg
Hydroxypolyethoxydodecane	20 mg
Chlorothymol	0.7 mg

Uses Symptomatic relief of haemorrhoids and pruritus ani.

Dosage and administration Rectal administration. Cleanse anal region after every bowel action. Insert one suppository every morning and night, also after every bowel action. Avoid straining during bowel action. Treatment should be carried out for at least six weeks, even though relief may be felt after only a few days.

Treatment should be discontinued only when advised by the doctor.

In addition, the usual precautions of strict cleanliness, avoidance of straining, and a bulky diet or a mild laxative to ensure soft stools, are essential.

Contra-indications, warnings, etc None reported. In a small number of cases the initial application may produce a burning sensation. The patient should persevere with the treatment as this feeling usually diminishes within two or three days.

Pharmaceutical precautions Store in a cool dry place.

Legal category P.

Package quantities Carton of 10 suppositories.

Further information Nil.

Product licence number 0322/0033.

CAMCOLIT*

Presentation *Camcolit 250*: White film coated tablets engraved on one side Camcolit, each containing 250 mg Lithium Carbonate BP (equivalent to 6.8 millimoles).

Camcolit 400: White film coated tablets, engraved one side Camcolit S with break line on reverse side, each containing 400 mg Lithium Carbonate BP (equivalent to 10.8 millimoles).

Uses Treatment and prophylaxis of mania, manic-depressive illness and recurrent depression.

Dosage and administration Tablets for oral administration.

Acute mania: Treatment of mania should be initiated in hospital where regular monitoring of serum lithium levels can be conducted.

The dosage of Camcolit should be adjusted to produce a serum lithium level between 0.6 and 1.2 mmol/l 12 hours after the last dose. The required serum lithium level may be achieved in one of two ways, but whichever is adopted regular estimations must be carried out to ensure maintenance of levels within the therapeutic range. For consistent results it is essential that the blood samples for serum lithium estimations are taken 12 hours after the last dose of lithium.

1. 1,500-2,000 mg of lithium carbonate are administered daily in divided doses for the first five or seven days. A blood sample for serum lithium estimation is taken 12 hours after the last dose on the fifth or seventh day, and the dosage of Camcolit is adjusted to keep the serum lithium level within the therapeutic range.

Subsequently, regular serum lithium estimations must be carried out and, where necessary, the dosage of Camcolit adjusted accordingly.

The precise initial dose of lithium should be decided in the light of the age and weight of the patient; young patients often require a dose higher than average and older patients a lower dose.

2. A lithium clearance test is carried out and the initial dosage calculated from the results. Even when the initial dosage is calculated in this way, it is still desirable that serum lithium levels should be determined at weekly intervals during the first three weeks of treatment, and any necessary adjustments to dosage made as a result of the levels actually obtained.

Most of the above applies in the treatment of hypomania as well as mania, but the patient (if not too ill) can be started on treatment as an outpatient provided that facilities for periodic serum lithium monitoring are available.

Prophylaxis of recurrent affective disorders (including unipolar mania, unipolar depressions and bipolar manic-depressive illness): A dosage of 500–1,200 mg of lithium carbonate can be administered daily in divided doses for the first seven days. A blood sample for serum lithium estimation is then taken 12 hours after the last dose, and the dosage of Camcolit is adjusted to keep the plasma lithium level within the effective range. Clinical improvement is usually associated with serum concentrations of 0.5 mmol/l or above. Toxic symptoms are usually associated with concentrations exceeding 1.5 mmol/l.

Use in elderly: Usually 500–1,000 mg/day given in divided doses.

Toxic symptoms are likely with serum concentrations above 1.0 mmol/l.

Use in children: Not recommended.

Measurement of serum lithium concentrations: Lithium therapy should not be initiated unless adequate facilities for routine monitoring of serum concentrations are available. On initiation of therapy serum concentrations should be measured weekly until stabilisation is achieved, then weekly for one month and at monthly intervals thereafter. Additional measurements should be made if signs of lithium toxicity occur (see below), on dosage alteration, development of significant intercurrent disease, signs of manic or depressive relapse and if significant change in sodium or fluid intake occurs.

As bioavailability varies from product to product a change of product should be regarded as initiation of new treatment. Blood levels should therefore be monitored weekly until re-stabilisation is achieved. More frequent monitoring is required if patients are receiving diuretics.

Contra-indications, warnings, etc The first consideration in lithium therapy is the selection of proper candidates. The second is the physical state of the patient, which must be adequate to handle the lithium ion when it is introduced into the body.

Contra-indications: Patients with renal disease, cardiovascular disease, Addison's disease or those breast feeding. There is epidemiological evidence that the drug may be harmful in human pregnancy. Should the use of lithium be unavoidable, close monitoring of serum concentrations should be made throughout the pregnancy and during parturition.

Precautions: Pre-treatment and periodic routine clinical monitoring is essential. This should include assessment of renal function, urine analysis, assessment of thyroid function and cardiac function, especially in patients with cardiovascular disease.

Patients should be euthyroid before the initiation of lithium therapy.

Clear instructions regarding the symptoms of impending toxicity should be given by the doctor to all patients receiving long-term lithium therapy (see Warnings and Adverse Effects). Patients should also be warned to report if polyuria or polydipsia develop. Episodes of nausea and vomiting or other conditions leading to salt/water depletion (including severe dieting) should also be reported. Patients should be advised to maintain their usual salt and fluid intake.

Elderly patients are particularly liable to lithium toxicity.

Lower doses of lithium may be needed during diuretic therapy as lithium clearance is reduced.

Raised plasma levels of ADH may occur during treatment.

Symptoms of nephrogenic diabetes are particularly prevalent in patients receiving concurrent treatment with tri/tetracyclic antidepressants.

Serum lithium concentrations may increase during concomitant therapy with indomethacin or tetracycline.

Warnings: Long-term treatment with lithium may result in permanent changes in the kidney and impairment of renal function. High serum concentrations of lithium, including episodes of acute lithium toxicity may enhance these changes. The minimum clinically effective dose of lithium should always be used. Patients should be maintained on lithium after 3–5 years only if, on assessment, benefit persists.

Renal function should be routinely monitored in patients with polyuria and polydipsia.

Side-effects: Side effects are usually related to serum lithium concentrations and are infrequent at levels below 1.0 mmol/l.

Mild gastro-intestinal effects, nausea, vertigo, muscle weakness and a dazed feeling may occur, but frequently disappear after stabilisation. Fine hand tremors, polyuria and mild thirst may persist. Some studies suggest that the tremor can be controlled by relatively small doses of propranolol.

Long term treatment with lithium is frequently associated with disturbances of thyroid function including goitre and hypothyroidism. These can be controlled by administration of small doses of thyroxine (0.05–0.2 mg daily) concomitantly with lithium. Thyrotoxicosis has also been reported.

Mild cognitive impairment may occur during long term use.

Hypercalcaemia, hypermagnesaemia, hyperparathyroidism and an increase in antinuclear antibodies have also been reported.

Exacerbation of psoriasis may occur.

Signs of impending toxicity: Appearance or aggravation of gastro-intestinal symptoms, muscle weakness, lack of co-ordination, drowsiness or lethargy may be early signs of intoxication. With increasing toxicity there is ataxia, giddiness, tinnitus, blurred vision, coarse tremor, muscle twitching and a large output of dilute urine. At blood levels above 2–3 mmol/l, there is increasing disorientation, seizures, coma and death.

Pharmaceutical precautions Store in a cool, dry place.

Legal category POM.

Package quantities Camcolit 250: 100 and 1,000 tablets.

Camcolit 400: 100 and 500 tablets.

Further information In view of recent reports of chronic nephrotoxicity attributed to lithium, it is important that for all lithium products the daily dose is divided and not given as a single dose. Such a procedure reduces the post-absorptive lithium peak and thus its concentration in the glomerular filtrate.

Product licence numbers Camcolit 250 0322/5900
Camcolit 400 0322/0015.

CYCLOBRAL*

Presentation Pink/brown hard gelatin capsules imprinted CYCLOBRAL. Each capsule contains 400 mg cycandelate.

Uses *Principal action:* Cyclobral is a vascular smooth muscle relaxant used to promote mild vasodilatation in peripheral and cerebrovascular diseases associated with impaired circulation.

Indications: Peripheral vascular disorders: Intermittent claudication, Raynaud's syndrome, night cramps, acrocyanosis, cold extremities, chilblains and 'restless legs'.

Cerebral vascular disorders: Chronic cerebral insufficiency, impaired mental function, dementia, confusion, dizziness and the sequelae of strokes.

Dosage and administration Cerebral and peripheral vascular disorders. Capsules for oral administration.

Adults: 1 capsule (400 mg) three or four times daily.

Children: Not recommended.

Contra-indications, warnings, etc

Contra-indications: Acute phase of cerebrovascular accidents or recent myocardial infarction. Actual or incipient peripheral gangrene or frostbite.

Special precautions: None.

Side-effects: Nausea, gastro-intestinal distress or flushing may occasionally occur.

Overdosage: Gastric lavage, followed, if necessary, by administration of vasopressors.

Pharmaceutical precautions Store in a cool dry place.

Legal category P.

Package quantities Capsules of 400 mg available in packs of 250.

Further information Cycandelate has a low order of toxicity and for maximum therapeutic effect it is recommended that four capsules daily should be given.

Product licence number 0322/0036.

ENZY PAN*

Presentation Chocolate-coloured, coated tablets containing: In the outer coat which dissolves in the stomach:

Pepsin BPC 1959 12 mg

In the inner core, which is specifically formulated to prevent solution in the stomach and to provide gradual release in the intestine:

Pancreatin BP 1968 180 mg

Desiccated ox bile 60 mg

Uses Replacement therapy in deficiencies of digestive enzymes. Loss of weight after surgery or in convalescence. Foetor-ex-ore.

Dosage and administration *Adults:* 2 or 3 tablets to be swallowed whole with water, during or after each meal.

No specific dosage recommendations can be made for children.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Store in a cool dry place.

Legal category GSL.

Package quantities 120 tablets.

Further information In the total absence of pancreatic secretion, e.g. after pancreatectomy and in chronic pancreatitis, up to 6 tablets with each meal may be necessary for complete replacement.

Product licence number 0322/5002.

FYBRANTA*

Presentation Mottled, light brown tablets. Active ingredients.

Bran 2 g in a base containing calcium phosphate to neutralise the natural phytic acid content of the bran.

Uses The treatment of all colonic and other gastro-enterological diseases where administration of bran is indicated, including the treatment of constipation symptomatic relief in diverticular disease and the 'irritable colon' syndrome. Treatment of conditions requiring a high-fibre regimen.

The inclusion of calcium phosphate ensures neutralisation of the phytic acid in bran, which may otherwise interfere with calcium absorption.

Dosage and administration *Adults:* Usually 1-3 tablets three or four times daily preferably with meals.

At the discretion of the physician, larger quantities may be prescribed in individual cases.

Fybranta tablets should be chewed, part of a tablet at a time, and swallowed with a drink of liquid.

No attempt should be made to swallow the tablets whole.

Contra-indications, warnings, etc Intestinal obstruction, gluten enteropathies.

Pharmaceutical precautions Store in a cool dry place.

Legal category P.

Package quantities 100 tablets.

Further information Most of the published clinical evidence supporting the administration of fibre to patients suffering from pressure diseases of the colon has reported on the administration of bran, not on fibre of other vegetable origin.

Fybranta presents natural cereal fibre in a portable and palatable form.

Product licence number 0322/0016.

KAMILLOSAN* OINTMENT

Presentation Light brown ointment. Active ingredients:

Volatile oil of chamomile	0.5%
Hexyl Resorcinol BP	0.4%
Extract of chamomile	10%

Uses Prophylaxis and treatment of nappy chafe, nappy rash, sore and cracked nipples in nursing mothers, and chapped hands.

Dosage and administration Spread ointment evenly on lint and apply twice daily until the condition clears up. For prevention and treatment of nappy rash, it is advisable to apply the ointment whenever the nappies are changed.

Contra-indications, warnings, etc None known.

Pharmaceutical precautions Store in a cool dry place.

Legal category GSL.

Package quantities 20 g tube.

Further information Nil.

Product licence number 0322/5914.

MURIPSIN*

Presentation Orange, coated tablets. Active ingredients of one tablet:

Glutamic Acid Hydrochloride USNF X111	500 mg
Pepsin BPC 1959	35 mg

Uses The symptomatic treatment of gastric hydrochloric acid deficiency.

Dosage and administration *Adults:* 1 or 2 tablets with each meal.

No specific dosage recommendations can be made for children.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Store in a cool dry place.

Legal category GSL.

Package quantities 50 tablets.

Further information Each Muripsin Tablet is approximately equivalent to the oral administration of 1 ml Dilute Hydrochloric Acid BP.

Product licence number 0322/5005.

NORGOTIN*

Presentation Colourless liquid. Active ingredients:

Ephedrine Hydrochloride BP	1%
Amethocaine Hydrochloride BP	1%
Chlorhexidine Acetate BP	0.1%
Propylene Glycol USP	to 100%

Uses Symptomatic relief of acute and subacute otitis media and otitis externa, used alone or as an adjunct to systemic chemotherapy.

Dosage and administration Twenty drops, or as much less as the ear will hold, instilled into the affected ear each hour until pain subsides, then every three hours.

Contra-indications, warnings, etc Should not be used in the presence of perforation of the tympanic membrane.

Pharmaceutical precautions Store in a cool dry place.

Legal category P.

Package quantities 16 ml dropper bottle.

Further information Nil.

Product licence number 0322/5008.

NORMACOL* ANTISPASMODIC

Presentation Orange, coated granules. Active ingredients:

Sterculia BP	62%
Alverine Citrate USNF X111	0.5%

Uses Treatment of spastic and hypertonic constipation. Treatment of the 'irritable colon' syndrome.

Dosage and administration *Adults:* 1–2 heaped 5 ml spoonfuls once or twice daily after meals.

Children: One half the above amount.

The granules should be placed dry on the tongue and, without chewing or crushing, swallowed with plenty of water.

When given to children, the granules may be administered conveniently by mixing with a little jam.

Contra-indications, warnings, etc Intestinal obstruction.

Pharmaceutical precautions Store in a cool dry place.

Legal category P.

Package quantities 500 g.

Further information Alverine citrate is a synthetic non-narcotic, non-habit-forming spasmolytic of a low order of toxicity in comparison with other anti-spasmodics. It is related to (but more than twice as active as) papaverine and has a specific effect on the smooth muscle of the gut, but not on those of the respiratory or cardiovascular system.

Product licence number 0322/5009.

NORMACOL* SPECIAL

Presentation White, coated granules. Active ingredient: Sterculia BP 62%.

Uses Treatment of constipation during pregnancy and lactation. Management of colostomies and ileostomies. 'High residue diet' management of diverticular disease of the colon. Administration after ingestion of sharp foreign bodies to provide a coating thus reducing the possibility of intestinal damage during transit.

Dosage and administration (other than in the management of ileostomy and colostomy). *Adults:* 1–2 heaped 5 ml spoonfuls once or twice daily after meals.

Children: One half the above amount.

The granules should be placed dry on the tongue and, without chewing or crushing, swallowed with plenty of water.

When given to children, the granules may be administered conveniently by mixing them with a little jam.

Contra-indications, warnings, etc Intestinal obstruction.

Pharmaceutical precautions Store in a cool dry place.

Legal category GSL.

Package quantities 500 g.

Further information Sterculia is a vegetable gum which absorbs up to 60 times its own volume of water, i.e. six times as much as methylcellulose or psyllium.

Product licence number 0322/5010.

NORMACOL* STANDARD

Presentation Brown, coated granules. Active ingredients:

Sterculia BP	62%
Frangula BPC 1949	8%

Uses Treatment of habitual constipation. The initiation and maintenance of bowel action after rectal surgery and after haemorrhoidectomy.

Dosage and administration *Adults:* 1–2 heaped 5 ml spoonfuls once or twice daily after meals.

Children: One half the above amount.

The granules should be placed dry on the tongue and, without chewing or crushing, swallowed with plenty of water.

When given to children, the granules may be administered conveniently by mixing them with a little jam.

Contra-indications, warnings, etc Intestinal obstruction.

Pharmaceutical precautions Store in a cool dry place.

Legal category GSL.

Package quantities 200 g and 500 g.

Further information Sterculia is a vegetable gum which absorbs up to 60 times its own volume of water, i.e. six times as much as methylcellulose or psyllium.

Product licence number 0322/5011.

NORMACOL* STANDARD SUGAR FREE FORMULA

Presentation Brown, sugarless, coated granules. Active ingredients:

Sterculia BP	62%
Frangula BPC 1949	8%

Uses Treatment of habitual constipation. The initiation and maintenance of bowel action after rectal surgery and after haemorrhoidectomy.

Dosage and administration *Adults:* 1–2 heaped 5 ml spoonfuls once or twice daily after meals.

Children: One half the above amount.

The granules should be placed dry on the tongue and, without chewing or crushing, swallowed with plenty of water.

Contra-indications, warnings, etc Intestinal obstruction.

Pharmaceutical precautions Store in a cool dry place.

Legal category GSL.

Package quantities 500 g.

Further information Use as Normacol Standard where carbohydrate intake must be restricted.

Product licence number 0322/5017.

NORMACOL-X*

Presentation White, coated granules accompanied by orange, uncoated tablets.

The active constituent of the granules is Sterculia BP 62%.

The active ingredient of each tablet is Danthron BP 200 mg.

Uses The preparation of patients for abdominal radiography.

Dosage and administration *Adults:* 2 heaped 5 ml spoonfuls of the granules after breakfast, and 1 tablet on retiring. This routine is maintained over the two days preceding that of the examination.

The granules should be placed dry on the tongue and, without chewing or crushing, swallowed with plenty of water.

Children: Not recommended.

Contra-indications, warnings, etc Intestinal obstruction.

In common with all contact laxatives Danthron may cause slight transient discomfort in a small percentage of patients. As the granules provide adequate bulk in the colon, such discomfort usually disappears with the resulting defaecation. Danthron may cause temporary harmless pink or red colouring of the urine.

Pharmaceutical precautions Store in a cool dry place.

Legal category P.

Package quantities Outers of 50 postal packs each containing 40 g granules and 2 tablets.

Further information Each pack contains sufficient granules to enable one further dose to be taken after examination to overcome the tendency to constipation due to dehydration or residual unevacuated barium.

Product licence number 0322/0014.

POSALFILIN*

Presentation Dark brown ointment (fatty base). Active ingredients:

Podophyllum Resin BP	20%
Salicylic Acid BP	25%

Uses Treatment of plantar warts.

Dosage and administration

1. Place a felt corn ring (not a corn plaster) around the wart, if necessary adjusting the size of the hole by snipping, allowing the wart to protrude through the hole.

2. Apply the ointment (using a minimum amount) to exposed wart only. Cover with a piece of plaster.

3. The dressing may be renewed two or three times weekly. When wart appears soft and spongy leave exposed to the air for a day or two when it will usually drop off. If not, repeat the above procedure.

4. Wash hands thoroughly after applying the ointment, and if a waterproof plaster is used normal washing will not effect the efficacy of the treatment.

The treatment can be applied by the patient at home, there are instructions in every pack.

Contra-indications, warnings, etc Posalfilin should only be used under medical supervision.

The patient should be warned that Posalfilin Ointment is extremely caustic to healthy skin.

It should be stressed that if any pain or inflammation is experienced during treatment with Posalfilin, application should be discontinued until the inflammation has subsided.

Pharmaceutical precautions Store in a cool dry place.

Legal category P.

Package quantities 10 g tube.

Further information Nil.

Product licence number 0322/5901.

PREFIL*

Presentation Brown, coated granules. Active ingredient: Sterculia BP 55%.

Uses *Principal action:* The active constituent of Prefil swells in the stomach, by absorption of water, to produce a feeling of satiety. Taken before meals as part of a planned dietary programme, Prefil facilitates appetite control.

Indications: Obesity.

Dosage and administration *Adults:* Two rounded 5 ml spoonfuls, $\frac{1}{2}$ to 1 hour before each meal. The granules should be placed dry on the tongue, in small quantities if necessary, and without chewing or crushing, swallowed with a tumblerful ($\frac{1}{2}$ pint) of water.

Children: At the discretion of the physician, when a reduced dosage may be given.

Contra-indications, warnings, etc

Contra-indications: Intestinal obstruction.

Precautions: Some patients who have become accustomed to an unusually low residue diet may experience slight abdominal discomfort from the increase in bulk which follows the administration of full doses of Prefil. These patients may be advised to take a smaller dose initially, increasing to the full dose over a period of one week. In these circumstances, the full clinical effect may not be experienced until the end of the first week.

Pharmaceutical precautions Store in a cool dry place.

Legal category GSL.

Package quantities 500 g.

Further information The active ingredient of Prefil is totally unabsorbed and therefore appetite control is

facilitated without inducing the systemic problems often associated with other anti-obesity preparations.

Available carbohydrate content approx. 1.6 g per spoonful (as sucrose) equivalent to 6 Cals.

Product licence number 0322/0035.

PYRALVEX*

Presentation Brown liquid. Active ingredients:

Extract of Anthraquinone glycosides	5%
Salicylic Acid BP	1%

Uses Treatment of inflammatory conditions of the oral mucosa.

Dosage and administration To be applied to the inflamed oral mucosa (after removing any dentures worn) three or four times daily using the brush provided.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities 10 ml bottle with brush.

Further information A double-blind study indicated that in topical treatment of inflammatory diseases of the oral and oropharyngeal mucosa, Pyralvex was more effective than corticosteroids.

Product licence number 0322/5013.

SOMNITE*

Presentation Round, white, uncoated, flat, bevel-edged tablets of 12 mm diameter with a single break line on one side and sailing boat design on the other. Each tablet contains Nitrazepam BP 5 mg.

Uses *Principal action:* Somnite is a non-barbiturate hypnotic agent which rapidly induces sleep lasting six to eight hours, by inhibiting stimuli to brain centres which maintain wakefulness.

Indications: Short term treatment of insomnia where daytime sedation is acceptable.

Dosage and administration *Adults:* 5 mg (1 tablet) before retiring. This average dose may, if necessary be increased up to 10 mg and for in-patients up to 20 mg.

Elderly patients: 2.5–5 mg.

Children: Not recommended.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to benzodiazepines. Acute pulmonary insufficiency.

There is no evidence as to drug safety in human pregnancy nor is there evidence from animal work that it is free from hazard. Do not use during pregnancy, especially during the first and last trimesters, unless there are compelling reasons.

Precautions: Chronic pulmonary insufficiency. In chronic renal or hepatic disease. In labour. High single doses or repeated low doses have been reported to produce hypotonia, poor sucking and hypothermia in the neonate and irregularities in the foetal heart. Avoid if possible in lactation. The concurrent use of other CNS depressant drugs should be avoided.

Warnings and side-effects: Common adverse effects include drowsiness, sedation, blurring of vision, un-

steadiness and ataxia. These effects occur following single as well as repeated dosage and may persist well into the following day. Performance at skilled tasks and alertness may be impaired. Patients should be warned of this hazard and advised not to drive or operate machinery during treatment. These effects are potentiated by alcohol. The elderly are particularly liable to experience these symptoms together with confusion especially if organic brain symptoms are present. See also Dependence Potential and Withdrawal Symptoms below.

Abnormal psychological reactions to benzodiazepines have been reported. Rare behavioural adverse effects include paradoxical aggressive outbursts, excitement, confusion, and the uncovering of depression with suicidal tendencies.

Other rare adverse effects including hypotension, gastro-intestinal and visual disturbances, skin rashes, urinary retention, headache, vertigo, changes in libido; blood dyscrasias and jaundice have also been reported.

Dependence potential and withdrawal symptoms: In general the dependence potential of benzodiazepines is low but this increases when high dosages are attained, especially when given over long periods. This is particularly so in patients with a history of alcoholism, drug abuse or in patients with marked personality disorders. Regular monitoring of treatment in such patients is essential and routine repeat prescriptions should be avoided.

Treatment in all patients should be withdrawn gradually as symptoms such as depression, nervousness, rebound insomnia, irritability, sweating and diarrhoea have been reported following abrupt cessation of treatment in patients receiving even normal therapeutic doses for short periods of time.

Abrupt withdrawal following excessive dosage may produce confusion, toxic psychosis, convulsions or a condition resembling delirium tremens.

Overdosage: The primary symptoms of overdosage are drowsiness, dizziness, ataxia and slurred speech. Treatment is symptomatic but gastric lavage may be useful if performed soon after ingestion.

Pharmaceutical precautions Somnite tablets should be stored in a cool, dry place and protected from light and moisture.

Legal category POM.

Package quantities Somnite tablets 5 mg are available in packs of 100 and 500.

Further information Somnite is a long acting benzodiazepine. Repeated dosage will lead to accumulation of whole drug and metabolites. The elderly and patients with impaired renal and/or hepatic function will be particularly susceptible to the adverse effects listed above. Treatment should be kept to a minimum and given only under close medical supervision.

Little is known regarding efficacy or safety of benzodiazepines in long-term use. It is advisable to review treatment regularly and to discontinue use as soon as possible.

Somnite does not induce microsomal enzymes as may occur with barbiturates and may be given together with commonly used cardiovascular drugs, anticoagulants, antihypertensives, stimulants, spasmolytics, antidepressants and chemotherapeutic agents.

Product licence number 0322/0034.

SPASMONAL*

Presentation Blue/grey opaque hard gelatin capsules, each containing 60 mg Alverine Citrate USNF XIII.

Uses Selective smooth muscle spasmolytic.

Dosage and administration *Adults:* 1 or 2 capsules one to three times daily, orally.

No specific dosage recommendations can be made for children.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Store in a cool dry place.

Legal category P.

Package quantities 100 capsules.

Further information Alverine citrate is a synthetic, non-narcotic, non-habit-forming spasmolytic of a low order of toxicity in comparison with other anti-spasmodics. It is related to (but more than twice as active as) papaverine, and has a specific effect on the smooth muscle of the intestine and uterus, but not on those of the respiratory or cardiovascular system.

Product licence number 0322/5014.

TAMPOVAGAN* 'N' (NEOMYCIN) PESSARIES

Presentation Off-white, hard vaginal pessaries. Active ingredient: Neomycin Sulphate BP 20 mg.

Uses Treatment of intractable vaginitis.

Dosage and administration Two pessaries to be inserted high into the vagina every night before retiring to bed. Treatment should be continued throughout the period of menstruation.

Contra-indications, warnings, etc None reported. Neomycin sulphate in the form of pessaries rarely causes irritation or allergic reaction, but should clearly not be used in patients with a known sensitivity to neomycin. Not recommended for children.

Pharmaceutical precautions Store in a cool dry place.

Legal category POM.

Package quantities Cartons of 10.

Further information Nil.

Product licence number 0322/5909.

TAMPOVAGAN* STILBOESTROL AND LACTIC ACID PESSARIES

Presentation Off-white, hard, vaginal pessary. Active ingredients:

Stilboestrol BP 0.5 mg in a base containing Lactic Acid BP 5%.

Uses Treatment of atrophic vaginitis, senile vaginitis and menopausal vaginitis.

Dosage and administration Two pessaries to be inserted high into the vagina at night.

Contra-indications, warnings, etc Should not be used in pregnancy or suspected pregnancy or in women who might become pregnant. Not recommended for children.

Pharmaceutical precautions Store in a cool dry place.

Legal category POM.

Package quantities Cartons of 10.

Further information Nil.

Product licence number 0322/5910.

WAXSOL*

Presentation Colourless liquid. Active ingredient: Docusate sodium 5% in a water-miscible base.

Uses Cerumenolytic.

Dosage and administration For aural use only. The patient should be directed to fill the ear with Waxsol on two consecutive nights only, before attending for syringing.

Contra-indications, warnings, etc Should not be used in the presence of perforation of the ear drum or when there is inflammation of the ear. Discontinue use if any pain or inflammation is experienced.

Pharmaceutical precautions Store in a cool place.

Legal category GSL.

Package quantities 16 ml dropper bottle.

Further information Waxsol, because of its low surface tension and its water-miscibility, rapidly penetrates the dry matrix of the ceruminous mass, reducing the solid material to a semi-solid debris which can be syringed away readily or, in less severe and in chronic cases, is ejected by normal physiological processes.

Product licence number 0322/5016.

**Trade Mark*

Norwich-Eaton Limited
Regent House
The Broadway, Woking
Surrey GU21 5AP



ALPHADERM*

Presentation Alphaderm is a translucent white cream containing hydrocortisone 1% and hypermolar urea 10% in a specially formulated powder-in-cream base which assists the percutaneous transportation of the active ingredients to the site of action. Alphaderm does *not* contain lanolin or parabens. The base is self-occlusive and ambiphilic and may be used either as a cream or an ointment.

Uses Alphaderm is indicated for the treatment of: eczema, including atopic, infantile and hyperkeratotic; intertrigo; neurodermatitis and all lichenoid conditions; contact dermatitis; photosensitivity reactions and prurigo.

Dosage and administration Alphaderm is applied topically. Wash affected areas well, dry, and apply directly to the lesions twice daily. Because it has a pH bordering on that of the skin, Alphaderm may be rubbed in well without causing irritation or stinging, even when applied to abrasions or to areas of broken skin. Occlusive dressings may be used but are usually unnecessary because of the self-occlusive nature of the special base.

Contra-indications, warnings, etc Alphaderm is contra-indicated in bacterial, viral and fungal diseases of the skin.

Precautions: In pregnant animals, administration of corticosteroids can cause abnormalities of foetal development. The relevance of this finding in human beings has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods. In infants, long-term continuous topical therapy should be avoided. Adrenal suppression can occur even without occlusion.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Alphaderm is available in tubes of 30 g and 100 g.

Further information Though the preparation has a non-greasy texture, the hydrocortisone content is micronised and dispersed in an oily medium. This is probably responsible for the long-lasting therapeutic effect which has been noted after the application of Alphaderm. Optimum rehydration of dry skin is achieved without the use of occlusive dressings.

Product licence number 0364/0019.

AQUADRATE*

Presentation Aquadrate is a translucent white cream containing hypermolar urea 10% in a specially formulated powder-in-cream base. Because of its keratolytic action it hydrates and penetrates the epidermis. Although Aquadrate has a non-greasy texture, the polysaccharide

matrix on to which the urea is adsorbed is dispersed in an ambiphilic medium which imparts a self-occlusive property. It therefore fulfils the functions of both an ointment and a cream. Aquadrate does *not* contain lanolin, parabens or any preservative likely to irritate or sensitise the skin.

Uses Aquadrate is indicated in ichthyosis, xeroderma, hyperkeratosis and other chronic dry skin conditions. It is also useful in the treatment of steroid-induced rosacea.

Dosage and administration Aquadrate is applied topically. Wash affected areas well, rinse off all traces of soap, dry, and apply sparingly. Use as often as necessary. Because it has a pH bordering on that of the skin, Aquadrate may be rubbed in well without causing stinging, even when applied to abrasions and areas of broken skin. Occlusive dressings may be used but are usually unnecessary because of the self-occlusive nature of the cream.

Contra-indications, warnings, etc There are no contra-indications to the use of Aquadrate.

Pharmaceutical precautions There are no special storage requirements.

Legal category P.

Package quantities Aquadrate is available in tubes of 30 g and 100 g.

Further information Nil.

Product licence number 0364/0018.

CHLORASEPTIC LIQUID

Presentation Chloraseptic liquid consists of a dark green, aqueous solution containing phenol BP and sodium phenolate (total phenol 1.4%), menthol, thymol and glycerin.

Uses Chloraseptic liquid is recommended for the relief of the pain associated with sore throat (pharyngitis), tonsillitis and superficial mucosal lesions as well as aphthous ulcers, Vincent's ulcers, moniliasis, and denture ulcers. Chloraseptic will also relieve post-operative pain following dental surgery. Chloraseptic will also control halitosis associated with minor mouth and throat infections.

Dosage and administration *Spray:* For sore throat – use full strength – Adults should spray throat five times at first; children from 6–12 years, three times. Repeat every two hours if necessary.

Gargle: As a gargle for sore throat – use full strength or dilute with equal parts of water. Rinse thoroughly, then expel remainder.

Mouthwash: For mouth and gum irritations – use full

strength. Rinse for 15 seconds, then expel remainder. As a deodorising mouthwash – use full strength or dilute with equal parts of water. Rinse thoroughly, then expel remainder.

Contra-indications, warnings, etc Not to be given to children under six years unless directed by physician. Consult physician if sore throat is severe or lasts more than two days, or is accompanied by high fever, headache, nausea or vomiting.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities 120 ml with spray attachment and 150 ml bottle.

Further information Nil.

Product licence number 0364/0023.

DANTRIUM*

Presentation Dantrium capsules are available in two strengths, containing either 25 mg or 100 mg dantrolene sodium per capsule.

Dantrium is presented in orange/cream capsules. The 25 mg capsule carries the monogram Eaton 030 on both sections of the capsule. The 100 mg capsule carries the monogram Eaton 033 on both sections.

Uses Dantrium produces relaxation of contracted skeletal muscle by affecting the contractile response at a site beyond the myoneural junction. Dantrium produces a dissociation of excitation-contraction coupling, probably by interfering with the release of Ca^{++} from the sarcoplasmic reticulum. The effect is seen in both fast and slow fibres but is more pronounced in the former.

Dantrium is indicated for the treatment of chronic, severe spasticity resulting from such disorders as stroke, multiple sclerosis, spinal cord injury and cerebral palsy. It is useful in these conditions whenever spasticity is so severe that increased muscular resistance to stretch, clonus or exaggerated reflex posturing interfere with the activities of daily living such as exercise, posture, equilibrium, walking, transfer manoeuvres or the use of braces.

Occasionally, only a subtle but perceptible improvement in spasticity may occur with Dantrium therapy. In such instances information regarding improvement should be sought from the patient and those who are in constant daily contact and attendance on him. Brief withdrawal of Dantrium for a period of two to four days will frequently demonstrate exacerbation of the spasticity and may help to reinforce a previously indefinable clinical impression.

Dosage and administration Before commencing Dantrium therapy, it is important to set an attainable therapeutic goal for the individual patient. Such a goal would be a reduction in spasticity which allows the patient or his attendants to carry out a function which could not previously be performed or one that he or his attendants consider important.

The need for patience and attention to the individual patient's needs in titrating Dantrium dosage is of paramount importance.

Dosage should be increased until the maximum benefit compatible with the patient's neurological deficit is achieved.

The lowest dose compatible with optimal response is

recommended, dosage in excess of 400 mg/day is not recommended.

A recommended dosage increment scale is shown below:

Week	Recommended dosage
First	One 25 mg capsule daily
Second	One 25 mg capsule twice daily
Third	Two 25 mg capsules twice daily
Fourth	Two 25 mg capsules three times daily
Fifth	Three 25 mg capsules three times daily
Sixth	Three 25 mg capsules four times daily
Seventh	One 100 mg capsule four times daily

Most patients will achieve their therapeutic goal at a titrated dose of 75 mg three times daily.

If no observable benefit is derived from the administration of Dantrium after a total of 45 days, therapy should be discontinued.

Many patients experience side effects such as weakness and fatigue during the first four weeks of therapy whilst the patient adjusts to the changes in muscle tone induced by the drug. They are usually transient and mild in nature. Patients should be warned of them and encouraged to persevere with treatment. Should it be necessary the dosage of Dantrium may be reduced and then gradually increased according to the patient's tolerance. It may be possible to reduce the duration of each dosage stage to four days, depending on the patient's reaction to the drug.

Contra-indications, warnings, etc

Contra-indications. Dantrium is contra-indicated where spasticity is utilised to sustain upright posture and balance in locomotion or whenever spasticity is utilised to obtain or maintain increased function.

Dantrium is contra-indicated in patients with evidence of hepatic dysfunction. Isolated cases of jaundice in patients receiving Dantrium have been reported.

Dantrium should not be administered to children.

Warnings: *Usage in pregnancy:* Although teratological studies in animals have proved satisfactory, as with all new medicines the safety of Dantrium in pregnancy has not been established. In such patients, the potential benefits must be weighed against the possible hazards.

Precautions: Dantrium has a potentially hepatotoxic action. Before beginning Dantrium therapy, liver function tests should be performed in all patients (SGOT or SGPT, alkaline phosphatase, total bilirubin, LDH, or their equivalents) to establish a base-line, and to rule out pre-existing liver disease. These tests should be repeated upon hospital discharge or at six weeks after starting therapy; further tests may be carried out at the physician's discretion. Generally, if these studies reveal abnormal values, therapy should not be commenced or should be discontinued when other causes for these abnormalities cannot be found. Some patients have reverted to normal laboratory values during continuation of therapy, whilst others have not.

The use of Dantrium with other potentially hepatotoxic drugs should be avoided.

Dantrium should be used with caution in patients with impaired pulmonary function, particularly those with obstructive pulmonary disease, and in patients with severely impaired cardiac function due to myocardial disease.

Patients should be advised not to drive a motor vehicle

or to undertake potentially dangerous work until Dantrium therapy has been stabilised.

Although the primary pharmacological effect of Dantrium is exerted directly on skeletal muscle, caution should be exercised in the concomitant administration of tranquillising agents.

Action in event of overdose: For acute overdose, general supportive measures should be employed along with immediate gastric lavage.

Fluids should be administered in large quantities to avert the theoretical possibility of crystalluria.

Side-effects and adverse reactions: The most frequently occurring side-effects of Dantrium have been drowsiness, dizziness, weakness, general malaise, fatigue and diarrhoea. These effects are generally transient, occur early in treatment, and can often be obviated by careful determination and regulation of the dosage.

Pharmaceutical precautions Dantrium capsules should be stored at room temperature.

Suitable containers are polypropylene, natural polyethylene, amber polyethylene, or amber glass bottles.

Legal category POM.

Package quantities Dantrium capsules 25 mg and Dantrium capsules 100 mg are supplied in containers of 100 capsules.

Further information The duration and intensity of skeletal muscle relaxation in patients on Dantrium is related to the dosage and blood levels. The mean biological half-life of Dantrium is about nine hours after a 100 mg dose.

Studies specifically designed to determine compatibility with diazepam and phenobarbitone revealed that neither of these drugs appears to affect Dantrium metabolism.

Product licence numbers

Dantrium capsules 25 mg 0364/0015
Dantrium capsules 100 mg 0364/0016

DANTRIUM* INTRAVENOUS ▼

Presentation Dantrium Intravenous is available as a sterile, lyophilized orange powder which is a mixture of 20 mg dantrolene sodium, 3000 mg mannitol and sufficient sodium hydroxide to yield a pH of approximately 9.5 when reconstituted with 60 ml of water for injection BP.

Uses Dantrium Intravenous is indicated for the treatment of malignant hyperthermia. It is for intravenous use only.

In isolated muscle preparations, dantrolene sodium uncouples the excitation and contraction of skeletal muscle, probably by interfering with the release of calcium from the sarcoplasmic reticulum.

In the malignant hyperthermia syndrome, evidence points to an intrinsic abnormality of muscle tissue. It has been postulated that 'triggering agents' (i.e. skeletal muscle relaxants and inhalation anaesthetics) induce a sudden rise in myoplasmic calcium, either by preventing the sarcoplasmic reticulum from accumulating calcium adequately, or by accelerating its release. This rise in myoplasmic calcium activates the acute catabolic processes common to the malignant hyperthermia crisis.

Dantrolene sodium may prevent the increases in myoplasmic calcium and the acute catabolism within the muscle cell by interfering with the release of calcium from the sarcoplasmic reticulum to the myoplasm. Thus the physiological, metabolic and biochemical changes associated with the crisis may be reversed or attenuated.

Dosage and administration As soon as the malignant hyperthermia syndrome is recognised all anaesthetic agents should be discontinued. An initial Dantrium Intravenous dose of 1 mg/kg should be given rapidly. If the physiological and metabolic abnormalities persist or reappear, this dose may be repeated up to a cumulative dose of 10 mg/kg. Clinical experience to date has shown that the average dose of Dantrium Intravenous required to reverse the manifestations of malignant hyperthermia has been 2.5 mg/kg. If a relapse or recurrence occurs, Dantrium Intravenous should be readministered at the last effective dose.

Contra-indications, warnings, etc Precautions:

1. In some subjects as much as 10 mg/kg of Dantrium Intravenous has been needed to reverse the crisis. In a 70 kg man this dose would require approximately 36 vials. Such a volume has been administered in approximately one and a half hours.

2. Because of the high pH of the intravenous formulation of Dantrium, care must be taken to prevent extravasation of the intravenous solution into the surrounding tissues.

3. **Pregnancy:** The safety of Dantrium Intravenous in pregnant women has not been established; it should be given only when the potential benefits have been weighed against the possible risk to mother and child.

Warnings: The use of Dantrium Intravenous in the management of malignant hyperthermia is not a substitute for previously known supportive measures. It will be necessary to discontinue the suspect triggering agents, attend to increased oxygen requirements and manage the metabolic acidosis. When necessary institute cooling, attend to urinary output and monitor for electrolyte imbalance.

Side-effects and adverse reactions: No side-effects have been attributed to Dantrium Intravenous. The nature of the emergency and the complexity of concomitant therapy will make it extremely difficult to isolate cause and effect relationships for any of the drugs used. Hepatotoxic reactions have been noted in a small number of subjects given long term oral dantrolene therapy.

Pharmaceutical precautions Each vial of Dantrium Intravenous should be reconstituted by adding 60 ml of water for injection BP, and shaking until the solution is clear. The contents of the vial must be protected from direct light and used within six hours after reconstitution. Protect the reconstituted solutions from temperatures above 30°C and below 15°C.

Unreconstituted product should be protected from light and stored below 30°C.

Legal category POM.

Package quantities Dantrium Intravenous is available in packs of twelve vials each containing 20 mg dantrolene sodium.

Further information Nil.

Product licence number 0364/0030.

FURACIN*

Presentation Furacin Soluble Ointment is a yellow ointment containing 0.2% nitrofurazone in a water-soluble polyethylene glycol base.

Furacin Solution (Sterile) is a yellow liquid containing 0.2% nitrofurazone in a water-miscible vehicle.

Uses Furacin is a broad-spectrum topical antibacterial effective in the presence of blood, pus and serum.

Furacin is indicated in bacterial skin infections including pyodermas, infected dermatoses and infections of wounds, burns and ulcers. Furacin is also of value in the treatment of skin-graft donor sites. Furacin Solution (Sterile) may be used as a bladder irrigant or instillate (diluted 1 in 6 with sterile water for injection).

Dosage and administration Furacin Soluble Ointment: Furacin Soluble Ointment is administered topically. Apply directly to the wound with sterile tongue-depressor or other spatula. Alternatively, melt the ointment in a beaker at a little above body temperature and pour gently on to the wound.

The ointment may also be applied on a gauze dressing. For extensive burned areas, large strips of sterile gauze impregnated with Furacin are often preferred. Bandages may be prevented from absorbing Furacin Soluble Ointment by covering the Furacin impregnated gauze with an impermeable layer, such as jaconet or gauze saturated with petroleum jelly. If bandages stick, remove them by saturating with sterile saline. Dressings may be left undisturbed on burns, cuts and wounds for 7–10 days.

Furacin Solution (Sterile): Furacin Solution (Sterile) may be administered either topically or as an instillate.

Furacin may be used for children at the doctor's discretion.

Contra-indications, warnings, etc Furacin is a contra-indicated in patients with known sensitivity to nitrofurazone.

It is not recommended to continue using Furacin when the infection is cleared.

Furacin Solution and Furacin Ointment should be used with caution in patients with known or suspected renal impairment. The polyethylene glycols in the base can be absorbed through denuded skin and may not be excreted normally by the compromised kidney. This may lead to symptoms of progressive renal impairment.

Side-effects and adverse reactions: Sensitisation to Furacin has been reported. Should this occur, treatment should be discontinued. Since the drug is not used systemically, sensitisation does not carry the implications for the patient that sensitisation to systemic therapy with antibiotics or sulphonamides may.

Pharmaceutical precautions Furacin Soluble Ointment is supplied in aluminium collapsible tubes. The ointment should be stored in light-proof containers and contact with metals other than stainless steel or aluminium should be avoided. There are no other special storage requirements.

Furacin Solution is supplied as a sterile product in 50 ml amber bottles. The product should be protected from light by storing in a dark place. Once opened Furacin Solution (Sterile) should be used immediately. Any unused solution must be discarded.

Legal category POM.

Package quantities Furacin Soluble Ointment is available in tubes of 25 g. Furacin Solution (Sterile) is available in bottles of 50 ml.

Further information Nil.

Product licence numbers

Furacin Soluble Ointment 0364/0013

Furacin Solution (Sterile) 0364/0012

FURADANTIN*

Presentation Furadantin Tablets are yellow in colour and have a pentagonal shape. Each tablet has a break line on one face and the tablet strength is shown on the opposite face. Furadantin Tablets are available in two strengths, containing 100 mg or 50 mg nitrofurantoin.

Furadantin Suspension is a yellow suspension containing 25 mg nitrofurantoin per 5 ml.

Uses Furadantin is a broad-spectrum antibacterial agent, active against the majority of urinary pathogens. It is bactericidal in renal tissue and throughout the urinary tract. After oral administration the nitrofurantoin is rapidly excreted in the urine, up to 45% being unchanged.

Therapeutic: Cystitis, pyelitis, pyelonephritis; also post-operative infections of the genito-urinary tract, particularly after the passage of instruments and after prostatectomy.

Prophylactic and suppressive: As cover for catheterisation or instrumentation of the urinary tract. To prevent reinfection in susceptible individuals.

Dosage and administration Furadantin is administered orally. The dose should be taken with each meal and at bedtime, with food or milk.

In the event of severe nausea the dose may be reduced, but not below the adult equivalent of 200 mg in 24 hours. Should it persist the drug should be withdrawn.

Therapeutic – Adults: Tablets: One 100 mg tablet (or two 50 mg) four times a day.

Suspension: Four 5 ml spoonfuls four times a day.

Therapeutic – Children: Furadantin Suspension or Furadantin Tablets 50 mg may be used. Dosage recommendations for children are given in the table below. It is not recommended to dilute Furadantin Suspension.

Body weight		Average age for weight	Dose to be taken four times daily	
lb	kg		Suspension	50 mg Tablets
10–30	5–13	3–30 months	2.5 ml	$\frac{1}{2}$
30–50	13–23	2½–6 years	5 ml	$\frac{1}{2}$
50–80	23–36	6–11 years	10 ml	1
80–110	36–50	11–14 years	15 ml	1½

Treatment at this dose level for more than 14 days is seldom necessary.

Prophylactic and suppressive: When such therapy is desirable one quarter to one half of the therapeutic dose is suggested.

Contra-indications, warnings, etc Infants under one month should not be given Furadantin.

Furadantin is contra-indicated in patients suffering from anuria or marked oliguria.

A small number of negroes and some people from the Eastern Mediterranean area suffer from a deficiency of glucose-6-phosphate dehydrogenase in their blood cells. In such people, nitrofurantoin in common with many other therapeutic agents may cause haemolysis. This enzyme deficiency is extremely rare in Caucasians. Any sign of haemolysis is an indication to discontinue the drug. Haemolysis ceases when the drug is withdrawn.

Precautions: Furadantin should only be used in pregnancy if considered essential by the physician. Foetal studies in animals with Furadantin do not suggest that it causes any increase in the incidence of congenital abnormalities. This is confirmed by over 28 years of clinical usage. However, it is recognised that caution should be observed when prescribing for the pregnant patient.

Action in event of overdose: Excessive intake would probably cause vomiting. Should overdose occur, stomach wash-out is recommended.

Side-effects: Nausea or vomiting may occur, but this can be minimised or eliminated by taking the drug with food or milk, or adjustment of dosage.

Adverse reactions: Peripheral neuropathy has been reported after treatment with Furadantin but has usually been associated with severe renal impairment and/or prolonged therapy. Should numbness or tingling occur in any part of the body, treatment should be discontinued.

Drug rashes, pyrexia and hepatitis associated with nitrofurantoin therapy have been reported. The hepatitis is of an allergic type and may be associated with antinuclear factor and lymphocyte sensitisation.

A respiratory syndrome with bronchospasm and/or dyspnoea, cough and sometimes chest pain has been reported. These symptoms have occasionally been associated with transitory pulmonary infiltration or pleural effusion.

These adverse reactions to nitrofurantoin therapy are rare.

Antidote: There is no known specific antidote to nitrofurantoin.

Pharmaceutical precautions Furadantin Tablets are supplied in polypropylene containers with polythene pilfer-proof caps. The tablets should be stored in light-proof and preferably moisture-proof containers. There are no other special storage requirements.

Furadantin Suspension is supplied in amber bottles and should be stored in a cool place. The suspension should be protected from light as exposure will cause darkening of the active principle. Because of this, amber bottles should be used in dispensing. The glass should preferably be neutral since discoloration will occur on contact with alkaline materials.

It is not recommended to dilute Furadantin Suspension.

Legal category POM.

Package quantities Furadantin Tablets 100 mg and 50 mg are supplied in packs of 100 and 1,000. Furadantin Suspension is supplied in bottles of 300 ml.

Further information Furadantin is not a sulphonamide; there is no need to increase fluid intake or give alkalis; forcing fluids beyond normal merely dilutes the antibacterial concentration in the urine.

The urine of patients receiving Furadantin may be coloured a dark yellow or brown. This results from the presence of metabolites and is quite harmless.

Product licence numbers

Furadantin Tablets 50 mg	0364/0008
Furadantin Tablets 100 mg	0364/0009
Furadantin Suspension	0364/0010

MACRODANTIN®

Presentation Macrochantin is presented in hard gelatin capsules, and is available in two strengths, containing 100 mg and 50 mg nitrofurantoin macrocrystals.

The 100 mg capsule has an opaque yellow body and cap, and bears the monogram 'Macrochantin' 100.

The 50 mg capsule has an opaque yellow cap, an opaque white body and bears the monogram 'Macrochantin' 50.

Uses Macrochantin is a broad-spectrum antibacterial agent, active against the majority of urinary pathogens. It is bactericidal in renal tissue and throughout the urinary tract.

The nitrofurantoin macrocrystals of Macrochantin are specially formulated. The controlled crystal size is designed to control the speed of absorption and thus reduce the incidence of nausea. Clinical and animal studies indicate that Macrochantin therapy decreases the likelihood of nausea in patients who might experience these symptoms on nitrofurantoin therapy. This special reformulation of nitrofurantoin has not caused any decrease in its bioavailability.

Therapeutic: Cystitis, pyelitis, pyelonephritis; also post-operative infections of the genito-urinary tract, particularly after the passage of instruments and after prostatectomy.

Prophylactic and suppressive: As cover for catheterisation or instrumentation of the urinary tract. To prevent reinfection in susceptible individuals.

Dosage and administration Macrochantin is administered orally. The dose should be taken with each meal and at bedtime, with food or milk.

Therapeutic - Adults: Capsules: One 100 mg capsule (or two 50 mg) four times a day.

Children: For children, Macrochantin 50 mg capsules may be used. Dosage recommendations for children are given in the table below. Treatment at this dose level for more than 14 days is seldom necessary.

Body weight		Average age for weight (years)	Dosage, 50 mg capsules
lb	kg		
30-50	13-23	2½-6	1 capsule twice a day
50-80	23-36	6-11	1 capsule four times a day
80-110	36-50	11-14	2 capsules three times a day

In the event of severe nausea the dose may be reduced, but not below the adult equivalent of 200 mg in 24 hours. Should it persist the drug should be withdrawn.

Prophylactic and suppressive: When such therapy is desirable one quarter to one half of the therapeutic dose is suggested.

Contra-indications, warnings, etc Infants under one month should not be given Macrochantin.

Macrochantin is contra-indicated in patients suffering from anuria or marked oliguria.

A small number of negroes and some people from the Eastern Mediterranean area suffer from a deficiency of glucose-6-phosphate dehydrogenase in their blood cells. In such people, nitrofurantoin in common with many other therapeutic agents may cause haemolysis. This enzyme deficiency is extremely rare in Caucasians. Any sign of haemolysis is an indication to discontinue the drug. Haemolysis ceases when the drug is withdrawn.

Precautions: Macrochantin should only be used in pregnancy if considered essential by the physician. Foetal studies with the active ingredient nitrofurantoin, do not suggest that Macrochantin causes any increase in the incidence of congenital abnormalities. This is confirmed by over 28 years of clinical use of nitrofurantoin. However it is recognised that caution should always be observed when prescribing for the pregnant patient.

Action in event of overdosage: Excessive intake would probably cause vomiting. Should overdosage occur stomach wash-out is recommended.

Side-effects: Nausea or vomiting may occur, but this can be minimised or eliminated by taking the drug with food or milk, or adjustment of dosage.

Adverse reactions: Peripheral neuropathy has been reported after treatment with nitrofurantoin but has usually been associated with severe renal impairment and/or prolonged therapy. Should numbness or tingling occur in any part of the body, treatment should be discontinued.

Drug rashes, pyrexia and hepatitis associated with nitrofurantoin therapy have been reported. The hepatitis is of an allergic type and may be associated with antinuclear factor and lymphocyte sensitisation.

A respiratory syndrome with bronchospasm and/or dyspnoea, cough and sometimes chest pain has been reported. These symptoms have occasionally been associated with transitory pulmonary infiltration or pleural effusion.

These adverse reactions to nitrofurantoin therapy are rare.

Antidote: There is no known specific antidote to nitrofurantoin.

Pharmaceutical precautions Macrochantin Capsules are supplied in polypropylene containers with polythene pilfer-proof caps. The capsules should be stored in light-proof and preferably moisture-proof containers. There are no other special storage requirements.

Legal category POM.

Package quantities Macrochantin Capsules 100 mg and 50 mg are supplied in containers of 100.

Further information Macrochantin is not a sulphonamide: there is no need to increase fluid intake or give alkalis; forcing fluids beyond normal merely dilutes the antibacterial concentration in the urine.

The urine of patients receiving Macrochantin may be coloured a dark yellow or brown. This results from the presence of metabolites and is quite harmless.

Product licence numbers

Macrochantin Capsules 50 mg 0364/0005
Macrochantin Capsules 100 mg 0364/0006

PSORADRATE CREAM*

Presentation Psoradrate cream is a smooth textured, unperfumed, bland, yellow cream containing 0.1%

dithranol BP or 0.2% dithranol BP in a specially formulated powder-in-cream base which includes stabilised, hypermolar urea to assist percutaneous transportation of the active ingredient.

Uses Psoradrate cream is indicated for the treatment of subacute and chronic psoriasis. In addition, Psoradrate 0.1% is indicated for the treatment of psoriasis of the scalp.

Dosage and administration Wash affected areas well, dry thoroughly and apply directly to the lesions twice daily. Treatment should be continued until the raised lesions have disappeared and the skin is smooth. Occlusive dressings should not be used because they may increase the incidence of staining and stinging on normal skin. For use on the scalp, shampoo and dry hair, then rub Psoradrate 0.1% into the lesions, preferably at night. Remove the next morning with shampoo.

Contra-indications, warnings, etc Psoradrate cream is contra-indicated in pustular psoriasis.

The active ingredient of Psoradrate cream, dithranol, may cause a tingling or stinging sensation when applied to skin or lesions. It is irritant to the eyes. If contact occurs wash out immediately with a neutral solution. Exercise care when applying to the face and intertriginous areas. Skin staining may occur and clothing may occasionally be discoloured. For external use only.

Pharmaceutical precautions Store in a cool place. Shelf life: two years. Keep out of reach of children.

Legal category POM.

Package quantities Psoradrate is available in tubes of 30 g and 100 g.

Further information Before using creams containing high concentrations of dithranol it is advisable to establish the patient's tolerance. In cases in which tolerance has not been established, treatment of psoriatic lesions should be commenced with a low concentration of dithranol, namely Psoradrate 0.1%. If the patient's skin can tolerate Psoradrate 0.1% cream, but the lesions appear resistant, then treatment should be changed to Psoradrate 0.2% cream to aid the clearance of the lesions. If, however, the patient is known to have a high tolerance to dithranol then therapy can be commenced using Psoradrate 0.2% cream.

Use of a descaling agent such as salicylic acid is not necessary with Psoradrate creams. The creams are absorbed into the skin and the inconvenience of removing the applications is avoided. Relapse rate with dithranol therapy has been reported as being less than that seen with steroids. Stains on clothes can be removed with a solvent such as trichloroethylene. Psoradrate cream does not contain lanolin or parabens.

Product licence numbers

Psoradrate Cream 0.1% 0364/0027
Psoradrate Cream 0.2% 0364/0031

VIVONEX* STANDARD

Presentation Vivonex Standard is an off-white, unflavoured water-soluble powder. The contents of one packet supply 300 kilocalories (1.256 MJ) and the following:

	<i>Grams</i>	<i>% by weight</i>
Available nitrogen in the form of pure amino acids (amino acid content 6.18 g)	0.98	1.22
Fat as highly purified safflower oil (80% as triglyceride of linoleic acid)	0.435	0.54
Carbohydrate as glucose solids	69.0	86.3

Caloric contribution:

Amino acids 8.2%

Fat 1.3%

Carbohydrate 90.5%

Six packets of Vivonex Standard supply 5.88 g of available nitrogen, 2.61 g fat, 414 g carbohydrate and the vitamins, amino acids and minerals shown in the following table.

<i>Vitamins</i>	<i>Per 80 g packet</i>	<i>In six 80 g packets</i>
Vitamin A (Retinol) IU	833.33	5,000
Vitamin D ₂ (Ergocalciferol) IU	66.67	400
Vitamin E IU	5	30
Vitamin C (Ascorbic acid) mg	10	60
Folic Acid mg	0.07	0.4
Vitamin B ₁ (Thiamine) mg	0.25	1.5
Vitamin B ₂ (Riboflavin) mg	0.28	1.7
Nicotinamide mg	3.33	20
Vitamin B ₆ mg	0.33	2
Vitamin B ₁₂ mcg	1	6
Biotin mg	0.05	0.3
Pantothenic Acid mg	1.67	10
Vitamin K mcg	11.17	67
Choline mg	12.28	73.7

Amino acids

<i>Essential amino acids</i>	<i>% total amino acids</i>	<i>g/6 packets</i>
L-Isoleucine	4.55	1.69
L-Leucine	7.20	2.67
L-Lysine	5.41	2.00
L-Methionine	4.66	1.73
L-Phenylalanine	5.18	1.93
L-Threonine	4.55	1.69
L-Tryptophan	1.41	0.52
L-Valine	5.02	1.86
Total	37.98	14.09

<i>Non-essential amino acids</i>	<i>% total amino acids</i>	<i>g/6 packets</i>
L-Alanine	4.85	1.80
L-Arginine	8.87	3.29
L-Aspartic acid	10.35	3.84
L-Glutamine	17.07	6.33
Glycine	7.91	2.93
L-Histidine	2.21	0.82
L-Proline	6.48	2.41
L-Serine	3.34	1.24
L-Tyrosine	0.94	0.35
Total	62.02	23.01

Electrolytes

<i>Cations</i>	<i>In normal dilution 80 g in 300 ml m-equiv/100 ml</i>	<i>In powder form</i>	
		<i>mg/80 g packet</i>	<i>mg/6 packets</i>
Sodium	3.74	258	1,548
Potassium	2.99	351.5	2,109
Calcium	2.77	166.7	1,000
Magnesium	1.83	66.67	400
Manganese	0.00567	0.468	2.81
Iron	0.0358	3	18
Copper	0.0035	0.333	2
Zinc	0.0255	2.5	15
<i>Anions</i>	<i>m-equiv/100 ml</i>	<i>mg/80 g packet</i>	<i>mg/6 packets</i>
Chloride	5.185	551.6	3,310
Phosphate (as P)	5.40	166.6	1,000
Acetate	0.0296	5.25	31.5
Iodide	0.000066	0.025	0.150
Gluconate	1.69	991.8	5,950
Sorbate	0.447	149	894

Six packets also contain 0.25 mcg Cobalt as Vitamin B₁₂.

Uses Vivonex Standard provides total enteral nutrition which requires minimal digestion and produces no exogenous residue.

It is indicated in the treatment of bowel fistulae, bowel obstruction, Crohn's disease, ulcerative colitis and other disorders of the digestive organs or of the alimentary tract where elemental nutrition with low fat and minimal residue is considered of value.

Vivonex Standard can be used to ensure a clear operative field for bowel surgery or diagnostic procedures. Use of Vivonex Standard pre-operatively can help to ensure that the negative nitrogen balance, often seen post-operatively in undernourished patients, is minimised or avoided.

Post-operatively Vivonex Standard provides a balanced, low residue, low fat, milk free nutritional regimen to maintain a positive nitrogen balance during the catabolic phase, and to simplify nursing during the recovery period. Vivonex Standard may also be used as an alternative to parenteral feeding and as supplementary feeding when a high energy intake is required.

Dosage and administration *Dosage - Adults:* Six packets (1,800 kilocalories) a day, which may be increased if thought necessary to meet the nutritional demands of some patients.

Children: Vivonex Standard may be given to children. However, when used for children under 10 years it may be necessary to adjust the quantity of Vivonex Standard consumed daily to meet the projected nutritional requirements for the patient involved.

Vivonex Standard may be used as a nutritional source in both infants and children. Vivonex Standard contains no cystine, a semi-essential amino acid in the newborn. The amount of Vivonex Standard required to maintain weight and nitrogen balance will vary with each individual.

As the recommended daily intake varies with the age of the infant or child, daily administration of a mineral and vitamin supplement may be necessary to meet individual needs, particularly when Vivonex Standard is used as the sole source of nutrition for more than a few days.

If Vivonex Standard, in standard dilution, is administered as the sole source of nutrition, additional fluid will be required to avoid dehydration.

Administration: Vivonex Standard may be administered orally, as a drink or frozen, or by nasogastric or enteric tube.

Contra-indications, warnings, etc

Contra-indications: There are no contra-indications.

Warnings: Vivonex Standard must not be administered parenterally.

Precautions: Because of the high caloric contribution from carbohydrates some depleted individuals may manifest elevated blood sugar levels requiring insulin for regulation. Vivonex Standard should be used with care in diabetics.

The electrolyte content of Vivonex Standard is based on requirements of normal individuals and may be excessive for patients with electrolyte imbalance.

Use during pregnancy or lactation may require supplementary vitamins and minerals.

Use for children under 10 years may require adjustment of the daily consumption to meet the projected nutritional requirements for the patient involved.

Most patients should be started slowly on Vivonex Standard. Begin the first day with Vivonex Standard at half strength and on the second day the patient may be tried with the standard dilution. Each 300 ml feed must be sipped slowly over at least a one hour period for best results.

Action in event of overdosage: Overdosage is unlikely to occur and would result in vomiting and/or diarrhoea. Should overdosage occur, stop feeding Vivonex Standard and give water to avoid dehydration.

Pharmaceutical precautions *Storage:* When packaged in cartons or in packets, Vivonex Standard should be stored in a cool, dry place.

In normal dilution Vivonex Standard is a perishable liquid. A full day's supply may be prepared at one time and stored in the refrigerator for up to 24 hours. Shake the liquid briefly before serving. Never leave at room temperature for more than a few hours.

Diluents: In no circumstances should Vivonex Standard be mixed with less than 250 ml (8½ oz) of water per 80 g packet.

Legal category POM.

Package quantities Vivonex Standard is supplied in cartons of six packets, each packet containing 80 g soluble powder.

Further information Vivonex Standard is a complete, elemental, minimal residue nutrition requiring little digestion. It is absorbed in the upper small intestine, leaving the lower bowel at rest. Vivonex Standard leaves no exogenous residue. On a Vivonex Standard-only regimen faecal volume and frequency are much reduced, and a bowel action every five to seven days is to be expected.

In severe catabolic states the Vivonex Standard

formulation may fail to achieve positive nitrogen balance. In such circumstances Vivonex HN is recommended.

Adult patients receiving Vivonex Standard do not normally require any additional supplements.

Vivonex Standard is available solely as an unflavoured powder. To ensure patient acceptance when feeding Vivonex orally, the drink should be served flavoured and chilled. Vivonex Flavour sachets are available in Orange, Strawberry, Beef Broth and Tomato flavours. Beef Broth and Tomato flavours may be blended with warm water. Alternatively, Vivonex may be flavoured using commercially available carbonated or still soft drinks.

Where accurate nutritional control is required, allowance must be made for any added calorie or mineral content, and for indigestible matter.

Vivonex Standard may be administered as a slow continuous naso-enteric infusion via any suitable naso-enteric feeding system.

For details of prescribing under the ACBS ruling see the current edition of MIMS.

Product licence number 0364/0014.

VIVONEX* HN

Presentation Vivonex HN is an off-white, unflavoured water-soluble powder. The contents of one packet supply 300 kilocalories (1.256 MJ) and the following:

	Grams	% by weight
Available nitrogen in the form of pure amino acids (amino acid content 13.31 g)	2.00	2.5
Fat as highly purified safflower oil (80% as triglyceride of linoleic acid)	0.261	0.326
Carbohydrate as glucose solids	63.3	79.1

Caloric contribution.

Amino acids	17.7%
Fat	0.78%
Carbohydrate	81.5%

Ten packets of Vivonex HN supply 20.0 g of available nitrogen, 2.61 g fat, 633g carbohydrate and the vitamins, amino acids and minerals shown in the table below.

Vitamins	Per 80 g packet	In ten 80 g packets
Vitamin A (Retinol) IU	500	5,000
Vitamin D ₂ (Ergocalciferol) IU	40	400
Vitamin E IU	3	30
Vitamin C (Ascorbic acid) mg	6	60
Folic Acid mg	0.04	0.4
Vitamin B ₁ (Thiamine) mg	0.15	1.5
Vitamin B ₂ (Riboflavine) mg	0.17	1.7
Nicotinamide mg	2	20
Vitamin B ₆ mg	0.2	2
Vitamin B ₁₂ mcg	0.6	6
Biotin mg	0.03	0.3
Pantothenic Acid mg	1	10
Vitamin K mcg	6.7	67
Choline mg	7.37	73.7

Amino acids

<i>Essential amino acids</i>	<i>% total amino acids</i>	<i>g/10 packets</i>
L-Isoleucine	4.15	5.53
L-Leucine	6.57	8.75
L-Lysine	4.94	6.58
L-Methionine	4.58	6.10
L-Phenylalanine	7.10	9.45
L-Threonine	4.16	5.53
L-Tryptophan	1.28	1.71
L-Valine	4.58	6.10
Total	37.36	49.75
<i>Non-essential amino acids</i>	<i>% total amino acids</i>	<i>g/10 packets</i>
L-Alanine	5.18	6.90
L-Arginine	4.07	5.41
L-Aspartic Acid	11.06	14.72
L-Glutamine	18.22	24.25
Glycine	9.84	13.09
L-Histidine	2.36	3.14
L-Proline	6.92	9.21
L-Serine	4.15	5.52
L-Tyrosine	0.84	1.12
Total	62.64	83.36

Electrolytes

<i>Cations</i>	<i>In normal dilution 80 g in 300 ml m-equiv/100 ml</i>	<i>In powder form</i>	
		<i>mg/80 g packet</i>	<i>mg/10 packets</i>
Sodium	3.35	231.3	2,313
Potassium	1.79	210.5	2,105
Calcium	1.66	100.0	1,000
Magnesium	1.097	40.0	400
Manganese	0.00341	0.281	2.81
Iron	0.02148	1.8	18
Copper	0.002098	0.2	2
Zinc	0.0153	1.5	15
<i>Anions</i>	<i>m-equiv/100 ml</i>	<i>mg/80 g packet</i>	<i>mg/10 packets</i>
Chloride	5.24	557.3	5,573
Phosphate (as P)	3.16	100	1,000
Acetate	0.0178	3.15	31.5
Iodide	0.000039	0.015	0.15
Gluconate	0.967	565.7	5,657
Sorbate	0.268	89.2	892

Ten packets also contain 0.25 mcg Cobalt as Vitamin B₁₂.

Uses Vivonex HN provides total enteral nutrition for patients who have increased calorie and nitrogen requirements. Vivonex HN requires minimal digestion and produces no exogenous residue.

Use of Vivonex HN prior to major surgery can help to avoid or minimise negative nitrogen balance.

The high nutritional value and minimal residue properties of Vivonex HN make it useful in the management

of malabsorption states, short bowel syndrome, bowel fistulae, bowel obstruction, Crohn's disease, ulcerative colitis and as a treatment following total gastrectomy; or for other conditions of the digestive organs or of the alimentary tract where elemental nutrition with low fat, minimal residue and a high nutritional contribution is considered of value.

Post-operatively Vivonex HN provides a balanced, low residue, low fat, milk free nutritional regimen to maintain a positive nitrogen balance during the catabolic phase and to simplify nursing during the recovery period.

Vivonex HN, which may be given orally or by continuous nasogastric infusion may be used as an alternative to parenteral feeding and/or as supplementary feeding when a high intake is required.

Dosage and administration *Dosage – Adults:* Ten packets (3,000 kilocalories) a day, which may be increased if thought necessary to meet the nutritional demands of some patients.

Children: Vivonex HN may be given to children. However, when used for children under 10 years it may be necessary to adjust the quantity of Vivonex HN consumed daily to meet the projected nutritional requirements for the patient involved.

Vivonex HN may be used as a nutritional source in both infants and children. Vivonex HN contains no cystine, a semi-essential amino acid in the newborn. The amount of Vivonex HN required to maintain weight and nitrogen balance will vary with each individual.

As the recommended daily intake varies with the age of the infant or child, daily administration of a mineral and vitamin supplement may be necessary to meet individual needs, particularly when Vivonex HN is used as the sole source of nutrition for more than a few days.

If Vivonex HN, in standard dilution, is administered as the sole source of nutrition, additional fluid will be required to avoid dehydration.

Administration: Vivonex HN may be administered by nasogastric or enteric tube or orally, as a drink or frozen.

Contra-indications, warnings, etc

Contra-indications: There are no contra-indications.

Warnings: Vivonex HN must not be administered parenterally.

Precautions: Because of the high caloric contribution from carbohydrates some depleted individuals may manifest elevated blood sugar levels requiring insulin for regulation. Vivonex HN should be used with care in diabetics.

The electrolyte content of Vivonex HN is based on requirements of normal individuals and may be excessive for patients with electrolyte imbalance.

Use during pregnancy or lactation may require supplementary vitamins and minerals.

Use for children under 10 years may require adjustment of the daily consumption to meet the projected nutritional requirements for the patient involved.

Most patients should be started slowly on Vivonex HN. Details of a suggested regimen for initiating tube feeding are given on the package insert inside each carton of Vivonex HN.

For oral feeding a similar regimen should be adopted to allow the body to adjust to liquid nutrition. It is essential that each 300 ml feed be sipped slowly over a period of at least an hour.

Action in event of overdosage: Overdosage is unlikely to occur and would result in vomiting and/or diarrhoea.

Should overdosage occur, stop feeding Vivonex HN and give water to avoid dehydration.

Pharmaceutical precautions *Storage:* When packaged in cartons or in packets, Vivonex HN should be stored in a cool, dry place.

In normal dilution, Vivonex HN is a perishable liquid. A full day's supply may be prepared at one time and stored in the refrigerator for up to 24 hours. Shake the liquid briefly before serving. Never leave at room temperature for more than a few hours.

Diluents: In no circumstances should Vivonex HN be mixed with less than 250 ml (8½ oz) of water per 80 g packet.

Legal category POM.

Package quantities Vivonex HN is supplied in cartons of 10 packets, each packet containing 80 g soluble powder.

Further information Vivonex HN is a complete, elemental, minimal residue, nutrition requiring little digestion. It is completely absorbed in the upper small intestine, leaving the lower bowel at rest. Vivonex HN leaves no exogenous residue. On a Vivonex HN only regimen faecal volume and frequency are much reduced, and a bowel action every five to seven days is to be expected.

When severe catabolic states do not exist the Vivonex Standard formulation may be the preparation of choice.

Adult patients receiving Vivonex HN do not normally require any additional supplements.

Vivonex HN is available solely as an unflavoured powder. To ensure patient acceptance when feeding Vivonex HN orally, the drink should be served flavoured and chilled. Vivonex Flavour sachets are available in Orange, Strawberry, Beef Broth and Tomato flavours. Beef Broth and Tomato flavours may be blended with warm water. Alternatively, Vivonex HN may be flavoured using commercially available carbonated or still soft drinks.

Where accurate nutritional control is required, allowance must be made for any added calorie or mineral content, and for indigestible matter.

Vivonex HN may be administered as a slow continuous nasoenteric infusion via any suitable naso-enteric feeding system.

For details of prescribing under ACBS ruling see the current edition of MIMS.

Product licence number 0364/0017.

**Trade Mark*

Novo Laboratories Ltd
Ringway House
Bell Road Daneshill East
Basingstoke, Hants, RG24 0QN



HUMAN ACTRAPID* ▼
HUMAN MONOTARD* ▼

Presentation Human Actrapid (Neutral Insulin Injection) is a neutral solution of Human Insulin (emp).

Human Monotard (Insulin Zinc Suspension) is a neutral suspension of amorphous (30%) and crystalline (70%) Human Insulin (emp).

When shaken it appears white and cloudy.

Both Human Monocomponent insulin preparations are available in strengths of 40 and 80 i.u./ml.

Uses The treatment of insulin-requiring diabetic patients. May be advantageous in the treatment of insulin induced fat atrophy, insulin allergy, insulin resistance and labile diabetes, and when intermittent short term therapy is required.

Human Actrapid may be used for all diabetics who require a quick and intense-acting insulin, e.g. in emergencies such as diabetic hyperglycaemic coma, during surgery and severe infection in diabetics, and in the management of pregnant diabetics.

Dosage and administration The dosage of insulin is determined by the physician according to the needs of the patient.

Human Actrapid may be given by injection or infusion, subcutaneously, intramuscularly or intravenously. It has a duration of action of some $\frac{1}{2}$ to 8 hours and its maximum effect is exerted between 2 $\frac{1}{2}$ and 5 hours after injection. Owing to its strong early effect the interval between the injection and the following meal should be 15–30 minutes.

Human Monotard may be given by subcutaneous or intramuscular injection. It may be given once or, more commonly, twice daily and may be combined with Human Actrapid. Human Monotard has a duration of action of some 2 $\frac{1}{2}$ to 22 hours and its maximum effect is exerted between 7 and 15 hours after injection.

Human Monocomponent insulin preparations may be admixed in the syringe and the injection given immediately.

Infusion pumps: Human Actrapid may be used in most infusion pumps; however, peristaltic pumps (roller pumps) are not suitable for use with Human Actrapid due to the risk of precipitation. The pump manufacturers instructions regarding type, strength and administration of insulin must be followed.

Human Monotard must not be used in insulin infusion pumps.

Use in pregnancy: It is essential to maintain continuous good control of the insulin requiring diabetic patient throughout pregnancy. In the insulin-treated (gestational or insulin dependent) pregnant diabetic patient the insulin requirements usually fall in the first trimester and increase during the second and third trimester.

Contra-indications, warnings, etc

Contra-indications: Insulin is contra-indicated in hypoglycaemia.

Precautions: On transfer from porcine monocomponent

insulins or other highly purified porcine insulins to Human Monocomponent insulin, no change in dosage is anticipated other than the routine adjustments made in order to maintain stable diabetic control.

Patients currently stabilised on mixed species or bovine insulin may require a dosage adjustment dependent upon the dosage, purity, species and formulation of the insulin(s) currently administered. Variations in glycaemic control may occur and adjustments in therapy should be made under the guidance of a physician.

Insulin resistant patients receiving over 100 units daily should be referred to hospital for transfer.

The addition of corticosteroids, oral contraceptives or thyroid hormone replacement therapy is likely to lead to an increase in insulin requirements. The addition of a beta-adrenergic blocking agent or a monoamine oxidase inhibitor, (MAOI) may also necessitate an adjustment of insulin dosage.

Side-effects: Lipodystrophy, insulin resistance and hypersensitivity reactions have been associated with insulin therapy, but the incidence and severity of these unwanted effects is minimal with the Human Monocomponent insulins. Severe local or generalised allergic reactions require immediate treatment and, in some cases, desensitisation may be necessary.

Overdosage: In the event of an overdose, glucose should be given orally if the patient is conscious. The unconscious patient should be treated with glucose intravenously or rectally and glucagon may be administered intramuscularly or subcutaneously.

Pharmaceutical precautions Human Monocomponent insulins should be stored between 2°C and 8°C. They should not be exposed to excessive heat or sunlight, neither should they be frozen. The vial in use may be kept at room temperature (max. 25°C) for one month. Human Monocomponent insulins have a shelf life of two years.

Legal category P.

Package quantities 10 ml glass vials of 40 i.u./ml or 80 i.u./ml.

Further information *Sole distributors* Farillon Limited, Bryant Avenue, Romford, Essex, RM3 0PJ. Tel: Ingrebourne 71136.

Human Actrapid	40 i.u./ml	4668/0001
	80 i.u./ml	4668/0002

Human Monotard	40 i.u./ml	4668/0004
	80 i.u./ml	4668/0005

ACTRAPID* MC
SEMITARD* MC
RAPITARD* MC
MONOTARD* MC
LENTARD* MC
ULTRATARD* MC

Presentation *Actrapid MC* (Neutral Insulin Injection BP) is a neutral solution of porcine MC insulin.

Semitard MC (Insulin Zinc Suspension Amorphous BP) is a neutral suspension of amorphous porcine MC insulin.

Rapitard MC (Biphasic Insulin Injection BP) is a neutral suspension comprising porcine MC insulin (25%) in solution and crystalline bovine MC insulin (75%).

Monotard MC (Insulin Zinc Suspension BP) is a neutral suspension of amorphous (30%) and crystalline (70%) porcine MC insulin.

Lentard MC (Insulin Zinc Suspension BP) is a neutral suspension of amorphous porcine MC insulin (30%) and crystalline bovine MC insulin (70%).

Ultratard MC (Insulin Zinc Suspension Crystalline BP) is a neutral suspension of crystalline bovine MC insulin.

When shaken the suspensions appear white and cloudy. All the above insulins are available in strengths of 40 and 80 i.u./ml.

Uses The treatment of insulin-requiring diabetic patients.

Actrapid MC may be used for all diabetics who require a quick and intense-acting insulin, e.g. in emergencies such as diabetic hyperglycaemic coma, during surgery and severe infections in diabetics and in the management of pregnant diabetics.

MC insulins may be advantageous in the treatment of insulin-induced fat atrophy, insulin allergy, insulin resistance and labile diabetes, and when intermittent short-term therapy is required.

Dosage and administration The dosage of insulin is determined by the physician according to the needs of the patient.

MC insulin preparations may be admixed in the syringe and the injection given immediately.

Actrapid MC may be given by injection or infusion, subcutaneously, intramuscularly or intravenously, and may be combined with other MC insulins.

Actrapid MC has a duration of action of some $\frac{1}{2}$ to 7 hours and its maximum effect is exerted between 2 $\frac{1}{2}$ and 5 hours after injection. Owing to its strong early effect, the interval between the injection and the following meal should be 15 to 30 minutes.

Suspensions may be given by subcutaneous or intramuscular injection.

Semitard MC is usually given twice daily and may be combined with Actrapid MC. Semitard MC has a duration of action of some 1 $\frac{1}{2}$ to 16 hours and its maximum effect is exerted between 5 and 10 hours after injection.

Rapitard MC is indicated as a once daily injection in patients with stable diabetes of moderate severity, especially when a fairly strong early effect is desired. Rapitard MC may also be used for the regulation of unstable severe diabetes on a twice daily injection regime. Rapitard MC has a duration of action of some 1 to 22 hours and its maximum effect is exerted between 4 and 12 hours after injection. Owing to its strong early effect the interval between the injection and the following meal should be approximately 30 minutes.

Monotard MC is given once or, more commonly, twice daily and may be combined with Actrapid MC. Monotard MC has a duration of action of some 2 $\frac{1}{2}$ to 22 hours and its maximum effect is exerted between 7 and 15 hours after injection.

Lentard MC as a once daily injection is an appropriate routine for 24 hour regulation of blood sugar in patients with stable diabetes of moderate severity. Lentard MC has a duration of action of some 2 $\frac{1}{2}$ to 24 hours and its

maximum effect is exerted between 7 and 15 hours after injection.

Ultratard MC can be used as a once daily injection in mild (type 2) diabetes when diet alone fails to produce good control and may also be combined with Actrapid MC in the management of type 1 or type 2 diabetes. Ultratard MC has a duration of action of some 4 to 36 hours and its maximum effect is exerted between 10 and 30 hours after injection.

Infusion pumps: Actrapid MC may be used in most infusion pumps; however, peristaltic pumps (roller pumps) are not suitable for use with Actrapid MC due to the risk of precipitation. The pump manufacturer's instructions regarding type, strength and administration of insulin must be followed.

Suspensions must not be used in insulin infusion pumps.

Use in pregnancy: It is essential to maintain continuous good control of the insulin-requiring diabetic patient throughout pregnancy. In the insulin-treated (gestational or insulin-dependent) pregnant diabetic patient the insulin requirements usually fall in the first trimester and increase during the second and third trimesters.

Contra-indications, warnings, etc *Contra-indications:* Insulin is contra-indicated in hypoglycaemia.

Precautions: Patients transferred from conventional (predominantly bovine) insulins may require a smaller dosage. The dosage reduction may occur immediately after transfer or gradually over a period of weeks or months. In order to reduce the risk of hypoglycaemia the patient and the physician should be aware of the possibility that the insulin requirement may be reduced. If the daily insulin dosage is below 40 i.u. the risk is considered minimal. However, when higher dosages are required, stricter supervision of the patient is necessary and possibly a 20% reduction should be made initially on transfer to the porcine MC insulins. Transfer to mixed species or bovine MC insulins may be associated with a smaller reduction in dosage. Insulin-resistant patients receiving over 100 units daily should be referred to hospital for transfer.

The addition of corticosteroids, oral contraceptives or thyroid hormone replacement therapy is likely to lead to an increase in insulin requirements. The addition of a beta-adrenergic blocking agent or a monoamine oxidase inhibitor (MAOI) may also necessitate an adjustment of insulin dosage.

Side-effects: Lipodystrophy, insulin resistance and hypersensitivity reactions have been associated with insulin therapy, but the incidence and severity of these unwanted effects is minimal with the MC insulins. Severe localised or generalised allergic reactions require immediate treatment and, in some cases, desensitisation may be necessary.

Overdosage: In the event of an overdose, glucose should be given orally if the patient is conscious. The unconscious patient should be treated with glucose intravenously or rectally, and glucagon may be administered intramuscularly or subcutaneously.

Pharmaceutical precautions MC insulins should be stored between 2°C and 8°C. They should not be exposed to excessive heat or sunlight, neither should they be frozen. MC insulins have a shelf life of two years. Expiry date is printed on the package.

Legal category P.

Package quantities 10 ml glass vials of 40 i.u./ml and 80 i.u./ml.

Further information *Sole distributors:* Farillon Limited, Bryant Avenue, Romford, Essex. RM3 0PJ. Tel: Ingrebourne 71136.

Product licence numbers

Actrapid MC	40 i.u./ml	0542/0013
	80 i.u./ml	0542/0014
Semitar MC	40 i.u./ml	0542/0011
	80 i.u./ml	0542/0012
Rapitard MC	40 i.u./ml	0542/5025
	80 i.u./ml	0542/5037
Monotard MC	40 i.u./ml	0542/0009
	80 i.u./ml	0542/0010
Lentard MC	40 i.u./ml	0542/5022
	80 i.u./ml	0542/5034
Ultratard MC	40 i.u./ml	0542/5021
	80 i.u./ml	0542/5033

GLUCAGON NOVO

Presentation Glucagon Novo is available as the hydrochloride in lyophilised freeze-dried form with accompanying diluent in two pack sizes:

1 mg – a vial containing glucagon hydrochloride 1 mg (1 i.u.) and lactose 107 mg, with a pre-sterilised disposable syringe containing Water for Injections 1.1 ml as diluent.

10 mg – a vial containing glucagon hydrochloride 10 mg (10 i.u.) and lactose 140 mg, with a vial containing 10 ml of diluent (comprised of glycerin 230 mg, methyl hydroxybenzoate 10 mg and propyl hydroxybenzoate 1.5 mg as preservatives, Water for Injections to 10 ml).

Uses Glucagon Novo is indicated in the treatment of severe hypoglycaemic reactions which may occur following insulin or oral therapy in the management of diabetic patients, or during insulin shock therapy in psychiatric patients. Glucagon Novo is also recommended as an adjunct for use in examinations of the gastro-intestinal tract by radiography or endoscopy.

Dosage and administration *Adults and children:*

1. Treatment of severe hypoglycaemic reactions. Dissolve the lyophilised glucagon in the accompanying diluent. Give 0.5 to 1 mg (0.5 to 1 i.u.) of Glucagon Novo by subcutaneous, intramuscular or intravenous injection. If the patient does not awaken within 20 minutes, intravenous glucose must be given. When the patient responds, administer oral carbohydrate to restore the liver glycogen and prevent secondary hypoglycaemia.

2. Insulin shock therapy. Dissolve the lyophilised glucagon in the accompanying diluent. After one hour of coma, give 0.5 to 1 mg (0.5 to 1 i.u.) of Glucagon Novo by subcutaneous, intramuscular or intravenous injection. If the patient does not awaken within 20 minutes, intravenous glucose must be given. When the patient responds, administer oral carbohydrate to restore the liver glycogen and prevent secondary hypoglycaemia.

In very deep states of coma, intravenous glucose may be given concurrently with Glucagon Novo.

3. Radiography and endoscopy of the gastro-intestinal tract. Dissolve the lyophilised glucagon in the accompanying diluent. The dosage required to dilate the stomach and duodenum and inhibit motility may range from 0.2 mg (0.2 i.u.) to 2 mg (2 i.u.) intravenously.

There is considerable variation in response between patients, depending on the technique of administration, so that no general dosage recommendations can be made but there is an upper dose limit of 2 mg.

The initial dilation and inhibition of motility lasts about 5 to 15 minutes, after which glucagon acts as a hurrying agent producing rapid transit of the barium through the small bowel to the lower gut.

Contra-indications, warnings, etc *Contra-indications:* Glucagon Novo is contra-indicated in phaeochromocytoma, insulinoma and glucagonoma.

Precautions: Caution must be observed if Glucagon Novo is used in diabetic patients as an adjunct in radiography or endoscopy of the gastro-intestinal tract. Since glucagon is a protein, there is a theoretical possibility of hypersensitivity.

Side-effects: Glucagon is relatively free of adverse effects except for occasional reports of nausea and vomiting which tends to be dose-related.

Pharmaceutical precautions Glucagon as the dry substance has a shelf life of two years when stored at room temperature below 25°C. Expiry date is printed on the package.

1 mg pack: The solution should be prepared immediately prior to use.

10 mg pack: The solution should preferably be prepared immediately prior to use but may be stored in a refrigerator at 4°C for up to one week. If fibril formation takes place or if solid particles are present in the solution the solution should not be used.

Legal category POM.

Package quantities A single dose pack consisting of a glass vial containing glucagon hydrochloride 1 mg (1 i.u.) in lyophilised freeze-dried form, with a pre-sterilised disposable syringe containing diluent. A multiple dose pack consisting of a glass vial containing glucagon hydrochloride 10 mg (10 i.u.) in lyophilised freeze-dried form, with a glass vial containing 10 ml diluent.

Further information *Sole distributors:* Farillon Limited, Bryant Avenue, Romford, Essex. RM3 0PJ. Tel: Ingrebourne 71136.

Product licence numbers

1 mg	0542/0016
10 mg	0542/0017

TRYPURE*

Presentation Trypure contains pure crystalline trypsin stabilised by the addition of a small quantity of inert calcium salt.

It is available in three presentations:

50 mg (dry powder) – a vial containing sterile trypsin 50 mg with a vial containing 15 ml diluent (each 1 ml comprised of sodium chloride 9 mg and methyl hydroxybenzoate/propyl hydroxybenzoate 1 mg).

5 g (dispersible powder) – a spray vial containing dispersed trypsin powder 5 g (trypsin 50 mg) with a spray vial containing 45 ml lidocaine solution 2% (each 1 ml comprised of lidocaine hydrochloride 20 mg, cetrimide 1 mg and sodium chloride 4.7 mg).

25 g (spray) – a pressurised aerosol can containing trypsin-freon suspension 25 g (trypsin 250 mg) with a spray vial containing 45 ml lidocaine solution 2% (each

1 ml comprised of lidocaine hydrochloride 20 mg, cetrimide 1 mg and sodium chloride 4.7 mg).

Uses Action: Trypsin is a proteolytic enzyme which directly promotes the hydrolysis of proteins in necrotic tissue, thereby supplementing the proteolytic enzymes of the body in the enzymatic debridement of wounds, ulcers, cavities and exudates.

Trypure has a proteolytic activity of approximately 4,000 NF units/mg equivalent to 25 Anson units.

Indications: The Trypure preparations are indicated for local use in the debridement of open wounds, ulcers or cavities, and for the liquefaction of coagulated blood and exudates.

Dosage and administration Approximately 50 mg Trypure (contained in the dry powder, dispersible powder or 5 bursts of one second from the spray) should be applied locally to each 100–200 sq cm of wound surface, but smaller doses should be used for small cavities. One application daily is normally sufficient.

After re-constitution of the dry powder by addition of the diluent, the resulting solution is suitable for application to surface wounds either directly or by means of a compress soaked in the solution. The dry powder in solution can also be used for instillation or local injection.

When using the dispersible powder or spray pack, pre-treatment of the area by spraying with the lidocaine solution 2% will reduce any transient pain experienced after the application of Trypure, and provide the moisture necessary to activate the Trypure.

The spray pack, which should be shaken before use and applied at a distance of 15 cm from the wound surface, may be used for larger or less accessible areas.

After the application of Trypure, the area of the lesion must be covered with a wet compress and a waterproof dressing. The compress should be kept moist at all times by re-soaking with physiological saline.

Wound debridement should always be carried out prior to each application of Trypure.

Contra-indications, warnings, etc *Contra-indications:* Known allergy to trypsin. Trypure powder in solution should never be given intravenously and should not be given by inhalation to patients prone to bronchospasm or asthma.

The dispersible powder and spray should not be used for inhalation therapy or for the treatment of nasal or oral lesions.

Precautions: Care should be taken to avoid getting Trypure into the eyes or nose. If this should happen, thorough irrigation of the eyes or nose with running water is indicated.

The spray pack should not be used near an open fire or any other strong source of heat.

Trypure should be used sparingly in ischaemic areas and caution is recommended when treating tuberculous empyema.

Warnings and adverse effects: The application of Trypure may be associated with transient pain which can be reduced by pre-treatment of the area with lidocaine solution 2% (available with the dispersible powder and spray pack).

Allergic or histamine-like reactions to trypsin occur rarely and respond to antihistamine therapy.

Pharmaceutical precautions *Storage:* Trypure powder in solution is stable for 24 hours at room temperature, and for one week at 4°C (in a refrigerator).

The dry powder has a shelf life of 3 years when stored at 15°C and the dispersible powder and spray pack each have a shelf life of 2 years when stored at this temperature. Expiry date is printed on the package.

The aerosol can in the spray pack should not be punctured or incinerated.

Compatibility: The use of Trypure can be combined, when necessary, with local or systemic antibiotic therapy. There is no evidence to suggest that Trypure is incompatible with hydrogen peroxide (when mixed at neutral pH), chlorhexidine and cetrimide solutions, whereas Trypure has been shown to be incompatible with potassium permanganate, chloramine, sodium hypochlorite, silver nitrate and iodine/iodide solutions.

Legal category POM.

Package quantities Dry powder pack consisting of a glass vial containing sterile trypsin 50 mg with a glass vial containing 15 ml diluent.

Dispersible powder pack consisting of a spray vial containing dispersed trypsin powder 5 g (trypsin 50 mg) with a spray vial containing 45 ml lidocaine solution 2%.

Spray pack consisting of a pressurised aerosol can containing trypsin-freon suspension 25 g (trypsin 250 mg) with a spray vial containing 45 ml lidocaine solution 2%.

Further information *Sole distributors:* Farillon Ltd., Bryant Avenue, Romford, Essex. RM3 0PJ. Tel: Ingrebourne 71136.

Product licence numbers

Trypure dry powder	0542/5019
Trypure dispersible powder	0542/5017
Trypure spray	0542/5018

**Trade Mark*

Organon Laboratories Limited

Cambridge Science Park

Milton Road

Cambridge CB4 4BH



BOLVIDON*

Presentation Yellow, film-coated, bi-convex tablets 6.5 mm in diameter, coded CT4 on one side and 'Organon' on the reverse side, each containing 10 mg mianserin hydrochloride.

White, film-coated, bi-convex tablets 7 mm in diameter, coded CT6 on one side and 'Organon' on the reverse side, each containing 20 mg mianserin hydrochloride.

White, film-coated, bi-convex tablets 8 mm in diameter, coded CT7 on one side and 'Organon' on the reverse side, each containing 30 mg mianserin hydrochloride.

Uses Symptoms of depressive illness.

Dosage and administration The tablets should be swallowed whole without chewing.

Adults: Bolvidon can be taken either in divided doses or as a single dose at night. Treatment should usually commence with 30 mg or 40 mg per day for the first few days. The effective daily dosage usually lies between 30 mg and 90 mg. Divided daily doses up to 200 mg are well tolerated.

It is often advantageous to maintain antidepressant treatment for several months after initial clinical improvement has occurred.

Elderly: Not more than 30 mg a day initially. The dose should be increased with caution under close supervision. A lower than the normal maintenance dose may be sufficient to produce a satisfactory clinical response.

Children: Not recommended.

Contra-indications, warnings, etc

Contra-indications: Mania. Severe liver disease. During breast feeding. Breast feeding should be discontinued if treatment with Bolvidon is considered essential.

Do not use during pregnancy unless there are compelling reasons. There is no evidence of safety in human pregnancy. Animal studies have not shown hazard.

Precautions: Care should always be taken in patients with recent myocardial infarction or heart block. Serious cardiotoxic effects appear to be rare at therapeutic dosage, even in patients with pre-existing cardiac disease, recent myocardial infarction or cardiac insufficiency.

The elderly are less liable to experience adverse reactions such as agitation, confusion and postural hypotension with Bolvidon than with tricyclics or bridged tricyclics, but all anti-depressant therapy should be used with caution in this group of patients.

Patients posing a high suicidal risk require close initial supervision.

Avoid if possible in patients with epilepsy. When treating patients with diabetes, hepatic or renal insufficiency, normal precautions should be exercised and the dosages of any concurrent therapy kept under review.

Patients with narrow angle glaucoma or symptoms suggestive of prostatic hypertrophy should also be monitored even though anticholinergic side-effects are not anticipated with Bolvidon therapy.

There are indications that Bolvidon, like other antidepressants, may precipitate hypomania in susceptible subjects with bipolar affective illness.

Bolvidon may potentiate the central nervous depressant action of alcohol.

If surgery is necessary during Bolvidon therapy the anaesthetist should be informed of the treatment being given.

Drug interactions: Bolvidon should not be given concurrently with, or within two weeks of cessation of therapy with monoamine oxidase inhibitors.

Phenytoin plasma levels should be monitored in patients treated concurrently with Bolvidon.

Interactions with sympathomimetic agents have not been reported, and are unlikely.

Clinical experience has shown that Bolvidon does not interact with the anti-hypertensives bethanidine, clonidine, hydralazine, guanethidine and propranolol. Nevertheless, the monitoring of blood pressure is recommended for those patients receiving concurrent anti-hypertensive therapy.

Concurrent anticoagulant therapy of the coumarin type (e.g. warfarin) is also permissible, but close additional monitoring procedures should be carried out.

Warnings and adverse effects: As improvement may not occur during the first 2-4 weeks of treatment, patients should be closely monitored during this period.

It is advisable to maintain treatment with Bolvidon for several months after initial clinical improvement.

The most commonly occurring side effect is drowsiness, particularly during the first few days of treatment. Patients should be warned of the possible hazard in driving or operating machinery. Any drowsiness may be potentiated by alcohol.

Serious adverse effects are uncommon. A small number of cases of bone marrow depression, usually presenting as a neutropenia, generally reversible on stopping treatment, have been reported. If a patient develops symptoms of infection, e.g. fever, sore throat or stomatitis, during treatment with Bolvidon, treatment must be stopped and a full blood count obtained.

Jaundice, usually mild, hypomania and convulsions have also been reported at therapeutic dosage and under such circumstances treatment should be withdrawn.

Additional adverse effects that may occur include breast disorders (gynaecomastia, nipple tenderness and non-puerperal lactation), dizziness, postural hypotension, polyarthralgia, skin rash, sweating and tremor.

Psychotic manifestations, including mania and paranoid delusions, may be exacerbated during antidepressant therapy.

The following adverse effects although not reported with Bolvidon can occur with tricyclics and bridged tricyclics: interference with sexual function; withdrawal symptoms in adults; withdrawal symptoms (e.g. neuromuscular irritability) in neonates whose mothers received tricyclic or bridged tricyclic antidepressants during pregnancy.

Overdosage: There is no specific antidote. Treatment is by gastric lavage with appropriate supportive therapy. Symptoms of overdosage are normally confined to prolonged sedation.

Cardiac arrhythmias, convulsions, severe hypotension and respiratory depression are unlikely to occur.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities

Bolvidon tablets 10 mg are supplied in push-through PVC/foil blister strips of 30 tablets. Packed in cartons containing three strips (90 tablets).

Bolvidon tablets 20 mg are supplied in push-through PVC/foil blister strips of 21 tablets. Packed in cartons containing three strips (63 tablets).

Bolvidon tablets 30 mg are supplied in push-through PVC/foil blister strips of 14 tablets. Packed in cartons containing three strips (42 tablets).

All strengths also available in Securitainers of 100 and 500 tablets.

Further information Bolvidon is a tetracyclic antidepressant which is structurally distinct from classical tricyclics and from bridged tricyclics, this difference is reflected in its pharmacology. Bolvidon is a potent histamine and serotonin antagonist with little influence on cholinergic receptors, selective for pre-synaptic alpha-2 rather than post-synaptic alpha-1 receptors. Bolvidon has no effect on serotonin re-uptake and only affects noradrenaline re-uptake in vitro. In vivo Bolvidon increases noradrenaline turnover. Bolvidon produces fewer and milder side effects than the tricyclics and bridged tricyclics especially in terms of anticholinergic effects and effects on the cardiovascular system. Bolvidon does not cause the severe complications in overdosage associated with tricyclics and bridged tricyclics, e.g. severe cardiac arrhythmias, respiratory depression, convulsions and coma.

Product licence numbers

10 mg tablets – 0065/0031R

20 mg tablets – 0065/0057R

30 mg tablets – 0065/0061R

COTAZYM®

Presentation Dark green gelatine capsules, containing pancreatic enzymes in powder form; administered by sprinkling on the food, or in milk.

Active ingredients: Lipase – not less than 14,000 FIP units; amylase – not less than 10,000 FIP units; protease – not less than 500 FIP units.

Uses Each Cotazym Capsule contains sufficient enzymes to digest 17 g dietary fat, 34 g dietary protein and 40 g dietary starch.

Indicated in pancreatic enzyme deficiency states, including fibrocystic disease, post-gastrectomy malabsorption, chronic pancreatitis, pancreatic carcinoma, and steatorrhoea.

Dosage and administration Cotazym is given in sufficient quantity to cover every gram of fat in the entire daily diet, including between-meal snacks. When dosage is calculated on the fat-digesting power of the lipase (17 g dietary fat per capsule) there will normally be sufficient trypsin and amylase to adequately cover protein and starch digestion. An average diet would take about 6 capsules a day to cover it. The capsules are opened and the contents sprinkled onto the food, or in milk; the total dose should be divided and taken throughout the day with each meal and each snack.

Contra-indications, warnings, etc There are no known contra-indications.

Pharmaceutical precautions Store in a cool dry place between 2° and 15°C and protect capsules from light.

Legal category P.

Package quantities Bottles of 100 capsules.

Further information Because Cotazym has an assayed lipase activity, the dosage required to digest a known amount of dietary fat can be easily determined.

Product licence number 0065/5054.

COTAZYM B®

Presentation Round, bi-convex, white, film-coated tablets, diameter 11 mm.

Active ingredients: Pancreas powder, lipase activity 5,400 FIP units; cellulase 2.25 Wallerstein units; and Ox Bile Extract NF XI equivalent to 30 mg cholic acid, in each tablet.

Uses Cotazym B is an enzyme preparation in tablet form. It has a broad spectrum of digestive activity and is valuable in the treatment of a variety of disorders of the gastro-intestinal tract, whether these are due to a permanent or temporary enzyme deficiency or even due to intolerance of certain foods, especially those of a fatty nature.

Dosage and administration Cotazym B Tablets should not be chewed; they should always be swallowed at mealtimes, with water if necessary. An average dose of 6 tablets daily (2 with each meal) will digest 50 g fat, 100 g protein, 250 g starch and 480 mg cellulose, which in a balanced diet represents about 2,000 calories.

Contra-indications, warnings, etc

Contra-indications: There are no known contra-indications.

Precautions and warnings: It will generally be necessary to restrict the fat intake in the diet. In patients with impaired renal function attention should be paid to the volume and acidity of the urine.

Pharmaceutical precautions Store in a cool dry place between 2 and 15°C.

Legal category P.

Package quantities Boxes of 120 tablets, individually foil-stripped.

Further information Nil.

Product licence number 0065/5023.

DECA-DURABOLIN*

Presentation Nandrolone Decanoate Injection BP. 1 ml ampoules in three strengths, 25 mg, 50 mg and 100 mg per ml: 1 ml Orgaject* disposable syringes 25 mg and 50 mg per ml.

Uses Deca-Durabolin is a long-acting anabolic agent with a duration of effect lasting up to three weeks. Indicated in all conditions requiring a powerful and prolonged anabolic or anti-catabolic stimulus. It can be used as an adjunct to specific anti-anaemic therapy in the treatment of certain refractory anaemias.

Dosage and administration Deca Durabolin should only be administered by deep injection into the gluteus maximus muscle.

Adults: For most indications 25–50 mg every three weeks.

Children: Up to 0.4 mg per kg every three weeks.

In the anaemias associated with chronic renal failure and in malignant disease treated with adjuvant chemotherapy, the following doses are recommended.

Adults: 100–200 mg weekly.

Children: 0.75–1.5 mg/kg weekly.

Contra-indications, warnings, etc

Contra-indications: Contra-indicated in pregnancy, carcinoma of prostate or testes, and mammary carcinoma in the male.

Precautions and warnings: Hypercalcaemia or hypercalciuria may develop either spontaneously or as a result of therapy in patients with certain tumours, especially in mammary carcinoma, hypernephroma and bronchial carcinoma. If hypercalcaemia or hypercalciuria develop during such treatment the preparation should be discontinued and appropriate measures should be taken to normalise calcium levels.

Patients with myocardial, hepatic or renal dysfunction, migraine, epilepsy, hypertension or a history of coronary artery disease should be observed carefully, since anabolic steroids may cause sodium and water retention.

Alterations in glucose tolerance may occur, requiring surveillance for latent diabetes, and possible changes in control for diabetic patients. The need for insulin or other anti-diabetic drugs may be reduced.

Skeletal maturation should be followed carefully when treating children, since anabolic steroids in high dosages may accelerate this process.

Adverse Reactions: Deca-Durabolin is usually free from virilising properties at the recommended dose levels. Larger doses than those recommended, prolonged treatment and/or too frequent administration may cause virilisation in some sensitive women. Hoarseness of the voice may be the first symptom of vocal change which may lead to irreversible lowering of the voice. If signs of virilisation, particularly lowering of the voice, develop, treatment should be discontinued in circumstances where the clinical condition is not sufficiently severe to warrant continuation. Other signs are acne, hirsutism, and increase of libido in women. There may be increased frequency of erections and phallic enlargement in prepubertal males, and clitoral hypertrophy and increase of pubic hair may occur in girls.

Prolonged treatment, use of high dosages, and/or too frequent administration may also increase the risk of amenorrhoea in women and inhibition of spermatogenesis in the male – both conditions probably resulting

from an inhibition of the release of gonadotrophins from the pituitary.

Occasionally, changes have been seen in the outcome of liver function tests, such as serum transaminases, in patients treated with Deca Durabolin. Treatment, however, need not be interrupted on this account. The changes appear to be reversible after discontinuation of the treatment.

Interactions: Although only one possible case of interaction with an oral anti-coagulant has been observed, it is advisable to check the prothrombin time regularly when Deca Durabolin is used in conjunction with such an agent.

Concurrent administration of liver enzyme inducing drugs such as rifampicin, barbiturates, phenylbutazone or phenytoin may decrease the effect of Deca Durabolin.

Pharmaceutical precautions Protect from light. Store at room temperature (15° to 25°C). After storage at lower temperatures precipitation of the arachis oil vehicle may occur. By heating the ampoules at 100°C for a few minutes or at 40°C for one hour the solution will become clear. The precipitation and rewarming does not affect the activity of the injection.

Legal category POM.

Package quantities 25 mg per ml: 1 ml ampoules in boxes of 3 and 1 ml Orgaject* Disposable Syringes singly.

50 mg per ml: 1 ml ampoules in boxes of 3 and 1 ml Orgaject* Disposable Syringes singly.

100 mg per ml: 1 ml ampoules in boxes of 3.

Further information Unlike the orally active anabolics (c-17 α -alkylated steroids) Nandrolone does not cause cholestatic jaundice and liver damage.

Product licence numbers

Deca-Durabolin 25 mg per ml 0065/5005

Deca-Durabolin 50 mg per ml 0065/5063

Deca-Durabolin 100 mg per ml 0065/0036

DURABOLIN*

Presentation Nandrolone Phenylpropionate Injection BP. 1 ml ampoules and 1 ml Orgaject* Disposable Syringes 25 mg per ml and 1 ml Orgaject* Disposable Syringes 50 mg per ml.

Active ingredient: Nandrolone Phenylpropionate BP 25 mg or 50 mg per ml.

Uses Durabolin is an anabolic agent with medium duration of action. The effects of a single intramuscular injection are apparent within a few hours and last for 7–10 days. Indicated in all conditions requiring a prolonged anabolic or anti-catabolic stimulus.

Dosage and administration Durabolin should only be administered by deep injection into the gluteus maximus muscle.

Adults: For most indications, 25–50 mg once weekly. In acute renal failure, doses as high as 50 mg daily may be required. Higher dosage may also be necessary in mammary carcinoma in females.

Children: Dosage should be adjusted to the weight of the child, and should not exceed 1 mg per kg per month.

Contra-indications, warnings, etc

Contra-indications: Contra-indicated in pregnancy, car-

cinoma of prostate or testes, and mammary carcinoma in the male.

Precautions and warnings: Hypercalcaemia or hypercalciuria may develop either spontaneously or as a result of therapy in patients with certain tumours, especially mammary carcinoma, hypernephroma and bronchial carcinoma. If hypercalcaemia or hypercalciuria develop during such treatment the preparation should be discontinued and appropriate measures should be taken to normalise calcium levels.

Patients with myocardial, hepatic or renal dysfunction, migraine, epilepsy, hypertension or a history of coronary artery disease should be observed carefully, since anabolic steroids may cause sodium and water retention.

Alterations in glucose tolerance may occur, requiring surveillance for latent diabetes, and possible changes in control for diabetic patients. The need for insulin or other anti-diabetic drugs may be reduced.

Skeletal maturation should be followed carefully when treating children, since anabolic steroids in high dosages may accelerate this process.

Adverse Reactions: Durabolin is usually free from virilising properties at the recommended dose levels. Larger doses than those recommended, prolonged treatment and/or too frequent administration may cause virilisation in some sensitive women. Hoarseness of the voice may be the first symptom of vocal change which may lead to irreversible lowering of the voice. If signs of virilisation, particularly lowering of the voice, develop, treatment should be discontinued in circumstances where the clinical condition is not sufficiently severe to warrant continuation. Other signs are acne, hirsutism, and increase of libido in women. There may be increased frequency of erections and phallic enlargement in prepubertal males, and clitoral hypertrophy and increase of pubic hair may occur in girls.

Prolonged treatment, use of high dosages, and/or too frequent administration may also increase the risk of amenorrhoea in women and inhibition of spermatogenesis in the male – both conditions probably resulting from an inhibition of the release of gonadotrophins from the pituitary.

Occasionally, changes have been seen in the outcome of liver function tests, such as serum transaminases, in patients treated with Durabolin. Treatment, however, need not be interrupted on this account. The changes appear to be reversible after discontinuation of the treatment.

Interactions: It is advisable to check the prothrombin time regularly when Durabolin is used in conjunction with an oral anti-coagulant.

Concurrent administration of liver enzyme inducing drugs such as rifampicin, barbiturates, phenylbutazone or phenytoin may decrease the effect of Durabolin.

Pharmaceutical precautions Protect from light. Store at room temperature (15° to 25°C). After storage at lower temperatures precipitation of the arachis oil vehicle may occur. By heating the ampoules at 100°C for a few minutes or at 40°C for one hour the solution will become clear. The precipitation and rewarming does not affect the activity of the injection.

Legal category POM.

Package quantities 25 mg per ml: 1 ml ampoules in boxes of 3 and 1 ml Orgaject* Disposable Syringes singly.

50 mg per ml: 1 ml Orgaject* Disposable Syringes singly.

Further information Unlike the orally active anabolics (c-17 α -alkylated steroids) Nandrolone does not cause cholestatic jaundice and liver damage.

Product licence numbers

25 mg/ml: 1 ml ampoules and	
1 ml Orgajects	0065/5007
50 mg/ml: 1 ml Orgajects	0065/5091

GESTANIN*

Presentation Round, flat, white tablets, diameter 6.5 mm, code-marked 'GK4' one side, with 'Organon' and a star on the reverse side.

Active ingredient: Allylestrenol 5 mg per tablet.

Uses Indicated where threatened abortion, recurrent abortion and failure of nidation is due to lack of endogenous progestogen.

Dosage and administration *Recurrent abortion:* As soon as pregnancy has been diagnosed, 1–2 tablets daily. Continue treatment for at least 16 weeks.

Threatened abortion: 3 tablets daily for at least five to seven days. If necessary, daily dosage may be increased and the treatment period extended, without risk.

Failure of nidation: 2–4 tablets daily from the sixteenth to the twenty-sixth day of each cycle until conception is achieved. Thereafter, 2 tablets daily for at least 16 weeks.

Contra-indications, warnings, etc

Contra-indications: Use in patients with a history of, or existent thromboembolic disorders, or with mammary or genital carcinoma.

Use in patients with impaired liver function, or with active liver disease.

Use in patients with undiagnosed, irregular vaginal bleeding.

Precautions and warnings: A decreased glucose tolerance may occur in diabetic patients on this treatment and their control must be carefully supervised. Patients receiving treatment with a progestogen should be kept under regular surveillance, and should have a thorough physical examination regularly. This product should be discontinued before elective surgery or during enforced bed rest.

Pharmaceutical precautions Protect tablets from light.

Legal category POM.

Package quantities Bottles of 100 tablets.

Further information Premature termination of pregnancy often follows a fall in placental hormone levels. Gestanin stimulates secretion of the endogenous placental hormones essential for the maintenance of pregnancy. Gestanin is non-virilising and is well tolerated.

Product licence number 0065/5030.

HYDROCORTISONE SODIUM SUCCINATE

Presentation Hydrocortisone Sodium Succinate Injection BP. In two strengths – ampoules and vials 100 mg; vials 500 mg. The white freeze-dried material contains sodium phosphates 16.6 mg per 100 mg hydrocortisone as buffering agents.

Active ingredient: Hydrocortisone Sodium Succinate equivalent to 100 mg or 500 mg hydrocortisone.

Uses Hydrocortisone Sodium Succinate is a readily soluble ester of hydrocortisone with the same actions as unesterified hydrocortisone. Indicated in the management of emergencies amenable to intensive corticosteroid therapy, such as status asthmaticus, acute adrenal crisis, cardiogenic, haemorrhagic or septic shock. Also valuable in shock states due to anaphylaxis, burns, severe diarrhoea or where the cause of shock is obscure, and in the treatment of ulcerative colitis.

Dosage and administration Rapid intravenous injection of massive doses of corticosteroids may sometimes cause cardiovascular collapse; the injection should therefore be given over a period of not less than 10 minutes.

For immediate use as a single injection of 500 mg dissolve the contents in 10 ml of Water for Injections BP.

Adults: Status asthmaticus: Initially, 500 mg intravenously; this dose should be repeated four to five hours later or followed by an infusion of 500 mg every four hours. Potassium supplements may be needed.

Acute adrenal crisis: 250 mg intravenously, then approximately 250 mg every 12 hours by intravenous infusion.

Shock states, e.g. cardiogenic, bacteraemic, anaphylactic, burns, etc.: 500 mg intravenously, repeated as necessary every two to six hours, either intravenously or by infusion.

Ulcerative colitis: 100 mg, dissolved in 120 ml saline and administered as a rectal drip.

Children: The usual daily dose is 6–10 mg/kg body weight but in life-threatening states 50 mg/kg body weight may be required.

Contra-indications, warnings, etc

Contra-indications: Systemic corticosteroids are generally contra-indicated in patients with Cushing's Syndrome, gastro-intestinal ulcers, systemic fungal infections or acute bacterial or viral infections, particularly ocular herpes infections, active tuberculosis and acute psychosis.

When pregnancy is present or suspected, the benefits of the use of corticosteroids should be weighed against the possible hazards to the foetus.

While on corticosteroid therapy, patients should not be vaccinated against smallpox. Other immunisation procedures should be undertaken under close observation as corticosteroid therapy may interfere with active immunisation due to the immuno-suppressive effects of corticosteroids.

No contra-indications exist when corticosteroids, in a large single dose, are used in conditions where life is endangered.

Precautions and warnings:

Patients currently on corticosteroid therapy or those who have been on such treatment within the previous year may require special control measures if involved in anaesthesia, surgical procedures and other stress. These special control measures usually involve increased dosage of rapidly-acting corticosteroids and are indicated before, during and after the stressful situation.

Withdrawal of corticosteroids should always be gradual and related to the duration of use and should be carried out under strict medical supervision. Withdrawal may result in acute rebound exacerbation of disease, acute adrenocortical insufficiency, polyarteritis.

The uses of corticosteroids in the presence of other disorders (e.g. diabetes mellitus, tuberculosis, amoebiasis, osteoporosis, a history of mental disorders, cardiomyopathy, hypertension and renal insufficiency) or of drugs with specific actions (e.g. hypoglycaemics), impinging on the effects of corticosteroids, may result in imbalance of control.

Corticosteroid administration will result in certain effects, the severity, significance and extent of which vary with the dosage and duration of treatment and the particular corticosteroid used. These include disturbance in electrolyte balance, mineral metabolism, glucose metabolism and gluconeogenesis, nitrogen depletion, diminished lymphoid tissue and immune response, inhibition of pituitary function, Cushingoid Syndrome, increase in blood coagulability, diminished inflammatory response.

Growth and development of children on prolonged corticosteroid therapy should be carefully observed (see 'adverse reactions').

Corticosteroid therapy is non-specific, suppresses the symptoms and signs of disease and enhances susceptibility to infections; appropriate anti-microbial therapy should accompany corticosteroid therapy when necessary.

Corticosteroids appear in breast milk in very small quantities. Mothers taking high doses of corticosteroids should be advised not to breast feed.

Adverse reactions: Adverse reactions associated with short-term corticosteroid therapy in high doses are uncommon.

The major adverse reactions with prolonged corticosteroid therapy are: peptic ulcers, acute pancreatitis, hypokalaemia, infections, suppression of growth in children, CNS effects (ranging from euphoria to frank psychotic manifestations), suppression of ACTH secretion and decreased reactive ability of the adrenal cortex, osteoporosis, ocular effects, negative nitrogen and calcium balance, atrophy of the skin, impaired wound healing, myopathy, diabetogenic effect, sodium and water retention (oedema), hypertension, and development of a Cushingoid state (e.g. 'moon-face', striae, 'central obesity', 'buffalo hump', supraclavicular fat pads, acne, hirsutism).

Pseudotumor cerebri (benign increased intracranial pressure) has been reported in some children receiving systemically administered corticosteroids for prolonged periods; vomiting and papilloedema tend to subside with reduction of dosage.

Anaphylactic reactions, such as urticaria and bronchospasm, have occurred, although very rarely, after intravenous administration of corticosteroids, particularly in patients with a history of hypersensitivity to drugs or allergy to food. If such anaphylactic reactions occur, the following measures are advisable; immediate intravenous injection of adrenaline (0.1–0.5 mg dependent on bodyweight), intermittent positive-pressure ventilation and administration of aminophylline.

When large doses are given intravenously, a transitory burning or tingling sensation, mainly in the perineal area, is often experienced.

Interactions: Concomitant use of corticosteroids and diuretics may result in an enhanced potassium loss.

Concurrent administration of liver enzyme inducing drugs such as rifampicin,ephedrine, barbiturates, phenylbutazone or phenytoin may decrease corticosteroid effects, while if anticoagulants are given with the

corticosteroid, adjustment of dosage of the former is usually necessary.

Salicylates should be used cautiously in conjunction with corticosteroids in hypoprothrombinaemia.

If patients undergoing long term therapy with corticosteroids are concomitantly given salicylates, any reduction in corticosteroid dosage should be made with caution, since cases of salicylate intoxication under these conditions have been reported.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities

100 mg strength: Boxes of 10 vials or ampoules, with 2 ml ampoules of solvent (Water for Injections BP)

500 mg strength: Boxes of 10 vials, without solvent.

Further information Hydrocortisone Sodium Succinate has a marked effect on inflammatory and allergic conditions. Its solubility in water makes it suitable for administration by intravenous injection or infusion in the treatment of acute emergencies. In such emergencies, massive doses can produce dramatic improvement; the required blood cortisol levels are best achieved with an initial intravenous injection, followed by further injections or infusions, and accompanied by appropriate supportive therapy.

Compatibility with Infusion Fluids:

Hydrocortisone Sodium Succinate is compatible with the following i.v fluids:

Dextrose 2½% to 10% in water or normal saline or half-strength saline, invert sugar 5% or 10% in water or saline, lactated Ringer's injection, Ringer's injection, sodium chloride injection. Sodium lactate (1/6M) injection.

Product licence numbers

100 mg 0065/5009

500 mg 0065/5071

MARVELON* ▼

Presentation White, round, biconvex tablets, coded TR5 on one side and ORGANON on the reverse side. Each tablet contains: 150 micrograms desogestrel and 30 micrograms ethinylestradiol.

Uses Oral contraception.

Dosage and administration The tablets are to be taken orally, without chewing, at the same time each day, e.g. at the time of the evening meal.

First course: One tablet daily for 21 days, starting on the first day of the menstrual cycle, with a tablet which is marked with the appropriate day of the week.

Subsequent courses: Each subsequent course is started after seven tablet-free days have followed the preceding course.

Post-partum use: After delivery or abortion, oral contraception should start on the first day of the first spontaneous menstruation. Since the first post-partum ovulation may precede the first bleeding, another method of non-hormonal contraception should therefore be used in the interval between childbirth and the fourteenth tablet-taking day of the first course. In general, Marvelon appears to have no adverse effect on lactation and the excretion of desogestrel in the milk is negligible. However, suppression of lactation may occur when administration is started immediately post-partum.

Changing from another oral contraceptive: Women may change without inconvenience from any other oral contraceptive to Marvelon. The first Marvelon tablet is taken on the first day of the withdrawal bleeding, provided that this bleeding starts with seven days of taking the last tablet. If no bleeding has occurred within seven days of taking the last tablet of the previous oral contraceptive, pregnancy should first be ruled out.

When a patient is changing from a combined oral contraceptive the pack must first be completed before administration of Marvelon commences.

When a patient is taking a combined oral contraceptive which has a 28 day tablet regime and which contains inactive tablets for the last few days (as opposed to a progestogen-only pill), withdrawal bleeding will occur during the inactive phase. When changing to Marvelon the tablets should be started on the first day of this bleeding and the remaining tablets of the previous oral contraceptive may be discarded.

When changing from a progestogen-only pill to Marvelon, the first tablet should be taken on the first day of bleeding, even if this occurs before completion of the previous pack.

Any remaining progestogen-only pills should be discarded.

Additionally, another method of non-hormonal contraception should be used for the first fourteen days.

Contra-indications, warnings, etc

Contra-indications:

- Thrombophlebitis, thrombo-embolic processes, or a history of these conditions.
 - Known or suspected oestrogen-dependent tumours e.g. mammary, genital carcinoma.
 - Undiagnosed irregular vaginal bleeding.
 - Acute or chronic liver disease or history of liver disease where the liver function tests have failed to return to normal. Jaundice or history of jaundice in pregnancy. Rotor syndrome or Dubin-Johnson syndrome.
- N.B.* The use of oral contraceptives is not contra-indicated in patients with a history of hepatitis whose liver functions are normal.
- Porphyria.
 - Cerebrovascular or cardiovascular disease.
 - Hyperlipoproteinaemia, especially in the presence of other risk factors which may indicate a predisposition to cerebrovascular or cardiovascular disorders.
 - A history during pregnancy of severe pruritis, herpes gestationis or a deterioration of otosclerosis.
 - Pregnancy or suspected pregnancy

Precautions and warnings: Pregnancy must be excluded before treatment is started. Whenever there is a reason to suspect pregnancy during treatment, this possibility must be investigated by the physician. If pregnancy has been confirmed, tablet-intake must be discontinued immediately.

Physical examination should precede the prescribing of any oral contraceptive and should be repeated regularly. Special attention should be paid to duration of the cycle, body weight, blood pressure, heart, breasts, pelvic organs, legs and skin.

A cervical smear should be taken at regular intervals.

The physician must be aware that the reliability of oral contraceptives is reduced when a tablet has been forgotten or if gastro-intestinal disturbances occur. If a

patient forgets to take a tablet, it should be taken as soon as possible, continuing thereafter with the normal dosage scheme. The omission of two or more tablets may significantly reduce the reliability of the method. In illness with vomiting or diarrhoea, failure to absorb the tablets can reduce contraceptive reliability.

In addition, the concomitant use of other drugs may interact with oral contraceptives. (See 'Interactions').

If efficacy is in doubt because of the above factors then additional non-hormonal contraceptive precautions are necessary and these should be continued until the next withdrawal bleeding. In some women using an oral contraceptive the amount and/or duration of blood loss during the withdrawal bleeding may be reduced. Occasionally the withdrawal bleeding may even fail to occur. When the aforementioned circumstances are excluded, pregnancy is unlikely and there is no reason to discontinue the use of Marvelon.

However, if during the use of Marvelon the previously regular withdrawal bleeding suddenly fails to occur, pregnancy should be excluded. When there are any reasons to suspect pregnancy, successive pregnancy tests may need to be performed at intervals of one week. While awaiting the outcome of these tests, the patient should be advised to discontinue tablet-intake and to use another method of non-hormonal contraception.

If any signs of thrombo-embolic processes occur, tablet-intake must be discontinued immediately.

The risk of arterial thrombosis associated with combined oral contraceptives increases with age and this risk is aggravated by cigarette smoking. The use of combined oral contraceptives by women in the older age group, especially those who are cigarette smokers, should therefore be discouraged and alternative methods advised.

Oral contraceptive preparations may increase the risk of thrombosis, and this should be taken into account when surgery is to be performed in patients using these preparations. Where possible, oral contraceptives should be discontinued approximately six weeks prior to elective surgery and not recommenced until the patient has recovered and is mobile.

Pre-existing uterine fibromyomata may increase in size under the influence of oestrogens, and if this is observed administration of the preparation should be discontinued.

Since the glucose tolerance may diminish during the use of oral contraceptives, diabetic patients should be monitored closely.

Patients with myocardial or renal disease, varicose veins, epilepsy, migraine, asthma, or a disease exacerbated by pregnancy require careful monitoring since fluid retention has been observed during continued use of oral contraceptives.

Young women whose cycles are not yet stabilised may experience irregular cycle control in the initial stages of oral contraceptive therapy.

Some women experience an increase in blood pressure during pregnancy and/or during oral contraceptive use. In these women the blood pressure should be checked regularly. In case of serious hypertension, further administration of the preparation must be withheld.

Hepatic cell adenomas have been reported in women on oral contraceptive preparations. The adenoma may present itself as an abdominal mass or with the signs and symptoms of an acute abdomen. A bleeding hepatic cell adenoma should be considered if the patient has abdominal pain or evidence of intra-abdominal bleeding.

Patients wearing contact lenses should be advised that they may experience some discomfort.

The use of oral contraceptive preparations may influence the results of certain laboratory tests.

Oral contraceptives have no significant influence on adreno-cortical function. The ACTH function test for the adrenal cortex remains unchanged. The reduction in corticosteroid excretion and the elevation of plasma corticosteroids are due to an increased cortisol-binding capacity of the plasma proteins.

The response to metyrapone is less pronounced in women receiving oral contraceptives and is thus similar to the response during pregnancy.

The radio-iodine uptake shows that thyroid function is unchanged. There is a rise in serum protein-bound iodine, similar to that in pregnancy and during the administration of oestrogens. This is due to the increased capacity of the plasma proteins for binding thyroid hormones, rather than to any change in glandular function. In women taking oral contraceptives, the content of protein-bound iodine in blood serum should, therefore, not be used for the evaluation of thyroid function.

Oral contraceptives may accelerate erythrocyte sedimentation in the absence of any disease. This effect is due to a change in the proportion of the plasma protein fractions.

Increases in plasma copper, iron and alkaline phosphatase have also been recorded.

Adverse reactions: During the first months of use of oral contraceptives, irregular bleeding may occur. Experience has shown that this is almost certainly a transient problem, therefore tablet-intake should be continued. If the irregular bleeding is heavy or prolonged, the physician should investigate.

Nausea, vomiting, headache and breast tenderness may be experienced during the initial months of use. These symptoms usually disappear rapidly; if not, the physician should investigate.

There are reports indicating an association between oral contraceptive preparations and the occurrence of cholelithiasis.

During the use of oral contraceptives, body weight may increase. Experience has shown that body weight stabilises after some time and in some cases can easily be controlled by a suitable diet.

During the use of oral contraceptives fluid retention may occur.

Symptoms such as sudden severe headaches, pains in the chest, visual disturbances, and a swollen arm or leg require immediate medical examination.

If jaundice, which is not necessarily treatment-related, occurs during the use of this preparation, administration must be discontinued immediately.

Chloasma is occasionally seen during the use of oral contraceptives, especially in women with a history of chloasma gravidarum. Women with a tendency to chloasma should avoid exposure to the sun whilst taking this preparation.

In some women who use oestrogen/progestogen preparations, depression may occur. In a number of these women there may be a disturbance of tryptophan metabolism and in such cases the administration of vitamin B₆ might be of therapeutic value.

Interactions: Irregular cycles and reduced reliability of oral contraceptives may occur when these preparations are used concomitantly with liver enzyme inducing drugs such as rifampicin, barbiturates and certain anti-epileptics, or with ampicillin. If no withdrawal bleeding occurs, it is advisable to make sure that these conditions have

not played a contributory role. If they cannot be excluded, the chance of pregnancy is high. In such cases the use of the oral contraceptive preparation should be stopped immediately and diagnosis established.

During this time other forms of non-hormonal contraception should be used.

Overdosage: There have been no reports of serious ill-effects from overdosage, even when a considerable number of tablets have been taken by a small child. In general, it is therefore unnecessary to treat overdosage. However, if overdosage is discovered within two or three hours and is large, then gastric lavage can be safely used.

There are no specific antidotes and further treatment should be symptomatic.

Pharmaceutical precautions Store in a cool, dry place and protect from light.

Legal category POM.

Package quantities Pack of 21 tablets (one month's supply).

Further information Nil.

Product licence number 0065/0071.

MINILYN[®]

Presentation Round, flat, white tablets, diameter 6 mm, code-marked with a circle on one side and Organon on the reverse side. Each tablet contains: Lynoestrenol BP 2.5 mg and Ethinyloestradiol BP 0.05 mg.

Uses Oral contraception.

Dosage and administration The tablets are to be taken orally without chewing, at the same time each day, e.g. at the time of the evening meal.

First course: One tablet daily for 22 days, starting on the first day of the menstrual cycle, with a tablet which is marked with the appropriate day of the week.

Subsequent courses: Each subsequent course is started after six tablet-free days have followed the preceding course; thus, if the 'last tablet' is taken on a Friday, then the first tablet from the next pack is taken on the following Friday.

Post-partum use: After delivery or abortion, oral contraception should start on the first day of the first spontaneous menstruation. Since the first post-partum ovulation may precede the first bleeding, another method of non-hormonal contraception should therefore be used in the interval between childbirth and the fourteenth tablet-taking day of the first course. In general, Minilyn appears to have no adverse effect on lactation and the excretion in the milk is negligible. However, suppression of lactation may occur when administration is started immediately post-partum.

Changing from another oral contraceptive: Women may change without inconvenience from any other oral contraceptive to Minilyn. The first Minilyn tablet is taken on the first day of the withdrawal bleeding, provided that this bleeding starts within six days of taking the last tablet. If no bleeding has occurred within six days of taking the last tablet of the previous oral contraceptive, pregnancy should first be ruled out.

When a patient is changing from a combined oral

contraceptive the pack must first be completed before administration of Minilyn commences.

When a patient is taking a combined oral contraceptive which has a 28 day tablet regime and which contains inactive tablets for the last few days (as opposed to a progestogen-only pill), withdrawal bleeding will occur during the inactive phase. When changing to Minilyn the tablets should be started on the first day of this bleeding and the remaining tablets of the previous oral contraceptive may be discarded.

When changing from a progestogen-only pill to Minilyn the first tablet should be taken on the first day of bleeding, even if this occurs before completion of the previous pack. Any remaining progestogen-only pills should be discarded.

Additionally, another method of non-hormonal contraception should be used for the first fourteen days.

Contra-indications, warnings, etc

Contra-indications:

- Thrombophlebitis, thrombo-embolic processes, or a history of these conditions.
- Known or suspected oestrogen-dependent tumours, e.g. mammary, genital carcinoma.
- Undiagnosed irregular vaginal bleeding.
- Acute or chronic liver disease or history of liver disease where the liver function tests have failed to return to normal. Jaundice or history of jaundice in pregnancy. Rotor syndrome or Dubin-Johnson syndrome.
- N.B.* The use of oral contraceptives is not contra-indicated in patients with a history of hepatitis whose liver functions are normal.
- Porphyria.
- Cerebrovascular or cardiovascular disease.
- Hyperlipoproteinaemia, especially in the presence of other risk factors which may indicate a predisposition to cerebrovascular or cardiovascular disorders.
- A history during pregnancy of severe pruritis, herpes gestationis or a deterioration of otosclerosis.
- Pregnancy or suspected pregnancy.

Precautions and warnings: Pregnancy must be excluded before treatment is started. Whenever there is a reason to suspect pregnancy during treatment, this possibility must be investigated by the physician. If pregnancy has been confirmed, tablet-intake must be discontinued immediately.

Physical examination should precede the prescribing of any oral contraceptive and should be repeated regularly. Special attention should be paid to duration of the cycle, body weight, blood pressure, heart, breasts, pelvic organs, legs and skin.

A cervical smear should be taken at regular intervals.

The physician must be aware that the reliability of oral contraceptives is reduced when a tablet has been forgotten or if gastro-intestinal disturbances occur. If a patient forgets to take a tablet, it should be taken as soon as possible, continuing thereafter with the normal dosage scheme. The omission of two or more tablets may significantly reduce the reliability of the method. In illness with vomiting or diarrhoea, failure to absorb the tablets can reduce contraceptive reliability.

In addition, the concomitant use of other drugs may interact with oral contraceptives. (See 'Interactions'.)

If efficacy is in doubt because of the above factors then additional non-hormonal contraceptive precautions are necessary and these should be continued until the next withdrawal bleeding.

In some women using an oral contraceptive the amount and/or duration of blood loss during the withdrawal bleeding may be reduced. Occasionally the withdrawal bleeding may even fail to occur. When the aforementioned circumstances are excluded, pregnancy is unlikely and there is no reason to discontinue the use of Minilyn. However, if during the use of Minilyn the previously regular withdrawal bleeding suddenly fails to occur, pregnancy should be excluded. When there are any reasons to suspect pregnancy, successive pregnancy tests may need to be performed at intervals of one week. While awaiting the outcome of these tests, the patient should be advised to discontinue tablet-intake and to use another method of non-hormonal contraception.

If any signs of thrombo-embolic processes occur, tablet-intake must be discontinued immediately.

The risk of arterial thrombosis associated with combined oral contraceptives increases with age and this risk is aggravated by cigarette smoking. The use of combined oral contraceptives by women in the older age group, especially those who are cigarette smokers, should therefore be discouraged and alternative methods advised.

Oral contraceptive preparations may increase the risk of thrombosis and this should be taken into account when surgery is to be performed in patients using these preparations. Where possible, oral contraceptives should be discontinued approximately six weeks prior to elective surgery and not recommenced until the patient has recovered and is mobile.

Pre-existing uterine fibromyomata may increase in size under the influence of oestrogens, and if this is observed administration of the preparation should be discontinued.

Since the glucose tolerance may diminish during the use of oral contraceptives, diabetic patients should be monitored closely.

Patients with myocardial or renal disease, varicose veins, epilepsy, migraine, asthma, or a disease exacerbated by pregnancy require careful monitoring since fluid retention has been observed during continued use of oral contraceptives.

Young women whose cycles are not yet stabilised may experience irregular cycle control in the initial stages of oral contraceptive therapy.

Some women experience an increase in blood pressure during pregnancy and/or during oral contraceptive use. In these women the blood pressure should be checked regularly. In case of serious hypertension, further administration of the preparation must be withheld.

Hepatic cell adenomas have been reported in women on oral contraceptive preparations. The adenoma may present itself as an abdominal mass or with the signs and symptoms of an acute abdomen. A bleeding hepatic cell adenoma should be considered if the patient has abdominal pain or evidence of intra-abdominal bleeding.

Patients wearing contact lenses should be advised that they may experience some discomfort.

The use of oral contraceptive preparations may influence the results of certain laboratory tests.

Oral contraceptives have no significant influence on adrenocortical function. The ACTH function test for the adrenal cortex remains unchanged. The reduction in corticosteroid excretion and the elevation of plasma corticosteroids are due to an increased cortisol-binding capacity of the plasma proteins.

The response to metyrapone is less pronounced in women receiving oral contraceptives and is thus similar to the response during pregnancy.

The radio-iodine uptake shows that thyroid function is unchanged. There is a rise in serum protein-bound iodine, similar to that in pregnancy and during the administration of oestrogens. This is due to the increased capacity of the plasma proteins for binding thyroid hormones, rather than to any change in glandular function. In women taking oral contraceptives, the content of protein-bound iodine in blood serum should, therefore, not be used for the evaluation of thyroid function.

Oral contraceptives may accelerate erythrocyte sedimentation in the absence of any disease. This effect is due to a change in the proportion of the plasma protein fractions. Increases in plasma copper, iron and alkaline phosphatase have also been recorded.

Adverse reactions: During the first months of use of oral contraceptives, irregular bleeding may occur. Experience has shown that this is almost certainly a transient problem, therefore tablet-intake should be continued. If the irregular bleeding is heavy or prolonged, the physician should investigate.

Nausea, vomiting, headache and breast tenderness may be experienced during the initial months of use. These symptoms usually disappear rapidly; if not, the physician should investigate.

There are reports indicating an association between oral contraceptive preparations and the occurrence of cholelithiasis.

During the use of oral contraceptives, body weight may increase. Experience has shown that body weight stabilises after some time and in some cases can easily be controlled by a suitable diet.

During the use of oral contraceptives fluid retention may occur.

Symptoms such as sudden severe headaches, pains in the chest, visual disturbances, and a swollen arm or leg require immediate medical examination.

If jaundice, which is not necessarily treatment-related, occurs during the use of this preparation, administration must be discontinued immediately.

Chloasma is occasionally seen during the use of oral contraceptives, especially in women with a history of chloasma gravidarum. Women with a tendency to chloasma should avoid exposure to the sun whilst taking this preparation.

In some women who use oestrogen/progestogen preparations, depression may occur. In a number of these women there may be a disturbance of tryptophan metabolism and in such cases the administration of vitamin B₆ might be of therapeutic value.

Interactions: Irregular cycles and reduced reliability of oral contraceptives may occur when these preparations are used concomitantly with liver enzyme inducing drugs such as rifampicin, barbiturates and certain anti-epileptics, or with ampicillin. If no withdrawal bleeding occurs, it is advisable to make sure that these conditions have not played a contributory role. If they cannot be excluded, the chance of pregnancy is high. In such cases the use of the oral contraceptive preparation should be stopped immediately and diagnosis established. During this time other forms of non-hormonal contraception should be used.

Overdosage: There have been no reports of serious ill-effects from overdosage, even when a considerable number of tablets have been taken by a small child. In general, it is therefore unnecessary to treat overdosage. However, if overdosage is discovered within two or three

hours and is large, then gastric lavage can be safely used.

There are no specific antidotes and further treatment should be symptomatic.

Pharmaceutical precautions Store in a cool, dry, place and protect from light.

Legal category POM.

Package quantities Pack of 22 tablets (one month's supply).

Further information Nil.

Product licence number 0065/5041.

MIXOGEN* INJECTION

Presentation 2 ml vials, for intramuscular injection. A clear oily solution, containing in each millilitre oestradiol benzoate 1 mg, oestradiol phenylpropionate 4 mg, testosterone propionate 20 mg, testosterone phenylpropionate 40 mg and testosterone isocaproate 40 mg.

Uses A combination of oestrogens and androgens which provides treatment for climacteric symptoms in women.

Dosage and administration Mixogen Injection should only be administered by deep injection into the gluteus maximus muscle.

Initially, 1 ml once every three weeks until symptoms are fully controlled, then 1 ml every four weeks.

Contra-indications, warnings, etc

Contra-indications:

- Thrombophlebitis, thrombo-embolic processes, or a history of these conditions.
- Known or suspected oestrogen-dependent tumours, e.g. mammary, genital carcinoma.
- Undiagnosed irregular vaginal bleeding.
- Acute or chronic liver disease or history of liver disease where the liver function tests have failed to return to normal. Jaundice or history of jaundice in pregnancy. Rotor syndrome or Dubin-Johnson syndrome.

N.B. The use of oestrogens is not contra-indicated in patients with a history of hepatitis whose liver functions are normal.

- Porphyria.
- Cerebrovascular or cardiovascular disease.
- Hyperlipoproteinaemia, especially in the presence of other risk factors which may indicate a predisposition to cerebrovascular or cardiovascular disorders.
- A history during pregnancy of severe pruritus, herpes gestationis or a deterioration of otosclerosis.
- Endometriosis.
- Pregnancy or suspected pregnancy.

Precautions and warnings: Pregnancy must be excluded before treatment is started. Whenever there is a reason to suspect pregnancy during treatment, this possibility must be investigated by the physician. If pregnancy has been confirmed the treatment must be discontinued immediately.

Physical examination should precede the prescribing of any oestrogen and should be repeated regularly. Special attention should be paid to duration of the cycle, body weight, blood pressure, heart, breasts, pelvic organs, legs and skin.

A cervical smear should be taken at regular intervals.

If any signs of thrombo-embolic processes occur, the use of the preparation must be discontinued immediately.

Oestrogen preparations may increase the risk of thrombosis and this should be taken into account when surgery is to be performed in patients using these preparations. Where possible, oestrogens should be discontinued approximately six weeks prior to elective surgery and not recommenced until the patient has recovered and is mobile.

Pre-existing uterine fibromyomata may increase in size under the influence of oestrogens, and if this is observed, administration of the preparation should be discontinued.

Since the glucose tolerance may diminish during the use of oestrogens, diabetic patients should be monitored closely.

Patients with myocardial or renal disease, varicose veins, epilepsy, migraine or asthma, require careful monitoring since sodium and water retention has been observed during continued use of oestrogens.

Since oestrogen preparations may cause an increase in blood pressure in predisposed patients, this should be checked regularly. In case of serious hypertension, further administration of the preparation must be withheld.

Patients wearing contact lenses should be advised that they may experience some discomfort.

If hypercalcaemia or hypercalciuria develop, treatment should be discontinued.

Administration to patients with nephrotic syndrome should be avoided.

Prolonged or excessive dosage of oestrogens inhibits pituitary function and on cessation of treatment, severe withdrawal bleeding may occur.

Interactions: Concurrent administration of liver enzyme inducing drugs such as rifampicin, barbiturates, phenylbutazone or phenytoin may decrease the effect of Mixogen.

Adverse reactions: There may be a risk of virilisation manifested by hoarseness of the voice, acne, hirsutism, enlarged clitoris and stimulation of libido. Hoarseness of the voice may be the first symptom of vocal change which may lead to an irreversible lowering of the voice. If signs of virilisation, particularly hoarseness of the voice, develop, treatment should be discontinued.

Other side-effects may be menstrual irregularities, nausea or vomiting, headache, sodium and water retention, breast tenderness, mood changes and uterine bleeding (during or on withdrawal of therapy).

Symptoms such as sudden severe headaches, pains in the chest, visual disturbances, or swelling of the arms or legs require immediate medical examination.

Pharmaceutical precautions Protect from light.

Legal category POM

Package quantities Single 2 ml vials.

Further information Nil.

Product licence number 0065/5010.

MIXOGEN* TABLETS

Presentation Round, white tablets, code-marked 'SZ7' on one side, with 'Organon' and a star on the reverse side.

Active ingredients: Ethinyloestradiol BP 0.0044 mg and Methyltestosterone BP 3.6 mg per tablet.

Uses A combination of oestrogen and androgen which provides treatment for climacteric symptoms in women.

Dosage and administration 1–2 tablets daily, more in severe cases, omitting treatment every fourth week. When symptoms are fully controlled, dosage may be gradually reduced to maintenance level.

Contra-indications, warnings, etc

Contra-indications:

- (a) Thrombophlebitis, thrombo-embolic processes, or a history of these conditions.
- (b) Known or suspected oestrogen-dependent tumours, e.g. mammary, genital carcinoma.
- (c) Undiagnosed irregular vaginal bleeding.
- (d) Acute or chronic liver disease or history of liver disease where the liver function tests have failed to return to normal. Jaundice or history of jaundice in pregnancy. Rotor syndrome or Dubin-Johnson syndrome.
- N.B.* The use of oestrogens is not contra-indicated in patients with a history of hepatitis whose liver functions are normal.
- (e) Porphyria.
- (f) Cerebrovascular or cardiovascular disease.
- (g) Hyperlipoproteinaemia, especially in the presence of other risk factors which may indicate a predisposition to cerebrovascular or cardiovascular disorders.
- (h) A history during pregnancy of severe pruritus, herpes gestationis or a deterioration of otosclerosis.
- (i) Endometriosis.
- (j) Pregnancy or suspected pregnancy.

Precautions and warnings: Pregnancy must be excluded before treatment is started. Whenever there is a reason to suspect pregnancy during treatment, this possibility must be investigated by the physician. If pregnancy has been confirmed, tablet-intake must be discontinued immediately.

Physical examination should precede the prescribing of any oestrogen and should be repeated regularly. Special attention should be paid to duration of the cycle, body weight, blood pressure, heart, breasts, pelvic organs, legs and skin.

A cervical smear should be taken at regular intervals.

If any signs of thrombo-embolic processes occur, the use of the preparation must be discontinued immediately.

Oestrogen preparations may increase the risk of thrombosis and this should be taken into account when surgery is to be performed in patients using these preparations. Where possible, oestrogens should be discontinued approximately six weeks prior to elective surgery and not recommenced until the patient has recovered and is mobile.

Pre-existing uterine fibromyomata may increase in size under the influence of oestrogens, and if this is observed, administration of the preparation should be discontinued.

Since the glucose tolerance may diminish during the use of oestrogens, diabetic patients should be monitored closely.

Patients with myocardial or renal disease, varicose veins, epilepsy, migraine or asthma, require careful monitoring since sodium and water retention has been observed during continued use of oestrogens.

Since oestrogen preparations may cause an increase in blood pressure in predisposed patients, this should be checked regularly. In case of serious hypertension, further administration of the preparation must be withheld.

Patients wearing contact lenses should be advised that they may experience some discomfort.

If hypercalcaemia or hypercalciuria develop, treatment should be discontinued.

Administration to patients with nephrotic syndrome should be avoided.

Tumours of the liver have been reported occasionally in patients subjected to prolonged treatment with C-17 α -alkylated androgenic-anabolic steroids. The possibility that these compounds may induce or enhance the development of hepatic tumours cannot at present be excluded and this should be considered when the use of this product is proposed, especially in young people who are not suffering from life-threatening disorders.

Prolonged or excessive dosage of oestrogens inhibits pituitary function and on cessation of treatment, severe withdrawal bleeding may occur.

Adverse reactions: There may be a risk of virilisation manifested by hoarseness of the voice, acne, hirsutism, enlarged clitoris and stimulation of libido. Hoarseness of the voice may be the first symptom of vocal change which may lead to an irreversible lowering of the voice. If signs of virilisation, particularly hoarseness of the voice, develop, treatment should be discontinued.

Other side-effects may be menstrual irregularities, nausea or vomiting, headache, sodium and water retention, breast tenderness, mood changes and uterine bleeding (during or on withdrawal of therapy).

Symptoms such as sudden severe headaches, pains in the chest, visual disturbances, or swelling of the arms or legs require immediate medical examination.

Interactions: Concurrent administration of liver enzyme inducing drugs such as rifampicin, barbiturates, phenylbutazone or phenytoin may decrease the effect of Mixogen.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Bottles of 100 tablets.

Further information Nil.

Product licence number 0065/5042.

MULTILOAD CU 250* ▼

Presentation The Multiload Cu 250 is an intrauterine device made of polyethylene, 3.6 cm in length with 27 cm of copper wire 0.3 mm diameter wrapped around the stem, giving a total surface area of 250 mm² of copper. The flexible side arms ensure that the Multiload Cu 250 remains in position as high as is possible against the fundus without the uterine cavity being stretched in any way. The device is preloaded on its inserter and a monofilament polypropylene thread is attached to the stem.

The Multiload Cu 250 can be regarded as a third generation IUD. As a result of its special shape the Multiload Cu 250 represents a breakaway from the principle that IUDs must be firmly embedded into the uterine cavity in order to prevent expulsion. In addition, with 250 mm² of copper wound around the vertical stem a very low pregnancy rate is obtained without using a maximum surface area.

As a result, the Multiload Cu 250 causes practically no cramp and no intermittent bleeding. Contractions of the uterus are cushioned by the wide upper end of the

Multiload Cu 250, resulting in flexure of the side arms which are designed to prevent expulsion.

The Multiload Cu 250 is suitable for both multiparous and nulliparous patients (however see Precautions and Warnings). The insertion procedure is simple and the device can be accurately positioned high up against the fundus. An expeller is not necessary.

Uses Intrauterine Contraception.

Dosage and administration It is recommended that the Multiload Cu 250 be replaced every three years.

Recommended procedure for inserting the Multiload Cu 250: Perform a bimanual examination of the uterus to determine its condition and position.

Expose the cervix with a bivalve speculum and hook a single tooth tenaculum to the posterior (sometimes anterior) lip of the cervix. A sufficiently good grip should be obtained with the tenaculum, without blocking the cervical canal, to align the uterine cavity with the canal. Cleanse the cervix with cotton wool soaked in antiseptic solution. Remove cellular debris from the external os of the cervix to prevent contamination of the uterine cavity. Lignocaine gel may be applied to produce local anaesthesia.

Sound the uterus to determine the depth and direction of the cavity. A good idea of the size and shape of the uterus is obtained by turning the sound carefully to and fro. If slight resistance is felt at the moment when the sound passes through the internal os it is advisable to dilate the cervical canal carefully with a No. 4 Hegar dilator.

The distance found between the external os and the fundus of the uterine cavity is set with a ring on the inserter; this ring is pre-set at 7 cm.

Introduce the Multiload Cu 250 with the inserter into the uterine cavity until it touches the fundus, bearing in mind the direction and depth determined with the sound. During this procedure it is desirable to pull the tenaculum in such a way that the axis of the cervical canal is stretched. Slight resistance may be encountered as the Multiload Cu 250 is pushed through the internal os uteri, particularly in nulliparous women, or women who have not had children for several years.

As soon as the Multiload Cu 250 and the inserter are resting against the fundus, the Multiload Cu 250 is removed from its housing by simply withdrawing the inserter while at the same time pulling the tenaculum in such a way that the axis of the cervical canal is stretched. It is important to ensure that the inserter is accurately removed in the correct direction, otherwise the Multiload Cu 250 may not be lodged as deeply as possible in the uterine cavity. Cut the thread of the Multiload Cu 250 to the required length.

Removal: The Multiload Cu 250 is usually removed after three years and replaced by a new one.

The ability to become pregnant is normally restored a short time after removal of the Multiload Cu 250.

In the case of pregnancy the Multiload Cu 250 must be removed upon diagnosis.

Removal procedure: Expose the cervix with a bivalve speculum. Grasp the thread of the Multiload Cu 250 firmly as near to the external os as possible. Pull it out carefully and steadily. There is a tendency for small quantities of calcium to form a sediment on the surface of all IUDs.

Contra-indications, warnings, etc

Contra-indications: Pregnancy, congenital or acquired

abnormalities of the uterine cavity, pelvic inflammatory disease either pre-existing or in a patient with a history of such conditions, acute cervicitis, acute or sub-acute salpingitis, endometritis or infected abortion in the past three months, dysfunctional uterine bleeding, cervical dysplasia, suspected or proven carcinoma of the cervix or endometrium, uterine polyps or fibroids, disturbance of the blood clotting mechanism and known allergy to copper.

Multiload Cu 250 should not be used with organic mercurial pessaries.

Precautions and warnings: When diathermy is used there is a possibility of heat injury to the endometrium in women with a copper IUD.

If pelvic infection occurs which is unresponsive to treatment, the Multiload Cu 250 should be removed. An association between the use of IUDs and pelvic infection has been reported. Appropriate antibiotic cover should be given three days prior to, and for at least ten days after insertion, in patients with a past history of rheumatic fever and certain known or suspected cardiac abnormalities, in order to preclude the possibility of precipitating sub-acute bacterial endocarditis.

The use of non-sterile techniques can result in sepsis. Spontaneous perforation is almost impossible; traumatic insertion procedures causing late perforation must be avoided. If a uterus is found to be less than 6 cm deep, insertion of a Multiload Cu 250 is not recommended.

Pain during and after insertion is more likely to occur in nulliparous than in multiparous women.

It has been demonstrated that the presence of an IUD in a pregnant uterus increases the risk of abortion and sepsis. Ectopic pregnancy may occur.

If in the unlikely event a patient presents with the Multiload Cu 250 in situ and she is pregnant, then as with all IUDs, the device must be removed.

The patient must be left in no doubt about the very slight chance of pregnancy and about the need to contact a doctor immediately if pregnancy should occur, as in this case the Multiload Cu 250 must be removed. After insertion the patient should be taught to examine herself to confirm the presence of the thread. It should also be pointed out to the patient that in the event of complications a doctor must always be consulted.

Some women are troubled by abdominal cramps after insertion. Post-insertion syncope may occur in some nulliparous patients. Intermittent bleeding or prolongation of menstruation may occur during the first two or three cycles.

Pharmaceutical precautions The Multiload Cu 250 is supplied sterile in a peel-open pouch, which should not be opened until required for insertion. Aseptic precautions should be carried out when handling the device. Care should be taken to ensure the sterile packages are not damaged; they should be stored in cool dry conditions.

Legal category POM.

Package quantities One outer package containing 10 Multiload Cu 250.

10 inner packs each containing 1 Multiload Cu 250 ready for immediate use and fitted with a disposable inserter.

Further information The amount of copper eluted from copper IUDs is well below the daily dietary intake of copper. No changes in blood levels of copper have been detected.

Product licence number 0065/0062.

OESTRADIOL* IMPLANTS

Presentation Pellets of fused, white crystalline hormone in several weights, for implantation.

Active ingredient: Oestradiol BPC 25 mg, 50 mg and 100 mg. The 25 mg weight has a diameter of 2.2 mm and the 50 mg and 100 mg a diameter of 4.5 mm.

Uses Implantation of fused implants of oestradiol provides a very slow release of the hormone. Approximate durations of effect are: 25 mg – 36 weeks. 50 mg – 44 weeks. 100 mg – 57 weeks. Indicated in females for long-term treatment in cases requiring oestrogen replacement, as in primary hypoplastic amenorrhoea, non-oestrogen-dependent mammary carcinoma (in women over 60), female castration and the climacteric.

In males, excessive libido and prostatic carcinoma.

Dosage and administration *Adults: Female:* Mammary carcinoma (in women over 60) 100–200 mg. Amenorrhoea (primary hypoplastic) 25 mg. Castration (with uterus) 25 mg. Castration (without uterus) 50 mg. Climacteric 25 mg.

Male: Prostatic carcinoma 100–300 mg; excessive libido 50 mg.

Frequency of replacement depends on the duration of activity of the implants administered.

Implants are inserted, either by means of a trocar and cannula or by open surgery, into an area where there is comparatively little movement, such as the lower abdominal wall or the buttock. Insertion is made under local anaesthetic and the wound is closed either with an adhesive dressing or a fine suture.

Oestradiol Implants are well tolerated but are so slowly absorbed that the endometrium is liable to progressive hypertrophy. For this reason, where the uterus is intact, Oestradiol Implants must invariably be placed superficially in case they have to be removed.

Whichever method is used for the insertion of implants, the following principles apply:

1. Full aseptic 'no touch' technique should be adopted.
2. Precautions should be taken to avoid the formation of haematoma at the site.
3. The rate of absorption of the active ingredient depends on the surface area of the implant. Thus the daily rate of absorption can be increased by supplying the total dose in a number of separate implants each sited on a separate track.

Contra-indications, warnings, etc

Contra-indications:

- (a) Thrombophlebitis, thrombo-embolic processes, or a history of these conditions.
 - (b) Known or suspected oestrogen-dependent tumours, e.g. mammary, genital carcinoma.
 - (c) Undiagnosed irregular vaginal bleeding.
 - (d) Acute or chronic liver disease or history of liver disease where the liver function tests have failed to return to normal. Jaundice or history of jaundice in pregnancy. Rotor syndrome or Dubin-Johnson syndrome.
- N.B.* The use of oestrogens is not contra-indicated in patients with a history of hepatitis whose liver functions are normal.
- (e) Porphyria.
 - (f) Cerebrovascular or cardiovascular disease.
 - (g) Hyperlipoproteinaemia, especially in the presence of other risk factors which may indicate a predis-

position to cerebrovascular or cardiovascular disorders.

- (h) A history during pregnancy of severe pruritus, herpes gestationis or a deterioration of otosclerosis.
- (i) Endometriosis.
- (j) Pregnancy or suspected pregnancy.

Precautions and warnings: Pregnancy must be excluded before treatment is started. Whenever there is a reason to suspect pregnancy during treatment, this possibility must be investigated by the physician. If pregnancy has been confirmed the implant must be removed immediately.

Physical examination should precede the prescribing of any oestrogen and should be repeated regularly. Special attention should be paid to duration of the cycle, body weight, blood pressure, heart, breasts, pelvic organs, legs and skin.

A cervical smear should be taken at regular intervals.

If any signs of thrombo-embolic processes occur, the implant must be removed immediately.

Oestrogen preparations may increase the risk of thrombosis and this should be taken into account when surgery is to be performed in patients using these preparations. Where possible, oestrogens should be discontinued approximately six weeks prior to elective surgery and not recommended until the patient has recovered and is mobile.

Pre-existing uterine fibromyomata may increase in size under the influence of oestrogens, and if this is observed the implant must be removed.

Since the glucose tolerance may diminish during the use of oestrogens, diabetic patients should be monitored closely.

Prolonged exposure to unopposed oestrogens may increase the risk of the development of endometrial carcinoma.

Patients with myocardial or renal disease, varicose veins, epilepsy, migraine or asthma, require careful monitoring since sodium and water retention has been observed during continued use of oestrogens.

Since oestrogen preparations may cause an increase in blood pressure in predisposed patients, this should be checked regularly. In case of serious hypertension, further administration of the preparation must be withheld.

Patients wearing contact lenses should be advised that they may experience some discomfort.

Hypercalcaemia or hypercalciuria may develop either spontaneously or as a result of hormonal therapy in patients with certain tumours, especially in mammary carcinoma, hypernephroma and bronchial carcinoma. If either hypercalcaemia or hypercalciuria develop during such treatment, the preparation should be removed and appropriate measures taken to normalise calcium levels.

Because oestrogens may accelerate epiphyseal closure, they should be used judiciously in those young patients in whom bone growth is not yet complete.

Prolonged or excessive dosage of oestrogens inhibits pituitary function and on cessation of treatment, severe withdrawal bleeding may occur.

Adverse reactions: Adverse reactions are rare and only appear if the dosage is too high or treatment is prolonged. These include nausea and vomiting, headache, sodium and water retention, breast tenderness and gynaecomastia (may occur in the treatment of prostatic carcinoma), menstrual disturbances, uterine bleeding (during or on withdrawal of therapy) and psychotic disturbances.

Symptoms such as sudden severe headaches, pains in

the chest, visual disturbances, swelling of the arms or legs require immediate medical examination.

In male patients reduced libido, impotence and disturbances of spermatogenesis may occur.

Interactions: Concurrent administration of liver enzyme inducing drugs such as rifampicin, barbiturates, phenylbutazone or phenytoin may decrease the effect of Oestradiol Implants.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Each sterile implant is supplied singly, in a sealed glass tube. Available in the following weights: 25 mg, 50 mg and 100 mg.

Further information Nil.

Product licence numbers

25 mg 0065/5074

50 mg 0065/5075

100 mg 0065/5076

ORABOLIN*

Presentation Round, flat white tablets, diameter 9 mm, code-marked 'SB3' on one side, with 'Organon' and star on the reverse side.

Active ingredient: Ethyloestrenol BP 2 mg per tablet.

Uses Ethyloestrenol is an orally active anabolic steroid.

Dosage and administration *Adults:* 1-2 tablets orally daily. Not recommended for children.

Contra-indications, warnings, etc

Contra-indications: Pregnancy, prostatic carcinoma, mammary carcinoma in the male and in severe disturbances of liver function.

Hypercalcaemia or hypercalciuria may develop either spontaneously or as a result of therapy in patients with certain tumours, especially in mammary carcinoma, hypernephroma and bronchial carcinoma. If hypercalcaemia or hypercalciuria develops during such treatment the preparation should be discontinued and appropriate measures should be taken to normalise calcium levels.

Treatment should be discontinued if cholestatic jaundice appears or liver function tests become abnormal.

Tumours of the liver have been reported occasionally in patients subjected to prolonged treatment with C-17 α alkylated androgenic-anabolic steroids. The possibility that these compounds may induce or enhance the development of hepatic tumours cannot at present be excluded and this should be considered when the use of this product is proposed, especially in young people who are not suffering from life-threatening disorders.

C-17 α -alkylated anabolic steroids have also been reported to increase the hypoprothrombinaemic action of oral anticoagulants. This should be taken into account when Orabolin is administered concomitantly with oral anticoagulants, in which case reduction of the anticoagulant dosage may be necessary.

Patients with myocardial or renal dysfunction, hypertension or epilepsy should be observed carefully, since anabolic steroids may cause sodium and water retention. The preparation should not be administered for periods longer than three months and the recommended dosage should not be exceeded.

Skeletal maturation should be followed carefully when treating young people, since anabolic steroids in high dosages may accelerate this process.

Precautions and warnings: Young women whose cycles are not yet stabilised may experience irregular cycle control in the initial stages of treatment.

In diabetics, the need for insulin or other anti-diabetic drugs may be reduced.

Adverse reactions: When administered in the recommended dosages and for short periods of time (up to four weeks) adverse reactions may occur very rarely. Occasionally after high dosages, some liver function tests have shown abnormal values. These deviations, however, were transient and completely reversible after discontinuation of treatment. In some cases, particularly those treated with high dosages, nausea and some sodium and water retention may occur.

The possibility of menstrual disturbances exists, probably resulting from an inhibition of the secretion of gonadotrophins from the pituitary and/or from the occurrence of a progestational effect. In such cases the treatment should be discontinued or the dosage decreased.

Interactions: Concurrent administration of liver enzyme inducing drugs such as rifampicin, barbiturates, phenylbutazone or phenytoin may decrease the effect of Orabolin.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Bottles of 100 tablets.

Further information Nil.

Product licence number 0065/5043.

ORADEXON-ORGANON* INJECTION

Presentation A clear aqueous solution for injection, available as 1 ml ampoules containing dexamethasone sodium phosphate 5 mg per ml and as 2 ml vials containing the equivalent of 4 mg dexamethasone per ml (5 mg/ml dexamethasone sodium phosphate is approximately equivalent to 4 mg/ml dexamethasone.)

Uses Dexamethasone has powerful anti-inflammatory effects, little mineralocorticoid activity, and it produces minimal fluid retention. Oradexon-Organon may be administered intravenously, intramuscularly or as a rectal drip. It is particularly useful for intravenous use in the treatment of all acute conditions in which corticosteroids may be life-saving. In addition, Oradexon-Organon has a wide range of uses by local injection in physical medicine, for the treatment of such conditions as rheumatoid arthritis, osteoarthritis, supraspinatus tendinitis, Dupuytren's contracture, humeral epicondylitis and for local treatment of ulcerative colitis by rectal drip. Oradexon-Organon injection is also of value in the control of cerebral oedema caused by neoplasms, injuries, surgery, or cerebrovascular accidents.

Dosage and administration All dosages indicated relate to dexamethasone.

Rapid intravenous injection of massive doses of corticosteroids may sometimes cause cardiovascular collapse; the injection should therefore be given over a period of not less than 10 minutes.

Suggested dosages for adults: *Intravenous injection or infusion:* In acute conditions endangering life, such as shock (haemorrhagic, bacteraemic, traumatic, cardiogenic, surgical, snake venom, shock from burns). In severe allergic reactions (drug hypersensitivity, anaphy-

laxis, status asthmaticus), in fulminating infections (peritonitis, pneumonia, meningitis, septicaemia) in hepatic coma, cerebral oedema: 8 to 40 mg, either as a slow intravenous injection or as an infusion in glucose, saline or Ringer's solution. Dosage should be adjusted according to the severity of the condition and the patient's response.

Injection into joints, bursae, tendon sheaths and local infiltration: In chronic conditions (rheumatoid arthritis, osteoarthritis, supraspinatus tendinitis, Dupuytren's contracture, humeral epicondylitis); intra-articular (large joints) 4 mg; intra-bursal 2 mg; tendon sheaths 2 mg; local infiltration 2 mg. Administration by these routes calls for strict asepsis.

Rectal Drip: In cases of ulcerative colitis, Oradexon-Organon may be administered in a dose of 4 mg diluted in 120 ml saline.

Suggested dosages for children: Dosage requirements are variable and may have to be changed according to individual needs. Usually 0.25 mg/kg to 0.50 mg/kg of body weight daily.

Contra-indications, warnings, etc

Contra-indications: Systemic corticosteroids are generally contraindicated in patients with Cushing's Syndrome, gastro-intestinal ulcers, systemic fungal infections or acute bacterial or viral infections, particularly ocular herpes infections, active tuberculosis and acute psychosis.

Local injection of a corticosteroid is contra-indicated in the presence of an infection at the injection site (e.g. infectious arthritides, resulting from gonorrhoea or tuberculosis).

When pregnancy is present or suspected, the benefits of the use of corticosteroids should be weighed against the possible hazards to the foetus.

While on corticosteroid therapy, patients should not be vaccinated against smallpox. Other immunisation procedures should be undertaken under close observation as corticosteroid therapy may interfere with active immunisation due to the immuno-suppressive effects of corticosteroids.

No contra-indications exist when corticosteroids, in a large single dose, are used in conditions where life is endangered.

Precautions and warnings:

1. Patients currently on corticosteroid therapy or those who have been on such treatment within the previous year may require special control measures if involved in anaesthesia, surgical procedures and other stress. These special control measures usually involve increased dosage of rapidly acting corticosteroids and are indicated before, during, and after the stressful situation.

2. Withdrawal of corticosteroids should always be gradual and related to the duration of use and should be carried out under strict medical supervision. Withdrawal may result in acute rebound exacerbation of disease, acute adrenocortical insufficiency, polyarteritis.

3. The use of corticosteroids in the presence of other disorders (e.g. diabetes mellitus, tuberculosis, amoebiasis, osteoporosis, a history of mental disorders, cardiomyopathy, hypertension and renal insufficiency) or of drugs with specific actions (e.g. hypoglycaemics), impinging on the effects of corticosteroids may result in imbalance of control.

4. Corticosteroid administration will result in certain effects, the severity, significance and extent of which

vary with the dosage and duration of treatment and the particular corticosteroid used. These include disturbance in electrolyte balance, mineral metabolism, glucose metabolism and gluconeogenesis, nitrogen depletion, diminished lymphoid tissue and immune response, inhibition of pituitary function, Cushingoid Syndrome, increase in blood coagulability, diminished inflammatory response.

5. Growth and development of children on prolonged corticosteroid therapy should be carefully observed (see 'adverse reactions').

6. Corticosteroid therapy is non-specific, suppresses the symptoms and signs of disease and enhances susceptibility to infections; appropriate antimicrobial therapy should accompany corticosteroid therapy when necessary.

Corticosteroids appear in breast milk in very small quantities. Mothers taking high doses of corticosteroids should be advised not to breast feed.

When injecting into joints or bursae appropriate examination of the fluid is necessary to exclude a septic process. If septic arthritis occurs, appropriate antimicrobial therapy should be instituted. Corticosteroids should not be injected into unstable joints. Intra-articular injections of a corticosteroid may produce systemic as well as local effects.

Cases of ruptured tendon have been reported following the injection of corticosteroids directly into a tendon. In the treatment of conditions such as tendinitis or tenosynovitis care should be taken to inject into the space between the tendon sheath and the tendon.

Interactions: Concomitant use of corticosteroids and diuretics may result in an enhanced potassium loss.

Concurrent administration of liver enzyme inducing drugs such as rifampicin, ephedrine, barbiturates, phenylbutazone or phenytoin may decrease corticosteroid effects, while if anticoagulants are given with the corticosteroid, adjustment of dosage of the former is usually necessary.

Salicylates should be used cautiously in conjunction with corticosteroids in hypoprothrombinaemia.

If patients undergoing long term therapy with corticosteroids are concomitantly given salicylates, any reduction in corticosteroid dosage should be made with caution, since cases of salicylate intoxication under these conditions have been reported.

Adverse reactions: Adverse reactions associated with short-term corticosteroid therapy in high doses are uncommon.

The major adverse reactions with prolonged corticosteroid therapy are: peptic ulcers, acute pancreatitis, hypokalaemia, infections, suppression of growth in children, CNS effects (ranging from euphoria to frank psychotic manifestations), suppression of ACTH secretion and decreased reactive ability of the adrenal cortex, osteoporosis, ocular effects, negative nitrogen and calcium balance, atrophy of the skin, impaired wound healing, myopathy, diabetogenic effect, sodium and water retention (oedema), hypertension, and development of a Cushingoid state (e.g. 'moon-face', striae, 'central obesity', 'buffalo hump', supraclavicular fat pads, acne, hirsutism).

Pseudotumor cerebri (benign increased intracranial pressure) has been reported in some children receiving systemically administered corticosteroids for prolonged periods; vomiting and papilloedema tend to subside with reduction of dosage.

Anaphylactic reactions, such as urticaria and bron-

chospasm, have occurred, although very rarely, after intravenous administration of corticosteroids, particularly in patients with a history of hypersensitivity to drugs or allergy to food. If such anaphylactic reactions occur, the following measures are advisable; immediate intravenous injection of adrenaline (0.1–0.5 mg dependent on bodyweight), intermittent positive-pressure ventilation and administration of aminophylline.

Local injection adverse reactions include post-injection flare and a painless destruction of the joint reminiscent of Charcot's arthropathy, especially with repeated intra-articular injections.

When large doses are given intravenously, a transitory burning or tingling sensation, mainly in the perineal area, is often experienced.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities 2 ml vials, singly containing 4 mg per ml dexamethasone, 1 ml ampoules in boxes of 25, containing 5 mg per ml dexamethasone sodium phosphate.

Further information Oradexon-Organon Injection is an important drug in the management of cerebral oedema which accompanies many intracranial conditions, e.g. neoplasms, trauma, thrombotic episodes, post-radiotherapy or post-surgery. The reduction in intracranial pressure which can be achieved by its usage relieves many of the unpleasant symptoms associated with this condition, enables early neurological investigative measures to be instigated and neurological procedures to be carried out.

Compatibility with infusion fluids: Oradexon-Organon Injection is compatible with the following i.v. fluids:

Dextrose 2.5% to 10% in water or normal saline or half-strength saline, invert sugar 5% or 10% in water or saline, lactated Ringer's injection, Ringer's injection, sodium chloride injection, sodium lactate (1/6M) injection.

Product licence number 0065/5013.

ORADEXON – ORGANON* TABLETS

Presentation Tablets of Dexamethasone BP. Round, flat, white tablets: 0.5 mg strength code-marked 'XC4', and 2 mg strength 'XC8', with 'Organon' and a star on reverse side.

Active ingredient: Dexamethasone BP 0.5 mg and 2 mg.

Uses Dexamethasone has powerful anti-inflammatory and anti-allergic properties and is indicated in a wide variety of disorders amenable to glucocorticoid therapy, as well as in the control of cerebral oedema. Dexamethasone has little mineralocorticoid activity and therefore has little influence on electrolyte metabolism. It is consequently not indicated in adrenal replacement therapy.

Dosage and administration *Adults:* In acute and chronic conditions 4 mg daily or more may initially be given if necessary; the dose is reduced to the minimum sufficient to control symptoms and signs of disease. Before terminating treatment the daily dose should be gradually reduced. A daily maintenance dose of 0.5–1.5 mg should be sufficient in most chronic diseases. In cerebral oedema daily doses of the order of 6–8 mg are usually appropriate.

Children: The usual daily dose is in the range of 0.01–0.04 mg/kg body weight.

Dosage of corticosteroids should be adjusted on the basis of the individual patient response.

Contra-indications, warnings, etc

Contra-indications: Systemic corticosteroids are generally contra-indicated in patients with Cushing's Syndrome, gastro-intestinal ulcers, systemic fungal infections or acute bacterial or viral infections, particularly ocular herpes infections, active tuberculosis and acute psychosis.

When pregnancy is present or suspected, the benefits of the use of corticosteroids should be weighed against the possible hazards to the foetus.

While on corticosteroid therapy, patients should not be vaccinated against smallpox. Other immunisation procedures should be undertaken under close observation as corticosteroid therapy may interfere with active immunisation due to the immuno-suppressive effects of corticosteroids.

Precautions and warnings:

Patients currently on corticosteroid therapy or those who have been on such treatment within the previous year may require special control measures if involved in anaesthesia, surgical procedures and other stress. These special control measures usually involve increased dosage of rapidly-acting corticosteroids and are indicated before, during and after the stressful situation.

Withdrawal of corticosteroids should always be gradual and related to the duration of use and should be carried out under strict medical supervision. Withdrawal may result in acute rebound exacerbation of disease, acute adrenocortical insufficiency, polyarteritis.

The use of corticosteroids in the presence of other disorders (e.g. diabetes mellitus, tuberculosis, amoebiasis, osteoporosis, a history of mental disorders, cardiomyopathy, hypertension, and renal insufficiency) or of drugs with specific actions (e.g. hypoglycaemics), impinging on the effects of corticosteroids may result in imbalance of control.

Corticosteroid administration will result in certain effects, the severity, significance and extent of which, vary with the dosage and duration of treatment and the particular corticosteroid used. These include disturbance in electrolyte balance, mineral metabolism, glucose metabolism and gluconeogenesis, nitrogen depletion, diminished lymphoid tissue and immune response, inhibition of pituitary function, Cushingoid Syndrome, increase in blood coagulability, diminished inflammatory response.

Growth and development of children on prolonged corticosteroid therapy should be carefully observed (see 'adverse reactions').

Corticosteroid therapy is non-specific, suppresses the symptoms and signs of disease, and enhances susceptibility to infections; appropriate antimicrobial therapy should accompany corticosteroid therapy when necessary.

Corticosteroids appear in breast milk in very small quantities. Mothers taking high doses of corticosteroids should be advised not to breast feed.

Interactions: Concomitant use of corticosteroids and diuretics may result in an enhanced potassium loss.

Concurrent administration of liver enzyme inducing drugs such as rifampicin,ephedrine, barbiturates, phenylbutazone or phenytoin may decrease corticosteroid effects, while if anticoagulants are given with the

corticosteroid, adjustment of dosage of the former is usually necessary.

Salicylates should be used cautiously in conjunction with corticosteroids in hypoprothrombinaemia.

If patients undergoing long term therapy with corticosteroids are concomitantly given salicylates, any reduction in corticosteroid dosage should be made with caution, since cases of salicylate intoxication under these conditions have been reported.

Antacids, especially those containing magnesium trisilicate, have been reported to impair the gastrointestinal absorption of corticosteroids. Therefore doses of one agent should be spaced as far as possible from the other.

Adverse reactions: Adverse reactions associated with short-term corticosteroid therapy in high doses are uncommon.

The major adverse reactions with prolonged corticosteroid therapy are: peptic ulcers, acute pancreatitis, hypokalaemia, suppression of growth in children, CNS effects (ranging from euphoria to frank psychotic manifestations), suppression of ACTH secretion and decreased reactive ability of the adrenal cortex, osteoporosis, ocular effects, negative nitrogen and calcium balance, atrophy of the skin, impaired wound healing, myopathy, diabetogenic effect, sodium and water retention (oedema), hypertension, and development of a Cushingoid state (e.g. 'moon-face', striae, 'central obesity', 'buffalo hump', supraclavicular fat pads, acne, hirsutism).

Pseudotumor cerebri (benign increased intracranial pressure) has been reported in some children receiving systemically administered corticosteroids for prolonged periods; vomiting and papilloedema tend to subside with reduction of dosage.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities *Oradexon-Organon 0.5 mg tablets:* Bottles of 500.

Oradexon-Organon 2 mg tablets: Bottles of 100 and 500.

Further information As Oradexon-Organon (dexamethasone) has little mineralocorticoid activity and there is minimal fluid retention, it is particularly suitable where increased blood pressure is to be avoided.

Product licence numbers

0.5 mg 0065/5044

2 mg 0065/5045

OVESTIN*

Presentation Round, flat, white tablets, diameter 8 mm, code-marked 'DG4' on one side, with 'Organon' and star on the reverse.

Active ingredient: Oestriol 0.25 mg per tablet.

Uses Oestriol is a naturally-occurring oestrogen with a selective action on the cervix and vagina; unlike most other oestrogenic hormones, oestriol has in therapeutic dosages relatively little proliferative effect on the endometrium, so that uterine bleedings occur only rarely.

Ovestin tablets are mainly indicated for the treatment of vaginal and cervical disorders and, in higher dosages, also for the treatment of symptoms of oestrogen deficiency, where they occur before or after the menopause.

Dosage and administration Initially 1 or 2 tablets, reducing to 1 tablet daily.

Contra-indications, warnings, etc

Contra-indications: Thrombophlebitis, thrombo-embolic processes, or a history of these conditions.

Known or suspected oestrogen-dependent tumours, e.g. mammary, genital carcinoma.

Undiagnosed irregular vaginal bleeding.

Acute or chronic liver disease or history of liver disease where the liver function tests have failed to return to normal. Jaundice or history of jaundice in pregnancy. Rotor syndrome or Dubin-Johnson syndrome.

N.B. The use of oestrogens is not contra-indicated in patients with a history of hepatitis whose liver functions are normal.

Porphyria.

Cerebrovascular or cardiovascular disease.

Hyperlipoproteinaemia, especially in the presence of other risk factors which may indicate a predisposition to cerebrovascular or cardiovascular disorders.

A history during pregnancy of severe pruritus, herpes gestationis or a deterioration or otosclerosis.

Endometriosis.

Pregnancy or suspected pregnancy.

Precautions and warnings: Pregnancy must be excluded before treatment is started. Whenever there is a reason to suspect pregnancy during treatment, this possibility must be investigated by the physician. If pregnancy has been confirmed, tablet-intake must be discontinued immediately.

Physical examination should precede the prescribing of any oestrogen and should be repeated regularly. Special attention should be paid to duration of the cycle, body weight, blood pressure, heart, breasts, pelvic organs, legs and skin.

A cervical smear should be taken at regular intervals.

If any signs of thrombo-embolic processes occur, treatment should be discontinued immediately.

Oestrogen preparations may increase the risk of thrombosis and this should be taken into account when surgery is to be performed in patients using these preparations. Where possible, oestrogens should be discontinued approximately six weeks prior to elective surgery and not recommenced until the patient has recovered and is mobile.

Pre-existing uterine fibromyomata may increase in size under the influence of oestrogens, and if this is observed administration of the preparation should be discontinued.

Since the glucose tolerance may diminish during the use of oestrogens, diabetic patients should be monitored closely.

Prolonged exposure to unopposed oestrogens may increase the risk of the development of endometrial carcinoma.

Patients with myocardial or renal disease, varicose veins, epilepsy, migraine or asthma, require careful monitoring since sodium and water retention has been observed during continued use of oestrogens.

Since oestrogen preparations may cause an increase in blood pressure in predisposed patients, this should be checked regularly. In case of serious hypertension, further administration of the preparation must be withheld.

Patients wearing contact lenses should be advised that they may experience some discomfort.

Because oestrogens may accelerate epiphyseal closure, they should be used judiciously in those young patients in whom bone growth is not yet complete.

Prolonged or excessive dosage of oestrogens inhibits pituitary function and on cessation of treatment, severe withdrawal bleeding may occur.

Adverse reactions: Adverse reactions are rare and only appear if the dosage is too high or treatment is prolonged. These include nausea and vomiting, headache, sodium and water retention, breast tenderness, menstrual disturbances, uterine bleeding (during or on withdrawal of therapy) and psychotic disturbances.

Symptoms such as sudden severe headaches, pains in the chest, visual disturbances, or swelling of the arms or legs require immediate medical examination.

Interactions: Concurrent administration of liver enzyme inducing drugs such as rifampicin, barbiturates, phenylbutazone or phenytoin may decrease the effect of Ovestin.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Bottles of 100 tablets.

Further information Nil.

Product licence number 0065/5049.

PREGNYL*

Presentation Pregnyl contains purified chorionic gonadotrophin prepared from the urine of pregnant women. Ampoules containing a white, freeze-dried plug, with 1 ml ampoules of solvent.

Active ingredient: Chorionic Gonadotrophin BP 500 i.u., 1,500 i.u. or 5,000 i.u. After addition of the solvent to the freeze dried substance, the solution should be used immediately.

Uses Chorionic gonadotrophin has physiological activity similar to that of the luteinising hormone of the anterior pituitary gland. It induces ovulation in the FSH-primed ovary, and facilitates corpus luteum formation; in the male, it stimulates the interstitial tissue of the testes to produce testosterone. The action of Pregnyl is identical with the stimulus which determines prenatal descent of the testes; when underdevelopment is associated with undescended testes, Pregnyl accelerates growth and development. Indicated in the female for anovulatory sterility and secondary amenorrhoea; in males, for undescended testes, ectopic testes requiring operation and delayed pubertal growth.

Dosage and administration *Adults: Anovulatory sterility:* 500 i.u. Serum Gonadotrophin BP intramuscularly daily from fifth to fourteenth day of cycle, followed by 5,000 i.u. Pregnyl intramuscularly daily from fifteenth to twenty-fourth day of cycle. If there is no response to the first course of injections, after one month a further course should be given with doubled dosage.

Secondary amenorrhoea: 3,000 i.u. Serum Gonadotrophin BP intramuscularly daily for five days, followed by three injections of 1,500 i.u. Pregnyl intramuscularly on alternate days. This course of treatment should be repeated for two or three cycles; menstruation will normally occur 8 to 12 days after the last injection in each course of treatment.

Undescended testes (in males over 17 years of age): 1,000 i.u. intramuscularly twice weekly; treatment should be continued for one or two months after testicular descent.

Ectopic testes requiring operation: Pre-medication with Pregnyl for one or two months before surgery ensures optimal blood supply and elasticity: 500 i.u. intramuscularly two or three times weekly.

Children: Undescended testes: 500 i.u. intramuscularly three times weekly; Pregnyl treatment should be continued for one or two months after testicular descent.

Delayed pubertal growth: 500 i.u. intramuscularly twice weekly for four to six weeks; if necessary, the course of treatment may be repeated later.

Contra-indications, warnings, etc

Contra-indications: Known or suspected androgen-dependent tumours, carcinoma of the prostate or mammary carcinoma in males.

Precautions and warnings: Evidence of sexual precocity is an indication for the immediate withdrawal of treatment. However after regression of undue development, therapy on a reduced dosage regime may be resumed in those cases in which continuation of therapy is necessary.

Patients with myocardial or renal dysfunction, epilepsy or migraine require careful monitoring, since fluid retention has been observed after administration of high dosages of HCG.

When treating anovulatory infertility by administration of an FSH-preparation followed by HCG, the stimulation of the ovaries by the FSH-preparation may give rise to excessive oestrogen levels. In such cases HCG should not be administered, since there is a risk of inducing multiple pregnancy or the ovarian hyperstimulation syndrome.

If pregnancy follows treatment with FSH and HCG preparations, the possibility of a multiple pregnancy is greater than normal.

Patients with a known allergic diathesis should be given an intradermal skin test prior to commencement of treatment with Pregnyl.

Adverse reactions: Administration of high HCG dosages may occasionally lead to development of oedema in males; this is usually regarded as a manifestation of sodium and water retention attributable to androgen secretion resulting from stimulation of the Leydig cells. Dosage should be considerably reduced in such cases.

Pharmaceutical precautions Protect from the light and store at a temperature not exceeding 20°C. In the dry state, in sealed containers, Pregnyl will retain its full activity for three years from the date of manufacture. Solutions are unstable and should be used freshly prepared.

Legal category POM.

Package quantities Boxes containing 12 ampoules of freeze-dried Chorionic Gonadotrophin BP 500 i.u., 1,500 i.u. or 5,000 i.u., with twin 1 ml ampoules of solvent.

Further information It is generally considered that active intervention should be instituted if a testis has not descended by the age of six years. If descent is not accomplished by using chorionic gonadotrophin, surgery is indicated. Prior use of chorionic gonadotrophin may, however, increase vascularity and reduce tissue friability of the surgical field.

Product licence numbers

500 i.u. 0065/5077

1,500 i.u. 0065/5078

5,000 i.u. 0065/5079

SUSTANON '100'

Presentation A clear, oily solution in 1 ml ampoules, each containing:

Testosterone Propionate BP	20 mg
Testosterone Phenylpropionate BP	40 mg
Testosterone Isocaproate	40 mg

Uses Sustanon is a combination of testosterone esters for intramuscular injection, with an extended duration of action. Indicated, in the male, for the treatment of the climacteric, delayed puberty, eunuchism, eunuchoidism, hypogonadism and impotence due to testicular insufficiency. Sustanon is also indicated in certain inoperable mammary carcinomas in the female.

Dosage and administration Sustanon '100' should only be administered by deep injection into the gluteus maximus muscle.

Adults: Generally, 1 ml Sustanon '100' every two weeks. In some conditions, e.g. mammary carcinoma, higher doses or increased frequency of injection may be necessary.

Contra-indications, warnings, etc

Contra-indications: Contraindicated in pregnancy and in cases of mammary or prostatic carcinoma in males.

Precautions and warnings: Hypercalcaemia or hypercalciuria may develop either spontaneously or as a result of hormonal therapy in patients with certain tumours especially mammary carcinoma, hypernephroma and bronchial carcinoma. If hypercalcaemia or hypercalciuria develop during such treatment the preparation should be discontinued and appropriate measures taken to normalise calcium levels.

Androgens should be used with great caution in patients with myocardial, renal or hepatic dysfunction, epilepsy, migraine or hypertension, since sodium and water retention may occur.

In treating males, stimulation to the point of increasing nervous, mental and physical activities beyond the patient's cardiovascular capacities should be avoided. If priapism or other signs of excessive sexual stimulation develop, therapy should be discontinued.

Androgens may reduce thyroxine-binding globulin and PBI levels without inducing clinical hypothyroidism; the significance of this is unknown.

Administration to patients with nephrotic syndrome should be avoided.

Androgens should be used cautiously in young boys to avoid possible premature epiphyseal closure or precocious sexual development.

Androgen therapy should only be used in male hypogonadism in which testosterone levels have been demonstrated to be low.

Adverse reactions: Sustanon '100', like any other androgen therapy, may give rise to the following adverse reactions:

- priapism and other signs of excessive sexual stimulation.
- phallic enlargement and increased frequency of erection in pre-pubertal males.
- sodium and water retention after prolonged administration of very high dosages.
- oligospermia and a decreased ejaculatory volume after prolonged administration of very high dosages.
- virilisation (e.g. hoarseness of the voice, acne, hirsutism) enlarged clitoris and stimulation of libido.
- menstrual irregularities in female patients.

Treatment should be interrupted until these symptoms have disappeared, after which it should be continued at a lower dosage.

Hoarseness of the voice may be the first symptom of vocal change which may lead to irreversible lowering of the voice. If signs of virilisation, particularly lowering of the voice, develop, treatment should be discontinued.

Interactions: Concurrent administration of liver enzyme inducing drugs such as rifampicin, barbiturates, phenylbutazone or phenytoin may decrease the effect of Sustanon '100'.

Pharmaceutical precautions Protect from light. Store at room temperature (15° to 25°C). After storage at lower temperatures precipitation of the arachis oil vehicle may occur. By heating the ampoules at 100°C for a few minutes or at 40°C for one hour the solution will become clear. The precipitation and rewarming does not affect the activity of the injection.

Legal category POM.

Package quantities 1 ml ampoules in boxes of 3.

Further information Sustanon is the ideal parenteral preparation for long-term androgen therapy; no single testosterone ester can provide the same sustained level of androgenic activity and rapid onset of action. The prolonged activity is such that only an occasional injection is needed to maintain the required therapeutic level.

Product licence number 0065/5019.

SUSTANON '250'

Presentation A clear, oily solution in 1 ml ampoules each containing:

Testosterone Propionate BP	30 mg
Testosterone Phenylpropionate BP	60 mg
Testosterone Isocaproate	60 mg
Testosterone Decanoate	100 mg

Uses Sustanon is a combination of testosterone esters for intramuscular injection, with an extended duration of action. Indicated, in the male, for the treatment of the climacteric, delayed puberty, eunuchism, eunuchoidism, hypogonadism, and impotence due to testicular insufficiency. Sustanon is also indicated in certain inoperable mammary carcinomas in the female.

Dosage and administration Sustanon 250 should only be administered by deep injection into the gluteus maximus muscle.

Adults: Generally, 1 ml Sustanon 250 every four weeks. In some conditions, e.g. mammary carcinoma, higher doses or increased frequency of injection may be necessary.

Contra-indications, warnings, etc

Contra-indications: Contraindicated in pregnancy and in cases of mammary or prostatic carcinoma in males.

Precautions and warnings: Hypercalcaemia or hypercalciuria may develop either spontaneously or as a result of hormonal therapy in patients with certain tumours, especially in mammary carcinoma, hypernephroma and bronchial carcinoma. If hypercalcaemia or hypercalciuria develop during such treatment, the preparation should be discontinued and appropriate measures taken to normalise calcium levels.

Androgens should be used with great caution in patients with myocardial, renal or hepatic dysfunction, epilepsy, migraine or hypertension, since sodium and water retention may occur.

In treating males, stimulation to the point of increasing nervous, mental and physical activities beyond the patient's cardiovascular capacities should be avoided. If priapism or other signs of excessive sexual stimulation develop, therapy should be discontinued.

Androgens may reduce thyroxine-binding globulin and PBI levels without inducing clinical hypothyroidism; the significance of this is unknown.

Administration to patients with nephrotic syndrome should be avoided.

Androgens should be used cautiously in young boys to avoid possible premature epiphyseal closure or precocious sexual development.

Androgen therapy should only be used in male hypogonadism in which testosterone levels have been demonstrated to be low.

Adverse reactions: Sustanon 250, like any other androgen therapy, may give rise to the following adverse reactions.

- Priapism and other signs of excessive sexual stimulation.
- phallic enlargement and increased frequency of erections in prepubertal males.
- sodium and water retention after prolonged administration of very high dosages.
- oligospermia and a decreased ejaculatory volume after prolonged administration of very high dosages.
- virilisation (e.g. hoarseness of the voice, acne, hirsutism) enlarged clitoris and stimulation of libido.
- menstrual irregularities in female patients.

Treatment should be interrupted until these symptoms have disappeared, after which it should be continued at a lower dosage.

Hoarseness of the voice may be the first symptom of vocal change which may lead to irreversible lowering of the voice. If signs of virilisation, particularly lowering of the voice, develop, treatment should be discontinued.

Interactions: Concurrent administration of liver enzyme inducing drugs such as rifampicin, barbiturates, phenylbutazone or phenytoin may decrease the effect of Sustanon 250.

Pharmaceutical precautions Protect from light. Store at room temperature (15° to 25°C). After storage at lower temperatures precipitation of the arachis oil vehicle may occur. By heating the ampoules at 100°C for a few minutes or at 40°C for one hour the solution will become clear. The precipitation and rewarming does not affect the activity of the injection.

Legal category POM.

Package quantities 1 ml ampoules in boxes of 3.

Further information Sustanon is the ideal parenteral preparation for long-term androgen therapy; no single testosterone ester can provide the same sustained level of androgenic activity and rapid onset of action. The prolonged activity is such that only an occasional injection is needed to maintain the required therapeutic level.

Product licence number 0065/5086.

TESTORAL SUBLINGS*

Presentation Testosterone BP sublingual tablets Round, bi-convex, white to creamy-white tablets, diameter 8 mm, code-marked with a 'T' surrounded by 'Subling' on one side, with 'Organon' and a star on the reverse side.

Active ingredient: Testosterone BP 10 mg per tablet.

Uses The male hormone, testosterone, although inactivated when swallowed, can be absorbed directly through the buccal mucosa. Sublings should be placed under the tongue or between cheek and gum. Indicated for androgen replacement therapy.

Dosage and administration For androgen replacement therapy, 1-3 Sublings daily, reducing to 1 daily for as long as necessary.

Contra-indications, warnings, etc

Contra-indications: Mammary or prostatic carcinoma in males.

Precautions and warnings: Testosterone should be used with great caution in patients with myocardial, renal or hepatic dysfunction, epilepsy, migraine or hypertension since androgens may cause sodium and water retention.

Stimulation to the point of increasing nervous, mental and physical activities beyond the patient's cardiovascular capacities should be avoided. If priapism or other signs of excessive sexual stimulation develop, therapy should be discontinued.

Androgens may reduce thyroxine-binding globulin and PBI levels without inducing clinical hypothyroidism; the significance of this is unknown.

If hypercalcaemia or hypercalciuria develop, treatment should be discontinued.

Administration to patients with nephrotic syndrome should be avoided.

Androgens should be used cautiously in young boys to avoid possible premature epiphyseal closure or precocious sexual development.

Androgen therapy should only be used in male hypogonadism in which testosterone levels have been demonstrated to be low.

Adverse reactions: Testoral Sublings, like any other androgen therapy, may give rise to the following adverse reactions:

- priapism and other signs of excessive sexual stimulation.
- phallic enlargement and increased frequency of erections in prepubertal males.
- sodium and water retention after prolonged administration of very high dosages.
- oligospermia and a decreased ejaculatory volume after prolonged administration of very high dosages.

Treatment should be interrupted until these symptoms have disappeared, after which it should be continued at a lower dosage.

Hoarseness of the voice may be the first symptom of vocal change which may lead to irreversible lowering of the voice. If signs of virilisation, particularly lowering of the voice, develop, treatment should be discontinued.

Interactions: Concurrent administration of liver enzyme inducing drugs such as rifampicin, barbiturates, phenylbutazone or phenytoin may decrease the effect of Testoral Sublings.

Overdosage: Treatment of overdosage is by gastric lavage with appropriate supportive therapy.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Bottles of 100 tablets.

Further information Sublings provide testosterone in smooth-texture tablets, specially prepared for sublingual absorption.

Product licence number 0065/5051.

TESTOSTERONE IMPLANTS

Presentation Pellets of fused, crystalline hormone for implantation.

Active ingredient: Testosterone BP 100 mg or 200 mg, each with a diameter of 4.5 mm.

Uses Implantation of fused implants of testosterone provides slow release of the hormone; approximate duration of effect: 100 mg – 30 weeks; 200 mg – 34 weeks. Indicated for conditions requiring maintenance therapy with androgens, i.e. in the male, castration, climacteric, eunuchoidism, deficient libido, hypogonadism: in the female, deficient libido, mammary fibroadenosis and mammary carcinoma.

Dosage and administration *Adults: Male:* 200–600 mg depending on individual requirements.

Female: Deficient libido, 100 mg; mammary fibroadenosis, 100 mg or 200 mg; mammary carcinoma, 500 – 1,500 mg.

Implants are inserted, either by means of a trocar and cannula or by open surgery, into an area where there is comparatively little movement, such as the lower abdominal wall or the buttock. Insertion is made under local anaesthetic and the wound is closed either with an adhesive dressing or a fine suture.

Whichever method is used for the insertion of implants, the following principles apply:

1. Full aseptic 'no touch' technique should be adopted.
2. Precautions should be taken to avoid the formation of haematoma at the site.
3. The rate of absorption of the active ingredient depends on the surface area of the implant. Thus the daily rate of absorption can be increased by supplying the total dosage in a number of separate implants each sited on a separate track.

Frequency of replacement depends on the duration of activity of the implants administered.

Contra-indications, warnings, etc

Contra-indications: Contra-indicated in pregnancy, and in cases of mammary or prostatic carcinoma in males.

Precautions and warnings: Hypercalcaemia or hypercalciuria may develop either spontaneously or as a result of hormonal therapy in patients with certain tumours especially in mammary carcinoma, hypernephroma and bronchial carcinoma. If hypercalcaemia or hypercalciuria develop during such treatment the preparation should be discontinued and appropriate measures should be taken to normalise calcium levels.

Androgens should be used with great caution in patients with myocardial, renal or hepatic dysfunction, epilepsy, migraine or hypertension, since sodium and water retention may occur.

Stimulation to the point of increasing nervous, mental and physical activities beyond the patient's cardio-

vascular capacities should be avoided. If priapism or other signs of excessive sexual stimulation develop, therapy should be discontinued.

Androgens may reduce thyroxine-binding globulin and PBI levels without inducing clinical hypothyroidism; the significance of this is unknown.

Administration to patients with nephrotic syndrome should be avoided.

Androgens should be used cautiously in young boys to avoid possible premature epiphyseal closure or precocious sexual development.

Androgen therapy should only be used in male hypogonadism in which testosterone levels have been demonstrated to be low.

Adverse reactions: Testosterone Implants, like any other androgen therapy, may give rise to the following adverse reactions.

- priapism and other signs of excessive sexual stimulation.
- phallic enlargement and increased frequency of erections in prepubertal males.
- sodium and water retention after prolonged administration of very high dosages.
- oligospermia and a decreased ejaculatory volume after prolonged administration of very high dosages.
- virilisation (e.g. hoarseness of the voice, acne, hirsutism) enlarged clitoris and stimulation of libido.
- menstrual irregularities in female patients.

Treatment should be interrupted until these symptoms have disappeared, after which it should be continued at a lower dosage.

Hoarseness of the voice may be the first symptom of vocal change which may lead to irreversible lowering of the voice; if signs of virilisation, particularly lowering of the voice, develop, treatment should be discontinued.

Interactions: Concurrent administration of liver enzyme inducing drugs such as rifampicin, barbiturates, phenylbutazone or phenytoin may decrease the effect of Testosterone Implants.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Each sterile implant is supplied singly, in a sealed glass tube. Available in 100 mg and 200 mg weights.

Further information Nil.

Product licence numbers

100 mg 0065/5083

200 mg 0065/5084

TETRABID-ORGANON*

Presentation Hard gelatin capsules (purple cap/yellow body).

Active ingredient: Each capsule contains Tetracycline Hydrochloride 250 mg.

Uses Tetrabid-Organon is a sustained-action tetracycline formulation which requires only half the daily dose and half the frequency of administration of conventional tetracycline. Indicated for the treatment of all infections caused by organisms sensitive to tetracycline, bronchitis and for the treatment and prophylaxis of acute exacerbations of chronic bronchitis. Tetrabid-Organon is also indicated in the treatment of acne vulgaris.

Dosage and administration *Adults and children over 12 years:* Two capsules initially, followed by one capsule every 12 hours. For more severe infections, dosage may be increased at the discretion of the physician. Treatment should continue for at least two or three days after achievement of the desired clinical response, and should continue for at least two months in the prophylaxis of acute exacerbations of chronic bronchitis.

In the treatment of acne vulgaris: One capsule daily for at least three months.

Capsules should preferably be taken one hour before, or two hours after meals.

Contra-indications, warnings, etc

Contra-indications: Contra-indicated in patients with a history of tetracycline sensitivity, pregnancy (unless specifically indicated by bacterial sensitivity tests and where the risk involved is justified) and during lactation. Tetrabid-Organon should not be administered to children under seven years of age.

Precautions and warnings: Tetracycline should be administered with caution in patients with renal or hepatic impairment; a reduction of the dosage or a greater interval between the administration of the capsules may be indicated.

Tetracycline is selectively taken up in developing bones and teeth of foetus and children, causing dental staining and enamel hypoplasia.

Broad-spectrum antibiotic therapy may result in overgrowth of non-susceptible organisms. If such superinfection should occur the antibiotic therapy should be discontinued and appropriate measures taken.

In long-term therapy, laboratory monitoring of certain functions (including haemopoietic, renal and hepatic studies) should be performed.

Adverse reactions: Skin photosensitivity reactions are occasionally observed in patients on tetracycline therapy. Treatment should be discontinued at the first evidence of skin erythema.

The incidence of adverse reactions such as nausea, vomiting and diarrhoea, is low.

Interactions: Antacids, iron haematinics and zinc sulphate have been reported to impair the intestinal absorption of tetracycline. Therefore doses of one preparation should be spaced as far as possible from the other.

Concurrent use of milk products interferes with absorption of tetracyclines to a variable degree, and should be avoided.

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, it is advisable to avoid administering tetracycline in conjunction with penicillin.

In general, the physician should be aware that interactions may occur when tetracycline is administered concomitantly with various drugs. In addition, tetracycline has been reported to interfere with some diagnostic tests.

Because the tetracyclines have been shown to depress plasma prothrombin activity, patients who are on anticoagulant therapy may require a reduction of their anticoagulant dosage.

Pharmaceutical precautions Store at a temperature below 30°C and in dry conditions. Capsules should not be used after the expiry date shown on the pack.

Legal category POM.

Package quantities Securitainer of 100 or 500 capsules.

Further information Twice-daily Tetrabid-Organon provides economical tetracycline therapy with a reduced incidence of side-effects. The formulation allows sustained release of tetracycline throughout the gastrointestinal tract and Fumaric Acid (33 mg) provides a localised low pH environment at the point of release which favours increased absorption.

Product licence number 0065/0028.

TRISEQUENS* ▼

Presentation Trisequens is supplied in a calendar dial-pack of 28 sequential tablets as follows:

(a) 12 blue biconvex tablets marked NOVO 270 on one side, blank on the other side, with a diameter of 6 mm, each containing 2 mg oestradiol and 1 mg oestriol.

(b) 10 white biconvex tablets, marked NOVO 271 on one side, blank on the other side, with a diameter of 6 mm each containing 2 mg oestradiol, 1 mg oestriol and 1 mg norethisterone acetate BP.

(c) 6 red biconvex tablets, marked NOVO 272 on one side, blank on the other side, with a diameter of 6 mm, each containing 1 mg oestradiol and 0.5 mg oestriol.

Uses Indicated for the treatment of symptoms due to oestrogen deficiency.

Dosage and administration Trisequens is administered orally, one tablet daily without interruption. Regular withdrawal bleeding will become established, usually during the administration of the low-oestrogen tablets, i.e. the 6 red tablets or possibly even during the last phase of the white tablets. In menstruating women, the first tablet should be taken on the fifth day of bleeding. Patients with menorrhagia or metrorrhagia should be curettaged and the first tablet taken on the fifth day afterwards. Patients with oligomenorrhoea may start therapy on the fifth day of bleeding or in cases of very long intervals between bleeding, therapy may commence at any time. Other patients may start at any time.

Contra-indications, warnings, etc

Contra-indications:

1. Known or suspected mammary or genital carcinoma.
2. Known or suspected oestrogen-dependent tumours.
3. Thrombophlebitis, thromboembolic disorders, or patients with a past history of these conditions.
4. Undiagnosed irregular vaginal bleeding.
5. Acute or chronic liver disease or history of liver disease where the liver function tests have failed to return to normal. Jaundice or history of jaundice in pregnancy. Rotor syndrome or Dubin-Johnson syndrome.
6. Haemoglobinopathies or sickle-cell anaemia.
7. Porphyria.
8. Hyperlipoproteinaemia, especially in the presence of other risk factors which may indicate a predisposition to cardiovascular or cerebrovascular disorders.
9. Pregnancy or suspected pregnancy.
10. A history during pregnancy of severe pruritus, herpes gestationis or a deterioration of otosclerosis.
11. Existing cerebrovascular or cardiovascular disease.

Precautions and Warnings: Before the initiation of therapy with Trisequens, it is advisable to undertake a thorough examination to exclude any possibility of genital or mammary tumours. A similar examination is

advisable at regular intervals throughout therapy, e.g. every 6 months. Special attention should be paid to duration of the cycle, body weight, blood pressure, heart, breasts, pelvic organs, legs and skin.

There is some evidence that obesity and possibly hypertension or diabetes mellitus, are predisposing factors to endometrial carcinoma. In view of this, special care should be taken in the presence of these conditions and also if a family history of endometrial carcinoma is present.

Patients with epilepsy, migraine, diabetes, asthma or cardiac dysfunction should be carefully controlled as oestrogens may worsen these conditions.

The indications for immediate withdrawal of therapy are as follows: thrombophlebitis, thromboembolic disorders, the appearance of jaundice, the occurrence of migraine-like headaches, sudden visual disturbances, or a significant increase in blood pressure. It is also advisable to withdraw treatment 6 weeks before elective surgery and during prolonged periods of immobilisation.

If abnormal irregular bleeding occurs during therapy diagnostic aspiration biopsy or curettage should be performed to rule out the possibility of uterine malignancy. (See also Dosage and Administration.)

Treatment may be stopped at approximately 6–12 monthly intervals to establish whether continued therapy is still required.

Trisequens has no contraceptive effect.

A decreased glucose tolerance may occur in diabetic patients on this treatment, and their control must be carefully supervised.

Studies in animals have indicated that administration of very high doses of oestrogen and/or progestogens will induce neoplastic tumours in some animal species. The relevance to man is unknown.

The results of recent studies in human beings suggest that there is a small but statistically increased incidence of endometrial carcinoma and of mammary carcinoma in women who have been receiving oestrogens in *high daily dosage over a prolonged period*. Combination with progestogen is not shown to be associated with an increased risk of endometrial carcinoma or mammary carcinoma.

Studies in animals, in particular the dog, have demonstrated that the progestogens including progesterone will induce neoplastic mammary tumours. Recent investigations suggest that results of dosing studies with progestogen in the dog are irrelevant to the potential for such effects in human beings, because of differences in mammary receptor susceptibility and responses.

Pre-existing uterine fibromyomata may increase in size under the influence of oestrogens and if this is observed administration of the preparation should be discontinued.

Side effects: There has only been a low incidence of side effects. Nausea occurs only rarely and oedema is infrequent. Breast tenderness or bleeding irregularities may occur especially during the first few months of treatment. Changes in weight may be seen, but the clinical evidence shows no clear tendency towards either weight increase or decrease. Blood pressure remains unchanged or shows a slight decrease during therapy.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Trisequens is supplied in a calendar dial-pack of 28 tablets.

Further information Total plasma oestrogen levels are restored thus causing a decrease or complete disappearance of subjective oestrogen deficiency symptoms. Suppression of subjective symptoms such as vasomotor disturbances and psychogenic disorders may primarily be ascribed to the oestradiol component. The anatrophy effects on the cervix and vagina may be ascribed both to the oestriol and oestradiol component.

A regular withdrawal bleeding is established with Trisequens due to the addition of norethisterone acetate in the second series of (white) tablets which induce a change in the endometrium to a secretory phase, followed by endometrial shedding usually during the third series of (red) tablets. The low oestrogen contents in the last series of tablets prevent the reappearance of symptoms without affecting withdrawal bleeding.

Product licence number 0065/0065.

***Trade Mark**



PAVULON®

Presentation Pancuronium bromide BP 2 ml ampoules. A clear, aqueous solution. Active ingredient: Each 2 ml ampoule contains pancuronium bromide BP 4 mg. Other ingredients: sodium chloride BP 16 mg, acetate buffers to pH 4, 1% benzyl alcohol.

Uses Pavulon is a neuromuscular blocking agent of the non-depolarising type with a medium duration of action. It is used as an adjuvant in surgical anaesthesia to obtain relaxation of the skeletal muscles in a wide range of surgical procedures.

Pavulon is also used for neuromuscular blockade during intensive care therapy for a variety of pathologies, including intractable status asthmaticus and tetanus. Pavulon is the relaxant of choice when other muscle relaxants might be inappropriate, e.g. shock, allergy, renal and hepatic insufficiency.

Dosage and administration Pavulon is usually administered by intravenous injection (but see recommendations for use in the intensive care patient, below). When calculating dosages of neuromuscular blocking agents the following factors must be taken into account: the anaesthetic technique used, the anticipated duration of the operation, potential interactions with the drugs used during (and before) anaesthesia, and the condition of the individual patient. The following may be used as a general guide to dosage:

General guide to dosage:

Adult surgery: Initial dose: 0.05–0.08 mg/kg (intubation accomplished within 150–120 seconds) or 0.08–0.1 mg/kg (intubation accomplished within 120–90 seconds). Incremental doses: 0.01–0.02 mg/kg.

Child surgery: Initial dose: 0.06–0.1 mg/kg. Incremental doses: 0.01–0.02 mg/kg.

Neonatal surgery: 0.03–0.04 mg/kg intravenously. Incremental doses: As neonates are sensitive this dose should be adjusted according to the initial response but generally incremental doses lie in the range 0.01–0.02 mg/kg body weight.

Following the administration of suxamethonium:

The dosage of Pavulon may be considerably reduced –

Adult surgery: Initial dose: 0.02–0.06 mg/kg. Incremental doses: 0.01–0.02 mg/kg.

Child surgery: Initial dose: 0.02–0.06 mg/kg. Incremental doses: 0.01–0.02 mg/kg.

If the recommended doses of Pavulon are exceeded this will increase the risk of prolonged neuromuscular block, difficulties with the reversal, and marked side effects. In heavy or obese patients calculation of the dosage of Pavulon on the basis of mg/kg leads to overdosing.

Pavulon is longer-acting in the intensive-care patient, and an intravenous dose of 0.06 mg/kg every one to one and a half hours, or even less frequently, is usually

adequate. It can also be given by intramuscular injection in a dose of 0.03–0.06 mg/kg every one to two hours. Onset of effect by this route is about 10 minutes.

The duration of action depends upon the clinical condition of the patient and the dose administered, but in normal subjects receiving preoperative muscle relaxant doses the duration of action is usually 40–45 minutes.

In the control of tetanus, duration of Pavulon relaxation probably depends on the severity of the spasm: duration of effect can therefore be variable.

Pavulon should not be mixed with other agents in the same syringe, or with solutions for intravenous infusion, as a change in pH may induce precipitation.

Contra-indications, warnings, etc

Contra-indications: Patients with a known hypersensitivity to Pavulon injection.

Concurrent use of a depolarising neuromuscular blocking drug e.g. suxamethonium.

Precautions and warnings: Generally speaking it is advisable to monitor the degree of neuromuscular block. Before the administration of Pavulon conditions such as electrolyte disturbance, altered pH and dehydration should if possible be corrected. Care should be exercised if there is a danger of regurgitation when intubating the patient.

Pavulon should be used with particular care in neonates, in ill or cachectic patients, in the presence of liver disease or obstructive jaundice (resistant to effects of drug) in states with altered plasma protein levels or when there is diminished renal blood flow or renal disease.

Care should be taken in patients with renal insufficiency since Pavulon is partially excreted, unchanged, in the urine.

Pavulon should be used cautiously in patients with a tendency to hypertension, as in adrenogenital syndrome, pheochromocytoma or hypertension caused by renal disease.

Extreme caution should be exercised, and very small doses used, in patients with myasthenia gravis or myasthenic syndrome, unless it is intended to administer prolonged post-operative respiratory assistance. In cases of myopathy (such as dystrophia myotonica), severe obesity, electrolyte disturbances (e.g. excessive potassium loss), altered pH and after poliomyelitis or dehydration, Pavulon should be dosed carefully as unwanted effects may occur. In the presence of liver disease the usual dose should be administered, but in certain cases a higher dose may be required, since, in some patients, there is increased resistance to the action of non-depolarising neuromuscular blocking agents.

In operations requiring hypothermia the neuromuscular blockade of non-depolarising drugs is decreased and increases when re-warming the patient. Hypothermia in neonates, therefore, requires a reduced dosage of Pavulon.

Care should be exercised during pregnancy, particu-

larly during the first 12 weeks. Since the consequences of the use of neuromuscular blocking agents on the developing foetus are extremely difficult to assess, one should carefully consider the advantages and the risks.

Pavulon should be administered only by anaesthetists familiar with its use, and only when facilities for controlled ventilation, insufflation with oxygen and endotracheal intubation are available for immediate use.

Since Pavulon in clinically effective doses affects the respiratory muscles, as well as other skeletal muscles, respiration must be assisted in all patients. It is essential to ensure that the patient is breathing spontaneously, deeply and regularly before leaving the theatre after anaesthesia. The neuromuscular blockade achieved with Pavulon can be reversed with a cholinesterase inhibiting agent (e.g. neostigmine) in an adequate dose, together with atropine as an anticholinergic agent.

Pavulon should be used with extreme caution in patients with acid base disturbances, (particularly metabolic acidosis), or electrolyte imbalance. Hypokalaemia or hypocalcaemia may cause an increased effect.

Pavulon may cause a rise in blood pressure and this should be borne in mind when used concurrently with other agents, e.g. halothane, ketamine.

Special care should be exercised if given to the same patient more than once in 24 hours, as a cumulative effect may develop.

Patients with carcinomatosis especially when associated with bronchial carcinoma may exhibit a marked sensitivity to this agent, and the neuromuscular block produced may respond poorly to neostigmine.

Allergic reactions including bronchospasm and hypotension occur rarely with Pavulon.

Interactions: Prior to surgery and during anaesthesia a number of medicines are commonly administered to the patient. This creates the possibility of interaction. In addition, the condition of the patient may influence the neuromuscular blocking (n.m.b.) activity of Pavulon.

The following medicines and conditions of the patient may interact with the n.m.b. activity of Pavulon:

Administration of depolarising drugs (e.g. suxamethonium chloride) following a non-depolarising drug (e.g. Pavulon) is dangerous.

The non-depolarising drug increases resistance towards the neuromuscular blocking effect of the depolarising drug. Therefore high doses of a depolarising drug are necessary before muscular relaxation can be obtained. These high doses of a depolarising drug may cause endplate desensitisation and prolonged post-operative apnoea. Unlike a non-depolarising block, a depolarising block cannot be overcome by an anticholinesterase agent and may even be worsened.

Recent evidence suggests that alkylating drugs (nitrogen mustards) should be considered a possible hazard when given to patients during anaesthesia involving the use of muscle relaxants.

There is a selective interaction between Pavulon and nitroglycerin in that the latter affects the process of recovery from neuromuscular blockade. When nitroglycerin infusion precedes Pavulon injection prolongation of the blockade will occur.

Care should be taken with anaesthesia involving the use of halothane and Pavulon in patients receiving chronic tricyclic antidepressant therapy, as this predisposes to the development of cardiac arrhythmias.

Anaesthetics: The following anaesthetics may influence the neuromuscular blocking activity of Pavulon:

Increased effect: halothane, ether, enflurane, isoflurane (Forane), methoxyflurane, neurolept analgesia, cyclopropane, propanidid, thiopentone, methohexitone.

Influence on the cardiovascular system: Pavulon does not intensify the hypotension induced by halothane; in addition the cardiac depression is partly restored. The excessive bradycardia induced by neurolept analgesia and some of the cholinergic effects of morphine derivatives are counteracted by Pavulon.

The tachycardia which may be induced by Pavulon can be corrected by Hydergine.

The following drugs may influence the duration of action of Pavulon and the intensity of the neuromuscular block:

Increased effect: other muscle relaxants (e.g. d-tubocurarine), antibiotics of the polypeptide and aminoglycoside groups (e.g. neomycin, streptomycin, kanamycin), diazepam, propranolol, thiamine (high dose), M.A.O. inhibiting agents, quinidine, magnesium sulphate, narcotic analgesics, protamine, nitroglycerin.

Decreased effect: neostigmine, edrophonium, corticosteroids (high dose), adrenaline, potassium chloride, sodium chloride, calcium chloride, heparin (temporary decrease), azathioprine, theophylline.

Condition of the patient: The following conditions may influence the neuromuscular blocking activity of Pavulon:

Increased effect: Hypokalaemia (e.g. after severe vomiting, diarrhoea, digitalisation), hypermagnesaemia, hypocalcaemia (after massive transfusion), hypoproteinaemia, dehydration, acidosis, hypercapnoea, cachexia, myasthenia gravis, myasthenic syndrome, renal and liver failure, profound anaesthesia.

Decreased effect: Hypothermia, hyperdiuresis, superficial anaesthesia.

Disturbances in renal function and hypocalcaemia are factors favouring the development of a syndrome resembling that of myasthenia gravis following administration of antibiotics. A disturbed plasma protein pattern requires prudence. Pavulon (like d-tubocurarine) causes a reduction in the partial thromboplastin time and the prothrombin time.

With respect to the frequently reported interactions involving other non-depolarising neuromuscular blocking agents the anaesthetist should be aware of the possibility that similar interactions may occur with Pavulon.

Side-effects: After Pavulon a slight to moderate rise in arterial pressure may occur. Increased pulse rate and cardiac output are frequently reported, showing Pavulon to have weak vagolytic activity. In general this is considered to be a favourable effect. Pavulon decreases intra-ocular pressure and induces miosis, both effects being favourable in ophthalmic surgery. A few cases of localised reactions at the site of injection have been reported.

Overdosage: In the event of an overdosage the patient should continue to be ventilated, and at the same time receive a cholinesterase inhibiting agent (e.g. pyridostigmine, neostigmine) in an adequate dose, as an antidote.

Pharmaceutical precautions In the pharmacy, Pavulon should be stored in a refrigerator at 0-4°C and protected from light, when it will retain its stability for two years. Pavulon is stable for six weeks at 25°C.

Opened ampoules of Pavulon should be discarded if the contents are not used within a few hours.

Legal category POM.

Package quantities Boxes of 25 ampoules 2 ml.

Further information The active substance of Pavulon is pancuronium bromide, an amino steroid which effectively blocks transmission of motor nerve impulses to the striated muscle receptors. Endplate depolarisation does not occur. Pancuronium bromide has no hormonal activity. An initial dose of Pavulon of 0.08 mg/kg i.v. has a mean onset of action of 45 seconds, a maximum effect after 90–120 seconds, and a mean duration of action of 60 minutes (these data are approximations since, as is well-known, all muscle relaxants display dose-response variability). The potency ratio of Pavulon/d-tubocurarine is approximately 6–7 : 1.

Pavulon is accepted as one of the standard preparations in anaesthesia, and is widely used in all fields of

surgery. It has a smooth onset of action, extremely low toxicity and the virtual absence of such side-effects as histamine release, and although rare instances of bronchospasm have been reported Pavulon has, in general, a lack of associated bronchospasm. There is lack of ganglion blockade and thus no hypotensive effect, unlike some other muscle relaxants.

Pavulon is of considerable value when used in conjunction with halothane, since it helps to counteract the cardiovascular depression normally induced by halothane. Pavulon is particularly suitable for use in poor risk patients and in intensive-care units. Pavulon is used widely with good results in Caesarean section.

Product licence number 0065/5014.

** Trade Mark*

Ortho-Cilag Pharmaceutical Limited

PO Box 79, Saunderton
High Wycombe
Buckinghamshire HP14 4HJ.



ACI-JEL* THERAPEUTIC VAGINAL JELLY

Presentation Acetic acid 0.92% w/w in a buffered (pH 4), gel base.

Uses In any case where the restoration and maintenance of vaginal acidity is desirable, as in the treatment of non-specific vaginal infection and in the milder forms of simple cervicitis. Aci-Jel Therapeutic Vaginal Jelly is also useful as an adjunct to systemic therapy in trichomoniasis, and prophylactically after courses of other, more specific therapy.

Dosage and administration One applicatorful intravaginally in the morning and upon retiring. The frequency of the application and duration of treatment depend upon the type of case and the degree of progress.

Contra-indications, warnings, etc None known.

Overdosage: Aci-Jel Therapeutic Vaginal Jelly is intended for intravaginal use. If accidental ingestion of large quantities of the product occurs, an appropriate method of gastric emptying may be used if considered desirable.

Pharmaceutical precautions Store at room temperature.

Legal category GSL.

Package quantities Tube containing 85 g. with or without the ORTHO* Plastic Vaginal Applicator.

Further information Nil.

Product licence number 0076/5015.

BINOVOUM*

Presentation $\frac{1}{2}$ -inch diameter, circular tablets with flat faces and bevelled edges bearing the engraving  on each face. 7 white tablets each containing 0.5 mg Norethisterone BP and 35 mcg Ethinyloestradiol BP, and 14 peach coloured tablets each containing 1.0 mg Norethisterone BP and 35 mcg Ethinyloestradiol BP.

Uses Contraception and the recognised indications for such oestrogen/progestogen combinations.

Action: Through the mechanism of gonadotrophin suppression by the oestrogenic and progestational actions of the ingredients. Although the primary mechanism of action is inhibition of ovulation, alterations to the cervical mucus and to the endometrium may also contribute to the efficacy of the product.

Dosage and administration The basic dosage regimen is a 28 day cycle, of 1 tablet daily for 21 days, followed by 7 tablet-free days. A white tablet is taken every day for 7 days, then a peach coloured tablet is taken every day for 14 days. For initial therapy, the first white tablet is taken on the first day of bleeding of the menstrual cycle. If BiNovum* Tablets are first taken later

than the first day of bleeding of the first menstrual cycle of medication, contraceptive reliance should be not placed on this product until after the first 14 consecutive days of administration.

Subsequent cycles: Each subsequent course is started after 7 tablet-free days have followed the preceding course.

Changing from another combined oral contraceptive: The first white tablet should be taken on the first day of the withdrawal bleed after the completion of the previous course of tablets.

Changing from a progestogen-only contraceptive: The first white tablet should be taken on the first day of bleeding that occurs either during the last course of tablets or following completion of the tablet course.

Post-partum use: After pregnancy, oral contraception may be initiated immediately post-partum in the non-nursing patient or as soon as spontaneous menstruation has been resumed. Another method of contraception should be used in the interval between delivery and the first course of tablets, unless it is started within seven days of delivery. After a miscarriage or first-trimester abortion, oral contraception may be started immediately.

If the patient forgets more than one tablet, she should recommence the course as soon as she remembers, taking the appropriate tablet for that day and omitting any tablets delayed more than 12 hours. She should then use an additional method of contraception until the next withdrawal bleed.

If the patient has vomiting or diarrhoea, absorption of the hormones will be impaired, making it advisable to use an additional reliable method of contraception until her next menstrual period. Should a bleeding fail to occur at the usual time, the possibility of pregnancy should be excluded before starting the next pack.

Contra-indications, warnings, etc

Contraindications: Existing thrombophlebitis, thromboembolic disorders, cerebrovascular disease, myocardial infarction, or a past history of these conditions. Sickle-cell anaemia. Markedly impaired liver function. Congenital or existing disorders of lipid metabolism. Known or suspected carcinoma of the breast. Known or suspected oestrogen-dependent neoplasia. History during pregnancy of idiopathic jaundice, severe pruritus, shingles or deterioration of otosclerosis. Dubin-Johnson syndrome. Rotor syndrome. Undiagnosed abnormal genital tract bleeding. Known or suspected pregnancy.

Warnings: An increased risk of thrombophlebitis, cerebrovascular disorders, myocardial infarction and pulmonary embolism associated with the use of oral contraceptives has been reported in several retrospective case control studies. The increased risk has been estimated in these studies to be approximately 4 to 11 times higher (for cerebral haemorrhage two times higher)

for users when compared to non users. This reported risk according to two of the studies is not related to duration of use nor does it persist after discontinuance according to one of the studies. An interim report of a large scale continuing prospective study has tended to confirm these retrospective studies for thrombophlebitis and possible cerebrovascular disorders. This study also reported that the risk of superficial and deep vein thrombosis was lower in women using preparations containing 50 mcg of oestrogen or less. There may not be full recovery from such disorders and it should be realised that in a few cases they are fatal.

Because of a possible increased risk of post surgical thromboembolic complications in oral contraceptive users, therapy should be discontinued at least six weeks prior to elective surgery. Caution should be exercised in administering oestrogen/progestogen combinations to women with a history of hypertension. An increased risk of surgically confirmed gall bladder disease associated with the use of oral contraceptives has been reported in a retrospective case control study.

Liver tumours, occasionally fatal, have been reported in women using oral contraceptives. These tumours may present as an abdominal mass, intra-abdominal bleeding and/or with signs and symptoms of acute abdomen. These have been reported in short term as well as long term users of oral contraceptives.

A small fraction of the active ingredients in oral contraceptives has been identified in the milk of mothers receiving these drugs. The effects, if any, on the breast-fed child have not been determined. If possible the use of oral contraceptives should be deferred until the infant is weaned.

When women have taken hormones during pregnancy there have been some reports of the possibility of adverse effects on the developing child. A direct relationship between such effects and oral contraceptives has not been confirmed, but as with any other drug, avoidance of continuing oral contraception in early pregnancy is desirable. Therefore pregnancy should be ruled out before initiating or continuing the administration of oral contraceptives to patients who have missed one menstrual period.

Certain factors may entail some risk of thrombosis, e.g. smoking, obesity, varicose veins, cardiovascular diseases, diabetes, and migraine. The suitability of a combined oral contraceptive should be judged according to the severity of such conditions in the individual case, and should be discussed with the patient before she decides to take it. The risk of arterial thrombosis associated with combined oral contraceptives increases with age and this risk is aggravated by cigarette smoking. The use of combined oral contraceptives in women in the older age group, especially those who are cigarette smokers, should therefore be discouraged and alternative methods advised.

Reduced efficacy and increased incidence of breakthrough bleeding have been associated with concomitant use of oral contraceptives and rifampicin. A similar association has been suggested with oral contraceptives and barbiturates, phenylbutazone, phenytoin sodium and ampicillin.

Reasons for stopping oral contraceptives immediately: Early manifestations of thrombotic or thromboembolic disorders, thrombophlebitis, cerebrovascular disorders (including haemorrhage), myocardial infarction, pulmonary embolism or retinal thrombosis. Hypertension. Gradual or sudden, partial or complete loss of vision.

Proptosis or diplopia. Onset or aggravation of migraine or development of headaches of a new pattern which are recurrent, persistent or severe. Papilloedema or any evidence of retinal vascular lesions. During periods of immobility (e.g. after accidents). Pregnancy. Manifestations of liver tumours.

Precautions: Examination of the pelvic organs, breasts and blood pressure should precede the prescribing of any oral contraceptive, and should be repeated regularly.

The following are some of the conditions reported to be influenced by oral contraceptive therapy, and where the physician will have to exercise medical judgement to commence, continue or discontinue therapy as appropriate.

- (a) Pre-existing uterine fibromyomata may increase in size.
- (b) A decrease in glucose tolerance in a significant number of women.
- (c) An increase in blood pressure in a small but significant number of women.
- (d) Cholestatic jaundice. Patients with a history of cholestatic jaundice of pregnancy are more likely to develop cholestatic jaundice during oral contraceptive therapy.
- (e) Amenorrhoea during and after oral contraceptive therapy. Women with a past history of oligomenorrhoea or secondary amenorrhoea or women with irregular cycles may be more likely to remain anovulatory or to become amenorrhoeic post oral contraceptive therapy.
- (f) Depression.
- (g) Fluid retention. Conditions which might be influenced by this factor include epilepsy, migraine, asthma, cardiac or renal dysfunction.
- (h) Varicose veins.
- (i) Multiple sclerosis.
- (j) Porphyria.
- (k) Tetany.
- (l) Wearing of contact lenses.

or any condition that is prone to worsen during pregnancy.

The following laboratory determinations may be altered in patients using oral contraceptives:

Hepatic: Increased BSP retention and other tests.

Coagulation: Increased prothrombin, Factors VII, VIII, IX and X, decreased antithrombin III, increased platelet aggregability.

Endocrine: Increased PBI and butanol extractable protein bound iodine and decreased T³ uptake, increased glucose blood levels.

Other: Increased phospholipids and tri-glycerides, decreased serum folate values and disturbance in tryptophan metabolism, decreased pregnanediol excretion, reduced response to metyrapone test.

These tests usually return to pre-therapy values after discontinuing oral contraceptive use. However, the physician should be aware that these altered determinations may mask an underlying disease.

Side effects: Those most commonly reported in early cycles of oral contraceptive therapy include breakthrough bleeding, spotting, nausea, vomiting and other gastrointestinal disturbances. These frequently decrease with continued use. Other common side-effects include: change in menstrual flow, change in weight, oedema, chloasma (which may persist post therapy), amenorrhoea, breast changes (tenderness, enlargement and secretion).

In addition to the conditions and disorders discussed above, the following have been reported as adverse reactions in patients using combined oral contraceptives:

Neuro-ocular lesions	Haemorrhagic eruptions
Rash	Cystitis-like syndrome
Cervical erosion and secretions	Headache
Suppression of lactation	Nervousness
Pre-menstrual like syndrome	Fatigue
Changes in libido	Hirsutism
Leg cramp	Loss of scalp hair
Relative pyridoxine deficiency	Erythema multiforme
	Erythema nodosum
	Itching
	Vaginal candidiasis
	Porphyria

Overdosage: Serious ill effects have not been reported following acute ingestion of large doses of oral contraceptives by young children. Overdosage may cause nausea, and withdrawal bleeding may occur in females. An appropriate method of gastric emptying may be used if considered desirable.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Carton containing 3 pushpaks each of 21 tablets – sufficient for 3 cycles.

Further information Nil.

Product licence number 0076/0090.

DELLEN* CONTRACEPTIVE CREAM

Presentation Delfen Contraceptive Cream contains nonoxonyl-9 5.0% w/w in a white, oil and water emulsion at pH 4.5.

Uses Delfen Contraceptive Cream is a spermicidal cream for the control of conception. A higher degree of protection against pregnancy will be afforded by using another method of contraception in addition to a spermicidal contraceptive.

Dosage and administration One applicatorful (5 cc) intravaginally prior to coitus. A fresh application must be made if intercourse is repeated or delayed by more than one hour. If a douche is desired, it should be deferred for at least six hours after intercourse.

Contra-indications, warnings, etc Hypersensitivity to the product.

Warnings: Where avoidance of pregnancy is essential the choice of contraceptive should be made in consultation with a doctor or a family planning clinic.

Side-effects: Irritation of the vagina or penis has been reported. In such cases the medication should be discontinued.

Overdosage: Delfen Contraceptive Cream is intended for intravaginal use only, and if taken orally by mistake is likely to taste unpleasant. If excess quantities are swallowed this may give rise to gastric irritation as the product contains a surfactant, and general supportive therapy should be carried out if necessary.

Pharmaceutical precautions None known.

Legal category GSL.

Package quantities Tube containing 70 g.

ORTHO* Plastic Vaginal Applicator available separately.

Further information Nil.

Product licence number 0076/5004.

DELLEN* CONTRACEPTIVE FOAM

Presentation Delfen Contraceptive Foam is a white, non-staining aerosol foam which contains nonoxonyl-9 12.5% w/w and buffered to normal vaginal pH of 4.5.

Uses Delfen Contraceptive Foam is a spermicidal foam for the control of conception. It provides rapid dispersion and extensive, uniform coverage of the cervix. A higher degree of protection against pregnancy will be afforded by using another method of contraception in addition to a spermicidal contraceptive. It is suitable for use with an occlusive device.

Dosage and administration One applicatorful intra-vaginally prior to coitus. A fresh application must be made if intercourse is repeated or delayed by more than one hour. If a douche is desired, it should be deferred for at least six hours after intercourse.

Contra-indications, warnings, etc Hypersensitivity to the product.

Warnings: Where avoidance of pregnancy is essential, the choice of contraceptive should be made in consultation with a doctor or a family planning clinic.

Side-effects: Irritation of the vagina or penis has been reported. In such cases the medication should be discontinued.

Overdosage: Delfen Contraceptive Foam is intended for intravaginal use only, and if taken orally by mistake is likely to taste unpleasant. If excess quantities are swallowed this may give rise to gastric irritation as the product contains a surfactant, and general supportive therapy should be carried out if necessary.

Pharmaceutical precautions Contents are under pressure. Do not burn or puncture container. Store at room temperature, not over 49°C (120°F).

Legal category GSL.

Package quantities 20 g aerosol container with or without the DELLEN* Contraceptive Foam Applicator.

Further information Nil.

Product licence number 0076/5003.

DERMONISTAT* CREAM

Presentation A smooth, white non-staining cream containing miconazole nitrate 2% w/w.

Uses A potent antimycotic cream for the treatment of fungal infections of the skin, hair and nails.

Dosage and administration May be applied topically to both adults and children.

Fungal infections of the skin: The cream should be applied to the lesions twice daily and continued for 10 days after the lesions have disappeared.

Fungal infections of the nail: The cream should be applied thinly to the infected nail once daily and the nail covered with a non-perforated plastic bandage. Nails should be clipped short at regular intervals and treatment continued until the growth of the new nail is established and a definite cure can be observed.

Contra-indications, warnings, etc Hypersensitivity to the product.

Side-effects: Isolated cases of sensitisation and irritation have been reported. If this occurs administration of the product should be discontinued.

Overdosage: Dermonistat Cream is intended for topical use. If accidental ingestion of large quantities of the product occurs, an appropriate method of gastric emptying may be used if considered desirable.

Pharmaceutical precautions None known.

Legal category P.

Package quantities 30 g tubes. A patient-instruction leaflet is enclosed in each package.

Further information Nil.

Product licence number 0076/0041.

GYNO-PEVARYL*150 VAGINAL PESSARIES GYNO-PEVARYL*150 VAGINAL PESSARIES AND CREAM COMBIPACK

Presentation *Pessaries:* White egg-shaped pessaries each containing 150 mg econazole nitrate and melting at 37°C.

Combipack: A combination pack comprising 3 Gyno-Pevaryl vaginal pessaries (each containing 150 mg econazole nitrate) plus a 15 g tube of Gyno-Pevaryl cream (containing 1% econazole nitrate).

Uses *Pessaries:* Vaginitis due to *Candida albicans* and other yeasts.

Combipack: Pessaries for vaginitis; cream for associated vulvitis and to treat the sexual partner to help prevent re-infection.

Dosage and administration *Pessaries:* One pessary should be inserted high into the vagina each evening for three consecutive days.

Combipack: Pessaries as above. The cream should be applied to the vulva and perianal region and/or to the sexual partner's penis, including under the foreskin.

Contra-indications, warnings, etc

Contra-indications: None known.

Side-effects: Rarely, transient local mild irritation may occur immediately after application.

Overdosage: Gyno-Pevaryl Vaginal Pessaries and Cream are intended for intravaginal use. If accidental ingestion of large quantities of the product occurs, an appropriate method of gastric emptying may be used if considered desirable.

Precautions: Hypersensitivity has rarely been recorded, if it should occur, administration of the product should be discontinued.

Gyno-Pevaryl 150 vaginal pessaries are effective in the treatment of vaginal candidiasis associated with pregnancy but as with any new product, caution should be exercised when prescribing during the first trimester.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities *Pessaries:* Each pack contains 3 pessaries and a patient instruction leaflet. The pessaries are individually sealed in a white plastic strip marked Gyno-Pevaryl 150 at regular intervals.

Combipack: Each pack contains 3 pessaries, a 15 g tube of cream and a patient instruction leaflet.

Further information Anogenital hygiene is important to help prevent re-infection.

Product licence numbers

Pessaries 0076/0058

Combipack 0076/0058 and 0076/0060

LIPPES LOOP* INTRAUTERINE CONTRACEPTIVE DEVICE

Presentation The Lippes Loop is manufactured from polyethylene in the shape of a double 'S'. Four different sizes are available to allow for the variability in the size of the uterus (see below). A fine double thread 'tail' made of polyethylene suture material (monofilament) is attached to the lower end to facilitate removal. In addition, palpation of the tail in the vagina by the patient, or visualization by the physician, can assist in determining whether or not an undetected expulsion has occurred. The Lippes Loop comes prepacked and sterilized with an introducer and insertion tube in a sealed envelope. The insertion tube is equipped with a flange which is used to determine the depth to which the tube should be inserted through the cervical canal and into the uterine cavity. The four available sizes are as follows:

Loop A – 22.5 mm. Blue thread. For nulliparous patients.

Loop B – 27.5 mm WITH REDUCED RADII. Black thread. Suggested for patients who have experienced premature pregnancy losses, and multiparous patients whose uteri measure less than 6 cm.

Loop C – 30 mm WITH REDUCED RADII. Yellow thread. Suggested for use in patients with one or more children.

Loop D – 30 mm. White thread. Suggested for use in multiparous patients where the risk of expulsion is thought to be greater than usual.

Uses Contraception.

Dosage and administration The Lippes Loop is inserted by a doctor into the patient's uterus. The insertion technique is described on the leaflet provided with each device.

Contra-indications, warnings, etc Contraindications: IUCD's should not be inserted when the following conditions exist:

1. Pregnancy or suspicion of pregnancy.
2. Abnormalities of the uterus resulting in distortion of the uterine cavity.
3. Pelvic inflammatory disease or a history of repeated pelvic inflammatory disease.
4. Postpartum endometritis or infected abortion in the past three months.
5. Known or suspected uterine or cervical malignancy including unresolved abnormal cervical smear.
6. Genital bleeding of unknown aetiology.
7. Cervicitis, until infection is controlled.
8. Large or multiple fibroids.
9. Menorrhagia and/or intermenstrual bleeding.
10. Severe dysmenorrhoea.

Warnings:

1. Pregnancy:
 - (a) Long-term effects: Long-term effects on the offspring, when pregnancy occurs with the Lippes Loop *in situ*, are unknown.

(b) Septic abortion: Reports have indicated an increased incidence of septic abortion associated in some instances with septicaemia, septic shock, and, rarely, death in patients becoming pregnant with an IUCD *in situ*. Most of these reports have been associated with the mid-trimester of pregnancy. In some cases the initial symptoms have been insidious and not easily recognised. If pregnancy should occur with an IUCD *in situ*, it is recommended that the IUCD be removed if the thread is visible. If the thread is not visible or device removal proves to be or would be difficult, the IUCD may be left *in situ* until the pregnancy goes to term or until a decision is made to terminate the pregnancy.

(c) Continuation of pregnancy: If the patient chooses to continue the pregnancy with the IUCD *in situ* there is an increased risk of spontaneous abortion and of sepsis, including, rarely, death. If the pregnancy is continued the patient should be closely observed and advised to report immediately all abnormal symptoms, such as flu-like syndrome, fever, abnormal cramping and pain, bleeding or vaginal discharge. The onset of septicaemia may be insidious with general symptoms rather than initial signs of spontaneous abortion.

2. Ectopic Pregnancy:

(a) A pregnancy that occurs with an IUCD *in situ* is more likely to be ectopic than a pregnancy occurring without an IUCD *in situ*. Accordingly, patients who become pregnant whilst using the IUCD require careful evaluation for the possibility of an ectopic pregnancy.

(b) Special attention as to whether an ectopic pregnancy has occurred is required for patients with delayed menses, slight metrorrhagia, and/or unilateral pelvic pain and for patients who wish to terminate the pregnancy with the device *in situ*.

3. Pelvic Infection: An increased risk of pelvic infection has been reported with the IUCD *in situ*. This, at times, may result in the development of bilateral or unilateral tubo-ovarian abscesses or general peritonitis which may lead to infertility if left untreated. Appropriate aerobic and anaerobic bacteriological studies are indicated at the time of initiation of antibiotic therapy. Removal of the IUCD is advised with reassessment of continuing treatment, based upon these bacteriological and sensitivity tests.

4. Embedding: Partial penetration or embedding of the IUCD in the endometrium may cause subsequent removal to be a difficult procedure.

5. Perforation: Partial or total perforation of the uterine wall or cervix may occur with the use of IUCD's. The possibility of perforation must be kept in mind during insertion and at the time of any subsequent examination. If perforation occurs, the IUCD should be removed. Adhesions, foreign body reactions, and intestinal obstruction may result if an IUCD is left in the peritoneal cavity. It is possible for the IUCD to penetrate the uterine wall at any time following insertion.

Precautions: Prior to insertion of an IUCD, a thorough history and physical examination, including a pelvic examination and Papanicolaou smear, should be performed.

Insertion of an IUCD into a uterine cavity measuring less than 6.5 cm may increase the incidence of expulsion, bleeding, pain and perforation.

The patient should be re-examined within 3 months

after insertion and thereafter at yearly intervals to ensure the device is still *in situ*. The patient should be advised to contact her doctor immediately if she misses a menstrual period or has any other reason to think she may be pregnant.

IUCD's should be used with caution in patients:

- With anaemia.
- Receiving anticoagulant therapy or having any disorder of coagulation.
- Receiving steroid therapy (possible masking of pelvic inflammatory disease should be borne in mind).
- With known or suspected rheumatic or congenital heart disease. The need for appropriate antibiotic cover during insertion of the device should be carefully considered.
- With a history of a previous uterine incision or perforation of the uterus.
- With a history of previous ectopic pregnancy.

Syncope, bradycardia or other neuro-vascular episodes may occur during insertion or removal of IUCD's, especially in patients susceptible to these conditions. The possibility of a seizure being precipitated in a patient suffering from epilepsy, at or shortly after the insertion of an IUCD, should also be borne in mind.

No method of contraception can be described as absolutely effective. In some cases it may be appropriate to recommend the use of an additional reliable method of contraception at mid-cycle.

Time of insertion: The Lippes Loop should be inserted preferably during or immediately after a normal menstrual period. Lippes Loop normally is not inserted until 6 weeks or more after delivery or an abortion.

To remove: To remove the Lippes Loop, pull gently on the exposed tail.

Spontaneous expulsion: Expulsion of the Lippes Loop occurs in some patients spontaneously. This expulsion occurs most frequently during the first or second cycle of use, usually at the time of the menstrual period. Expulsion can, however, occur at any time, even several months after insertion.

Confirmation of the expulsion of the device is necessary prior to inserting a second device. Pregnancy must be ruled out before any method of locating the device is undertaken.

Adverse reactions:

1. **Effect on menstrual patterns:** Post-insertion: Almost all patients will experience varying amounts of vaginal bleeding after insertion of the Lippes Loop. In approximately 25% of patients, post-insertion bleeding should cease in a few days.

Intermenstrual Bleeding: Spotting or light bleeding may occur intermenstrually in approximately 25% of patients in the first cycle following insertion. A few patients may experience mid-cycle spotting for several consecutive cycles.

Menstrual Periods: Variation in the first menstrual period following insertion is frequent. This occurs most often as spotting or a brown discharge for 2 days before the period. The first menstrual flow will be longer and slightly heavier than usual, and occasionally the bleeding may be extremely heavy. If this bleeding persists, consideration may be given to removal of the device. A few patients may have heavier than normal bleeding during the second postinsertion menstrual period. The bleeding pattern usually returns to normal by the third cycle. Pelvic pathology should be considered if heavy bleeding occurs beyond this point.

2. **Cramps:** Insertion of the Lippes Loop in multiparous patients usually causes no pain. Slight cramps lasting a few minutes are reported by about 10% of patients in this group and rarely require analgesic therapy.

In contrast, most nulliparous patients complain of moderate to severe cramps which may last for several days following insertion. Analgesics are often required for relief of discomfort in this group; occasionally, removal of the device may be necessary.

3. **Syncope:** Syncope may occur immediately following insertion, particularly in nulliparous patients; it is uncommon in the multiparous patient. A few minutes in a horizontal position may be needed for stabilisation in some patients.

4. **Pelvic inflammatory disease:** Recent studies have indicated that there may be an increased incidence of pelvic inflammatory disease amongst patients fitted with any intrauterine contraceptive device.

Handling precautions If the seal of the sterile envelope is broken, the device inside should not be used.

Legal category POM. Also available through family planning clinics.

Package Quantities Each sterile Lippes Loop is supplied in a sealed envelope. A 'Direction for the Patient' leaflet is also supplied.

Further information Nil.

Product licence numbers

Size A 0076/0077

Size B 0076/0078

Size C 0076/0079

Size D 0076/0080

MASSE[®] BREAST CREAM

Presentation - A white oil in water cream containing Glycerin, Lanolin, Arachis Oil, Sorbitan monostearate, Glyceryl monostearate, Cetyl alcohol, Stearic acid, Polysorbate 60, Propyl p-hydroxybenzoate, Potassium hydroxide, Purified Water.

Uses For pre-natal and post-natal nipple care. Use pre-natally for preparing the nipples for breast feeding including the massage of flat and inverted nipples. Use post-natally for routine application to the nipples of lactating women.

Dosage and administration *Pre-natal nipple care:* Masse Breast Cream is applied once or twice daily during the last two or three months of pregnancy. A $\frac{1}{2}$ " ribbon of cream is massaged gently into the nipples and the surrounding pigmented area with the fingertips until the cream is absorbed. The massage should be with gentle outward motion from the areola to the apex of the nipple.

Post-natal nipple care: Masse Breast Cream is massaged gently around the nipple and areola after the breast has been cleansed after each nursing.

Contra-indications, warnings, etc Acute mastitis or breast abscess. Lanolin sensitivity.

Overdosage: Masse Breast Cream is intended for topical use. If accidental ingestion of large quantities of the product occurs, an appropriate method of gastric emptying may be used if considered desirable.

Pharmaceutical precautions None known.

Legal category GSL.

Package 28 g tubes. A patient instruction leaflet is enclosed in each package.

Further information Nil.

Product licence number 0076/5009.

MICRONOR[®] ORAL CONTRACEPTIVE TABLETS

Presentation White, $\frac{1}{4}$ inch diameter, circular tablets with flat faces and bevelled edges, bearing on each face the engraving 'ORTHO 0.35'. Micronor Oral Contraceptive Tablets each contain 0.35 mg Norethisterone BP.

Uses Contraception.

Action: Micronor has a progestational effect on the endometrium and on the cervical mucus. The exact mechanism of how it prevents conception has not been confirmed.

Dosage and administration Micronor is administered orally on a continuous daily dosage regimen starting on the first day of menstruation. One tablet is taken at the same time each day, every day of the year, whether menstruation occurs or not. When starting Micronor therapy the patient should be instructed to use an additional reliable non-hormonal method of contraception during the first 14 days of the first cycle.

The non-nursing patient may be prescribed Micronor in the post partum period whether or not menstruation has resumed provided the possibility of pregnancy has been excluded.

The possibility of ovulation and conception prior to initiation of medication should be considered.

Strict adherence to the dosage regimen is important. If the patient should fail to take 1 tablet at the usual time protection is reduced. She should take the missed tablet as soon as she remembers and take the next tablet on the day it is due. When a tablet is missed an additional reliable means of contraception should be used in addition to taking Micronor until her next period occurs.

If the patient does not have a period within 45 days of her last period, pregnancy should be excluded.

If the patient has vomiting or diarrhoea, absorption of the hormone will be impaired, making it advisable to use an additional reliable method of contraception until the next menstrual period.

Contra-indications, warnings, etc Any of the following conditions should be regarded as contra-indications for the use of Micronor. Existing thrombophlebitis, thromboembolic disorders, cerebral vascular disease, myocardial infarction, or a past history of these conditions. Markedly impaired liver function, known or suspected hormone dependent neoplasia, known or suspected carcinoma of the breast, undiagnosed abnormal genital tract bleeding, known or suspected pregnancy.

Warnings: Because of a possible increased risk of post surgery thromboembolic complications in oral contraceptive users, therapy should be discontinued six weeks prior to elective surgery.

Masculinisation of the female foetus has occurred when progestogens have been used in pregnant women, although this has been observed at doses much higher than that contained in Micronor. Pregnancy should be ruled out before continuing administration of Micronor to patients who have gone 45 days without a menstrual period.

small doses of oral steroids should be used. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

In infants, long-term continuous topical therapy should be avoided. Adrenal suppression can occur even without occlusion.

Eurax-Hydrocortisone should not be allowed to come into contact with the conjunctiva.

Side-effects: Eurax-Hydrocortisone is generally well tolerated. Only in exceptional cases may the cromolone component give rise to skin sensitisation; in such cases, the preparation should be withdrawn.

Pharmaceutical precautions *Storage:* Protect from heat.

Dilutions: Diluents and additives to this formulation are not recommended.

Legal category POM.

Package quantities Tubes of 30 g.

Further information Cromolone is effective against all common forms of pruritus. The relief it affords sets in rapidly and lasts for approximately 6 hours. Cromolone minimises the risk of secondary skin infection by relieving itching and thus preventing damage to the skin caused by scratching. In addition, cromolone exerts a bacteriostatic action on streptococci and staphylococci. Hydrocortisone possesses anti-inflammatory, anti-allergic, anti-exudative, and anti-pruritic activity. The therapeutic properties of cromolone and hydrocortisone complement one another, the combined preparation being particularly effective in the treatment of eczema and pruritus.

Product licence number 0001/5010.

FABROL* ▼

Presentation Pale yellow orange flavoured granules in sachets containing 200 mg acetylcysteine.

Uses *Mode of action:* Fabrol has an intense mucolytic action on mucoid and mucopurulent secretions, due to its ability to split disulphide bonds in mucus glycoprotein. This property allows it to be used as adjuvant therapy in many clinical conditions characterized by the presence of viscous mucoid or mucopurulent secretions, particularly in the respiratory tract.

Indications: Fabrol is indicated in acute and chronic bronchitis and other respiratory tract infections where the condition is associated with the production of viscous mucus. Given on a long term basis in chronic bronchitis, it progressively improves symptoms due to mucus hypersecretion and substantially reduces the rate of infectious exacerbations.

Dosage and administration

Adults: 1 sachet (200 mg) three times daily.

Children: Up to 2 years: 1 sachet (200 mg) daily.

2-6 years: 1 sachet (200 mg) twice daily.

The granules should be dissolved before administration in a glass of water.

In acute cases a treatment period of 5-10 days is usually adequate but may be extended if necessary.

In chronic bronchitis relief of symptoms may be noticeable after treatment for 1-2 months but treatment

may be continued for up to six months e.g. during the winter season.

Fabrol can be administered concurrently with amoxycillin, doxycillin, and erythromycin. When other oral antibiotics or drugs are required, they should be administered 1-2 hours apart from Fabrol.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to acetylcysteine.

Precautions: Each Fabrol sachet contains the equivalent of 2.70 g sucrose. This should be taken into account when treating diabetic patients.

Side-effects: Nausea, heart-burn, vomiting, urticaria, headache and tinnitus have infrequently been reported but these rarely necessitate withdrawal of treatment.

Pregnancy: The administration of Fabrol during pregnancy is advised only if there are compelling reasons.

Accidental overdosage: There is no specific antidote for Fabrol and treatment is symptomatic. It consists of postural drainage, bronchial suction and supportive therapy as indicated.

Pharmaceutical precautions The addition of other drugs to the Fabrol solution should be avoided.

Legal category POM.

Package quantities Packages of 30 sachets.

Further information Nil.

Product licence number 0001/0092

HYGROTON*

Presentation Pale yellow compressed tablets, containing 50 mg chlorthalidone, approximately 7 mm diameter, flat with bevelled edge and impressed GEIGY on one side, breakline and ZA on the other.

White compressed tablets, containing 100 mg chlorthalidone, 7 mm diameter, flat with bevelled edge and impressed GEIGY on one side, breakline and BA on the other.

Uses Hygroton has been shown to have two separate therapeutic actions:

Diuretic: Following a single oral dose a marked salt and water diuresis is evident within two hours and a maximum effect within 12 hours. This natriuretic activity of Hygroton persists for 48-72 hours.

Antihypertensive: In hypertensive subjects Hygroton lowers both systolic and diastolic pressure, the degree of reduction depending on the original blood pressure of the patient. In general, the higher the blood pressure the greater the fall brought about by Hygroton.

Hygroton is indicated for: Hypertension. Oedema due to cardiac failure, hepatic cirrhosis, nephrosis.

Pathological oedema of pregnancy. Diabetes insipidus.

Dosage and administration Hygroton is given orally in tablet form.

Hygroton tablets should be taken orally as a single daily dose at breakfast time.

Hypertension: In mild to moderate hypertension, 25 mg of Hygroton at breakfast time, increasing to 50 mg if necessary.

In more severe cases Hygroton may be combined with other antihypertensive agents in order to increase their hypotensive effects or to allow the use of a lower dose

of the latter where side-effects are becoming troublesome.

Oedema: 1 to 2 × 100 mg tablets on alternate dates. If preferred the 50 mg tablets may be given on a daily basis. In severe cases of oedema, a single loading dose of 4 × 100 mg Hygroton tablets may be required.

The maintenance dose should be the minimum amount needed to keep the patient free from oedema and may be as low as 100 mg twice weekly.

Pathological oedema of pregnancy: The dose of Hygroton used in the treatment of oedema in pregnancy is similar to that in other forms of oedema.

Diabetes insipidus: Hygroton, when used in the treatment of diabetes insipidus can be used either alone or as an adjunct to treatment with antidiuretic hormone. In either case the usual starting dose is 100 mg twice daily, reducing where possible to a maintenance dose of 50 mg daily.

Potassium supplementation: Potassium supplements may be required in digitalised patients, severe cases of oedema, hepatic cirrhosis and in long-term therapy. In digitalised patients, the dose of digoxin may need to be reduced.

Routine supplementation with potassium is not necessary in patients with uncomplicated hypertension.

Paediatric dosage: The recommended dosage for babies up to 10 kg (22 lb) in weight is 5 mg/kg on alternative days. In older children the recommended dose is 50 mg on alternate days for children up to the age of five years, and 50–100 mg on alternate days for children over the age of five years.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to chlorthalidone.

Severe renal or hepatic insufficiency. Concomitant lithium therapy.

Side-effects: In the majority of patients Hygroton is well tolerated. Side-effects are infrequent and generally mild. Gastro-intestinal disturbances may occasionally occur. In rare cases, especially at the start of treatment, patients may complain of slight dizziness and tiredness, which generally resolves spontaneously or following a temporary reduction in the dosage.

There have also been occasional reports of the occurrence of cardiac arrhythmias, disturbances of vision, allergic skin reactions, neutropenia and thrombocytopenia.

Precautions: As with the use of other sulphonamide-type oral diuretics decreased glucose tolerance, as shown by hyperglycaemia and glycosuria, may occur. Hygroton may occasionally aggravate diabetes mellitus or precipitate diabetes in patients who have not previously displayed symptoms. This condition is usually reversible on cessation of therapy. During prolonged Hygroton therapy regular tests for glycosuria should be carried out and any unexpected polyuria investigated.

Hyperuricaemia may occasionally occur and acute attacks of gout may be precipitated. In cases where prolonged elevation of serum uric acid occurs, the concurrent use of a uricosuric agent will reverse the hyperuricaemia without loss of therapeutic effect.

Hypokalaemia may occur, but in most patients this appears to be of little clinical significance. Muscle weakness, cramps, lassitude and ECG changes are signs of significant potassium depletion which may be remedied by the use of oral potassium supplements (16–40 mEq/day). Supplementary potassium medication is

indicated in the presence of an underlying disease (hepatic cirrhosis) associated with increased potassium excretion or in patients receiving concomitant treatment with digitalis, glucocorticoids or ACTH.

As with all antihypertensive agents a cautious dosage schedule is indicated in patients with severe coronary or cerebral arteriosclerosis. In cases where renal function is impaired, creatinine clearance and the electrolyte balance should be monitored. The marked loss of fluid and electrolytes occurring during long-term treatment with large doses of diuretics may aggravate signs of renal failure.

In patients under treatment with lithium, diuretics should be prescribed with caution, because they diminish the excretion of lithium and thus raise the blood lithium levels. Where lithium has induced polyuria, ingestion of diuretics has been observed to exert a paradoxical anti-diuretic effect.

Pregnancy and lactation: Since Hygroton, like other diuretics, is liable during pregnancy to reduce plasma volume as well as the blood supply to the uterus and placenta, its use in pregnant women calls for careful consideration. Diuretics should not be prescribed as treatment for eclampsia or pre-eclampsia or non-pathological oedema occurring during pregnancy.

Chlorthalidone passes into the breast milk and thus mothers taking Hygroton should refrain from breast-feeding their infants.

Accidental overdosage: Symptoms of overdosage include nausea, weakness, dizziness and disturbances of electrolyte balance. There is no specific antidote, but gastric lavage has been recommended. Supportive treatment aimed at maintaining normal fluid and electrolyte balance is essential.

Pharmaceutical precautions *Storage:* Protect from moisture.

Legal category POM.

Package quantities *Tablets 50 mg:* Containers of 100 and 500.

Tablets 100 mg: Containers of 100 and 500.

Further information Nil.

Product licence numbers

Tablets 50 mg 0001/5011

Tablets 100 mg 0001/5012

HYGROTON®-K

Presentation Round, red, sugar coated tablets of approximately 11.3 mm diameter and imprinted GEIGY on one side, containing 25 mg chlorthalidone BP and 500 mg potassium chloride BP–6.7 mEqK (controlled release).

Uses Hygroton has been shown to have two separate therapeutic actions.

Diuretic: Following a single oral dose, a marked salt and water diuresis is evident within two hours and a maximum effect within 12 hours. The natriuretic activity of Hygroton persists for 48–72 hours.

Antihypertensive: In hypertensive subjects Hygroton lowers both systolic and diastolic pressure, the degree of reduction depending on the original blood pressure of the patient. In general the higher the blood pressure the greater the fall brought about by Hygroton.

Potassium supplementation: Hygroton-K contains 500 mg controlled release potassium chloride providing 6.7 mEqK.

Hygroton-K is indicated for the same conditions as for Hygroton but particularly where the physician believes that potassium supplementation is indicated, as in the long-term treatment of hypertension, oedema due to cardiac failure, hepatic cirrhosis, nephrosis, pathological oedema of pregnancy, diabetes insipidus and patients receiving concomitant medication with digitalis, glucocorticoids or ACTH.

Dosage and administration Hygroton-K tablets should be swallowed whole with meals and not chewed.

Hypertension: In mild to moderate hypertension, 1 tablet of Hygroton-K at breakfast time, increasing to 2 tablets if necessary.

In more severe cases Hygroton-K may be combined with other antihypertensive agents in order to increase their hypotensive effect, or to allow the use of a lower dose of the latter, where side-effects are becoming troublesome.

Oedema: 1 or 2 tablets of Hygroton-K once or twice daily. The maintenance dose should be the minimum amount needed to keep the patient free from oedema.

Pathological oedema of pregnancy: The dosage of Hygroton-K is similar to that used in other forms of oedema.

Diabetes insipidus: When Hygroton is indicated for maintenance or as an adjunct to maintenance with antidiuretic hormone the determined dose of Hygroton may be given as Hygroton-K if potassium supplementation is desired.

Where possible the maintenance dose of Hygroton-K should be 2 tablets daily.

Paediatric dosage: Hygroton-K tablets must be swallowed whole and not crushed. Consequently this dosage form of Hygroton is not convenient for paediatric use.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to chlorthalidone. Hyperkalaemia. Severe renal or hepatic failure. Concomitant lithium therapy.

All solid dosage forms of potassium salts are contra-indicated in patients suffering from obstructions in the digestive tract (e.g. oesophageal compression due to enlargement of the left atrium, stenosis of the gut).

Side-effects: In the majority of patients Hygroton-K is well tolerated. Side-effects are infrequent and generally mild. Gastro-intestinal disturbances may occasionally occur. In rare cases, especially at the start of treatment, patients may complain of slight dizziness and tiredness, which generally resolves spontaneously or following a temporary reduction in the dosage.

There have also been the occasional reports of the occurrence of cardiac arrhythmias, disturbances of vision, allergic skin reactions, neutropenia and thrombocytopenia.

Hygroton-K tablets are designed to minimise gastrointestinal irritation. However, complaints of abdominal pain, distension, nausea, vomiting or gastro-intestinal bleeding are indications for stopping treatment with potassium containing preparations immediately.

Precautions: As with the use of other sulphonamide type diuretics, decreased glucose tolerance as shown by hyperglycaemia and glycosuria may occur. Hygroton may occasionally aggravate diabetes mellitus or precipitate diabetes in patients who have not previously

displayed symptoms. This condition is usually reversible on cessation of therapy. During prolonged Hygroton therapy regular tests for glycosuria should be carried out and any unexpected polyuria investigated.

Hyperuricaemia may occasionally occur and acute attacks of gout may be precipitated. In cases where prolonged elevation of serum uric acid occurs the concurrent use of a uricosuric agent will reverse the hyperuricaemia without loss of therapeutic effect.

Muscle weakness, cramps, lassitude and ECG changes are signs of significant potassium depletion which may be remedied by adding additional oral potassium supplements.

When Hygroton-K is used particular care should be taken not to combine it with potassium sparing diuretics.

As with all antihypertensive agents a cautious dosage schedule is indicated in patients with severe coronary or cerebral arteriosclerosis.

In cases where renal function is impaired, creatinine clearance and the electrolyte balance should be monitored. The marked loss of fluid and electrolytes occurring during long-term treatment with large doses of diuretics may aggravate signs of renal failure.

In patients under treatment with lithium, diuretics should only be prescribed with caution, because they diminish the excretion of lithium and thus raise the blood lithium levels. Where lithium has induced polyuria, ingestion of diuretics has been observed to exert a paradoxical anti-diuretic effect.

Pregnancy and lactation: Since chlorthalidone, like other diuretics, is liable during pregnancy to reduce plasma volume as well as the blood supply to the uterus and placenta, its use in pregnant women calls for careful consideration. Diuretics should not be prescribed as treatment for eclampsia or pre-eclampsia, or non-pathological oedema occurring during pregnancy.

As chlorthalidone passes into the breast-milk, mothers taking Hygroton-K should refrain from breast-feeding their infants.

Accidental overdose: Symptoms of Hygroton overdose include nausea, weakness, dizziness and disturbances of electrolyte balance. There is no specific antidote but gastric lavage has been recommended.

Supportive treatment aimed at maintaining normal fluid and electrolyte balance is essential. Particular care should be taken to prevent serum potassium levels from exceeding normal values.

Pharmaceutical precautions Protect from heat and moisture.

Legal category POM.

Package quantities Containers of 100 and 250 tablets.

Further information *Note* - Hygroton-K alone is not considered to be effective therapy for hypokalaemia from any cause.

Product licence number 0001/0059.

LAMPRENE*

Presentation The active ingredient, clofazimine, is presented as: red-brown, soft gelatin capsules, containing 100 mg clofazimine in each capsule.

Uses Antileprotic agent:

Prevention of the development of *M. leprae* resistant

to sulphones, in patients with lepromatous and borderline leprosy.

Prevention of lepra reactions in patients with lepromatous and borderline leprosy.

Treatment for lepromatous and borderline forms of leprosy resistant to sulphones.

Treatment of lepra reactions e.g. Erythema nodosum leprosum (ENL).

Treatment of *M. ulcerans* infection (Buruli ulcer).

Dosage and administration For the treatment of leprosy, Lampréne should be employed in combination with other suitable anti-leprosy agents.

The capsules should preferably be taken during meals or together with milk. The dosage of Lampréne must be adapted to the patient's body weight and to the state of activity of the disease.

For the prevention of resistance to sulphones and for the prevention of lepra reactions in cases of lepromatous and borderline leprosy: 50–100 mg Lampréne daily or 100 mg 3 times weekly, during the first 4–6 months of long-term treatment with dapsone (50–100 mg daily).

In cases resistant to sulphones: Long-term treatment with Lampréne in a dosage of 100 mg daily, combined during the first 2–3 months with rifampicin 600 mg daily.

In lepra reactions: If lepra reactions (e.g. ENL) occur, the basic therapy given hitherto should be continued. To suppress the lepra reactions, Lampréne should be administered under surveillance in relatively large, individually determined doses. The dosage generally recommended is one of 300 mg daily for 3 months. As soon as the lepra reaction has been brought under control, the dosage should be gradually lowered to a level at which its suppressant effect is still just sufficient.

Contra-indications, warnings, etc

Contra-indications: There are no known conditions in which Lampréne would be contra-indicated.

Precautions: Treatment with Lampréne should be given only under medical supervision. Daily doses of 300 mg or more should not be administered for longer than 3 months.

If gastro-intestinal symptoms develop during treatment with Lampréne, the dosage should be reduced or the interval between doses prolonged. In the event of persistent diarrhoea or vomiting, the patient should be hospitalised.

During long-term medication with Lampréne, as well as in patients with a history of liver or kidney disease, it is advisable to perform clinical examinations and hepatic or renal tests every 3 months. The use of Lampréne in patients complaining of recurrent abdominal pains, or suffering from damage to the liver or kidneys, should wherever possible be avoided.

Pregnancy: For general medical reasons, it is not advisable to prescribe Lampréne during the first three months of pregnancy unless the drug's use is urgently indicated. The active substance of Lampréne crosses the placental barrier; newborn infants of women under treatment with the drug may therefore show relatively pronounced discolouration.

Side-effects: Lampréne is generally well tolerated. The side-effects occasionally met with are mostly of a mild nature and disappear after the daily dose has been reduced or the medication withdrawn.

The following side-effects have been observed:

Red to brownish-black discolouration of the skin and of the leprosy lesions in lighter-skinned patients at sites

exposed to light; discolouration of the hair, the conjunctiva, and the lacrimal fluid, as well as discolouration of sweat, sputum, urine and faeces.

Dryness of the skin, ichthyosis, pruritus, photosensitivity, acneiform eruptions and non-specific skin rashes. Nausea, vomiting, abdominal pains, diarrhoea, anorexia, and loss of weight are sometimes encountered. These occur mainly in the presence of accompanying gastro-intestinal disease (e.g. amoebiasis or bacterial infections of the gut) or in cases where large daily doses (>300 mg) have been given for a prolonged period (>3 months).

Accidental overdosage: There is no specific antidote for Lampréne and treatment is symptomatic.

Pharmaceutical precautions *Storage:* Protect from heat and moisture.

Legal category POM.

Package quantities *Capsules:* Containers of 100.

Further information Lampréne (clofazimine) is a highly active preparation which exerts a potent inhibitory effect on the growth of *Mycobacterium leprae* (Hansen's bacillus) and which almost invariably also elicits good effects in patients intolerant of, or resistant to, other anti-leprosy drugs. During long-term treatment with sulphone preparations, Lampréne serves to guard against the development of resistance. No cross-resistance between Lampréne and either dapsone or rifampicin has been reported.

Lampréne also possesses anti-inflammatory properties and is suitable for treating lepra reactions occurring in the course of treatment with other drugs. Not only can such reactions be suppressed by administering Lampréne, but in patients previously requiring corticosteroid therapy it is possible to reduce the dosage of corticosteroids gradually and finally to withdraw them completely. During treatment with sulphone preparations, concomitant administration of Lampréne reduces the frequency of lepra reactions.

In rare cases where lepra reactions also occur under treatment with Lampréne, they can be combated by temporarily increasing the dosage.

Product licence number 0001/5041.

LOPRESOR®

Presentation The active ingredient metoprolol tartrate is presented as: pale red, round, slightly biconvex, film-coated tablets with slightly bevelled edges: approximately 9 mm diameter, engraved GEIGY on one side and scored on the other side. Each tablet contains 50 mg.

Lopresor is also available as: light blue, round, slightly biconvex, film-coated tablets with slightly bevelled edges: approximately 10 mm diameter, engraved GEIGY on one side and scored on the other. Each tablet contains 100 mg.

Uses Beta-adrenergic receptor blocking agent.

Indications: Hypertension and angina pectoris, cardiac arrhythmias, especially supraventricular tachyarrhythmias. Adjunct to treatment of thyrotoxicosis.

Dosage and administration *Administration:* Lopresor tablets should be administered orally.

Dosage: Hypertension: Initially a dose of 100 mg in the morning should be prescribed.

Depending upon the response the dosage may be increased to 400 mg daily given in single or divided doses. Over the dosage range most patients may be expected to respond rapidly and satisfactorily. A further reduction in blood pressure may be achieved if Lopresor is used in conjunction with an antihypertensive diuretic such as chlorthalidone or a vasodilator such as hydralazine.

Lopresor may be administered with benefit both to previously untreated patients with hypertension and to those in whom the response to previous therapy is inadequate. In the latter type of patient the previous therapy may be continued and Lopresor added in to the regime with adjustment of the previous therapy if necessary.

Angina Pectoris: 50–100 mg, twice or three times daily.

In general a significant improvement in exercise tolerance and reduction of anginal attacks may be expected with a dose of 50–100 mg twice daily.

Cardiac arrhythmias: A dosage of 50 mg two or three times daily is usually sufficient. If necessary the dose can be increased up to 300 mg per day administered in divided doses.

Following the treatment of an acute arrhythmia with Lopresor Injection (see separate Data Sheet) continuation therapy with Lopresor tablets should be initiated 4–5 hours later. In such cases, the initial oral dose should not exceed 50 mg three times daily.

Thyrotoxicosis: 50 mg four times daily.

If it becomes necessary to discontinue treatment with a beta-blocker, one should withdraw the drug gradually, i.e. over a period of 8–10 days, because abrupt interruption of the medication – particularly in cases of ischaemic heart disease – may be followed by an acute deterioration in the patient's condition.

Contra-indications, warnings, etc

Contra-indications: Atrioventricular block of second or third degree, uncontrolled heart failure, severe bradycardia and cardiogenic shock.

Precautions: Metoprolol has proved safe in a large number of asthmatic patients: although it is a selective beta-blocker it is prudent to exercise care in the treatment of patients with chronic obstructive pulmonary disease. Therapy with a β_2 -stimulant may become necessary or current therapy require adjustment.

Lopresor must not be used in patients with untreated heart failure, but may be administered when the failure has been brought under control. Where heart failure appears during treatment with Lopresor the drug may be temporarily withdrawn until the failure has been controlled.

Lopresor should be given cautiously to patients with metabolic acidosis.

Lopresor may mask some of the symptoms of hypoglycaemia. Since treatment with a beta-blocker may affect carbohydrate metabolism, it may be necessary to adjust the dose of the hypoglycaemic agent in labile and insulin dependent diabetics.

Lopresor therapy should be brought to the attention of the anaesthetist prior to general anaesthesia. In a patient under beta-blockade, the anaesthetic selected should be one exhibiting as little negative inotropic activity as possible (halothane/nitrous oxide).

Like other beta-blockers, Lopresor should not be given in combination with antiarrhythmic agents of the verapamil type because their concomitant use may result in bradycardia, hypotension or even cardiac arrest.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenoceptor blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuance of the beta-adrenoceptor blocking drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-blocker should be gradual.

Pregnancy: The administration of Lopresor during pregnancy, as with other drugs is advised only if there are compelling reasons. If Lopresor is used during pregnancy and lactation special attention should be paid to the foetus, neonate and breast fed infant for undesirable effects of the drug's beta-blocking action (e.g. slowing of heart rate).

Side-effects: Gastro-intestinal upsets; sleep disturbances and exertional tiredness may occasionally occur. In most cases these effects have been transient or have disappeared after a reduction in dosage. In rare cases, feelings of coldness in the extremities may occur. As with other beta-blockers excessive bradycardia may occasionally occur; bronchospasm and heart failure may occasionally be precipitated in susceptible patients.

Accidental overdosage: The symptoms of overdosage will be marked bradycardia and possible hypotension. Bradycardia may be overcome by the administration of intravenous atropine sulphate (0.25–2.0 mg) which will decrease vagal tone. If bradycardia persists sympathomimetic drugs such as metaraminol or noradrenaline should be employed. These drugs have a pressor effect which may also help to overcome hypotension. The positive inotropic and chronotropic properties of glucagon may be useful when it is given in doses of 1–5 mg (max. 10 mg).

Pharmaceutical precautions *Storage:* Protect from heat, light and moisture.

Legal category POM.

Package quantities *Lopresor 50 mg:* Bottles of 100 tablets.

Lopresor 100 mg: Bottles of 100 tablets. Calendar packs of 56 tablets.

Further information Lopresor is a cardioselective beta-adrenergic blocking agent. It has a relatively greater blocking effect on beta₁-receptors (i.e. those mediating adrenergic stimulation of heart rate and contractility and release of free fatty acids from fat stores) than on beta₂-receptors, which are chiefly involved in broncho- and vasodilation.

Lopresor therefore possesses the therapeutically desirable effects of shielding the heart and blood vessels from the harmful effects of excessive adrenergic challenge during stress or exercise with minimal interference with respiratory function or vascular tone.

In hypertension Lopresor is effective during the first few days of treatment and reaches its full effect in a few weeks. No orthostatic hypotension or tendency to collapse has been observed even with fairly high doses.

In angina pectoris Lopresor diminishes the elevation of pulse rate and blood pressure in response to exercise or stress so permitting more efficient use of the oxygen supply to the myocardium. Ischaemic ECG changes are usually prevented or normalised and the patient's capacity for exercise is increased.

Because of its cardioselectivity, Lopresor can be administered even to patients with obstructive respira-

tory disorders, provided that adequate precautions are taken.

Product licence numbers

Tablets 50 mg 0001/0065

Tablets 100 mg 0001/0066

LOPRESOR* INJECTION ▼

Presentation Lopresor ampoules each containing 5 mg metoprolol tartrate in a clear, colourless solution of 5 ml volume.

Uses *Mode of action:* Lopresor is a cardioselective β_1 -receptor blocker exhibiting no intrinsic sympathomimetic activity.

Indications: Beta-adrenergic receptor blocking agent: Disturbances of cardiac rhythm, especially supraventricular tachyarrhythmias.

Dosage and administration Initially up to 5 mg, injected i.v. (1–2 mg/minute). The injection can be repeated at 5 minute intervals until a satisfactory response has been obtained. A total dose of 10–15 mg generally proves sufficient; raising the dose to 20 mg or more does not usually yield better results.

During anaesthesia: 2–4 mg injected slowly i.v. at induction is usually sufficient to prevent the development of dysrhythmias during anaesthesia. The same dosage can also be used to control dysrhythmias developing during anaesthesia. Further injections of 2 mg may be given as required to a maximum overall dose of 10 mg.

The active substance of Lopresor has a plasma half-life of 3–5 hours. The duration of its beta-blocking effect is dose-dependent: 4 hours after intravenous administration of 20 mg Lopresor, for example, its beta-blocking effect in healthy subjects is reduced by one-half.

Contra-indications, warnings, etc

Contra-indications: Atrioventricular block of second or third degree, uncontrolled heart failure, severe bradycardia or cardiogenic shock.

Precautions: Intravenous injections of Lopresor are suitable only for acute administration in hospitalised patients and should be given only if facilities are available for monitoring the electrocardiogram and blood pressure.

The i.v. administration of Lopresor to patients with a systolic blood pressure below 100 mm Hg (13.3 kPa) should only be made with special care as it can result in a further significant decrease of blood pressure.

In a patient under beta-blockade, the anaesthetic selected should be one exhibiting as little negative inotropic activity as possible (e.g. halothane/nitrous oxide).

Metoprolol has proved safe in a large number of asthmatic patients, although it is a selective beta-blocker it is prudent to exercise care in the treatment of patients with chronic obstructive pulmonary disease. Therapy with a β_2 stimulant may become necessary or current therapy require adjustment.

Lopresor must not be used in patients with untreated heart failure, but may be administered when the failure has been brought under control. Where heart failure appears during treatment with Lopresor the drug may be temporarily withdrawn until the failure has been controlled.

Lopresor may mask some of the symptoms of hypoglycaemia. Since treatment with a beta-blocker may affect carbohydrate metabolism, it may be necessary to

adjust the dose of the hypoglycaemic agent in labile and insulin dependent diabetics.

Lopresor should be given cautiously to patients with metabolic acidosis.

Like other beta-blockers, Lopresor should not be given in combination with antiarrhythmic agents of the verapamil type, because their concomitant use may result in bradycardia, hypotension, or even cardiac arrest.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenoceptor blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuance of the beta-adrenoceptor blocking drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-blocker should be gradual.

Pregnancy: The administration of Lopresor during pregnancy as with other drugs is advised only if there are compelling reasons. If Lopresor is used during pregnancy and lactation special attention should be paid to the foetus, neonate and breast fed infants for undesirable effects of the drug's beta-blocking action (e.g. slowing of heart rate).

Side-effects: As with other beta-blockers, a marked fall in blood pressure may sometimes occur following intravenous injection of Lopresor.

Excessive bradycardia may also occasionally occur and bronchospasm and heart failure may occasionally be precipitated in susceptible patients.

Overdosage: The symptoms of overdosage will be marked bradycardia and possible hypotension. Bradycardia may be overcome by the administration of intravenous atropine sulphate (0.25–2.0 mg) which will decrease vagal tone. If bradycardia persists – sympathomimetic drugs such as metaraminol or noradrenaline should be employed. These drugs have a pressor effect which may also help to overcome hypotension. The positive inotropic and chronotropic properties of glucagon may be useful when it is given in doses of 1–5 mg (max. 10 mg).

Pharmaceutical precautions *Storage:* Protect from light.

Legal category POM.

Package quantities Packs of 10 ampoules.

Further information In patients with paroxysmal atrial tachycardia, use of Lopresor often enables normal sinus rhythm to be re-established or the ventricular rate to be reduced. Similarly, in cases of atrial fibrillation or flutter, Lopresor is not only capable of lowering the ventricular rate but, in some instances, may, also restore sinus rhythm. In addition, it diminishes the number of ventricular extrasystoles. When given in therapeutic doses, Lopresor exerts less influence on peripheral blood vessels and bronchial muscle than non-cardioselective beta-blockers. Provided adequate caution is observed it can therefore also be administered in the presence of obstructive pulmonary diseases. When employed at higher dosage ranges, however, Lopresor may in rare cases increase airways resistance in the same manner as other selective beta-blockers.

Product licence number 0001/0086.

LOPRESOR* SR

Presentation The active ingredient metoprolol tartrate

is presented as pale yellow, round, film-coated tablets with slightly convex faces; approximately 10.1 mm diameter, imprinted GEIGY on one side and CDC on the other. Each tablet contains 200 mg metoprolol tartrate in a sustained release formulation.

Uses Selective beta-adrenergic receptor blocking agent.

Indications: Hypertension and angina pectoris.

Dosage and administration *Administration:* Lopresor SR tablets should be administered orally.

Dosage: Hypertension: Initially one Lopresor SR tablet should be given in the morning. Most patients may be expected to respond satisfactorily within 14 days to one or two tablets once daily. Further antihypertensive effect may be achieved by the addition of a diuretic such as chlorthalidone or a vasodilator such as hydralazine.

Lopresor SR may be administered with benefit to both previously untreated patients with hypertension and to those in whom the response to previous therapy is inadequate. In the latter type of patient therapy may be continued and Lopresor SR added to the regime with adjustment of previous therapy if necessary.

Angina pectoris: Initially, one Lopresor SR tablet daily. The dose may be increased to two tablets once daily if required. In general a significant improvement in exercise tolerance and a reduction of anginal attacks may be expected with a dose of one Lopresor SR tablet daily.

Contra-indications, warnings, etc

Contra-indications: Atrioventricular block of second or third degree, uncontrolled heart failure, severe bradycardia and cardiogenic shock.

Precautions: Metoprolol has proved safe in a large number of asthmatic patients, although it is a selective beta-blocker it is prudent to exercise care in the treatment of patients with chronic obstructive pulmonary disease. Therapy with a β_2 stimulant may become necessary or current therapy require adjustment.

Lopresor SR must not be used in patients with untreated heart failure, but may be administered when the failure has been brought under control. Where heart failure appears during treatment with Lopresor SR the drug may be temporarily withdrawn until the failure has been controlled.

Lopresor SR may mask some of the symptoms of hypoglycaemia. Since treatment with a beta-blocker may affect carbohydrate metabolism, it may be necessary to adjust the dose of the hypoglycaemic agent in labile and insulin dependent diabetics.

Lopresor SR should be given cautiously to patients with metabolic acidosis.

Lopresor SR therapy should be brought to the attention of the anaesthetist prior to general anaesthesia. In a patient under beta-blockade, the anaesthetic selected should be one exhibiting as little negative inotropic activity as possible, (e.g. halothane/nitrous oxide).

There have been reports of skin rash and/or dry eyes associated with the use of beta-adrenergic blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuance of the beta-adrenoceptor blocking drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-blocker should be gradual.

Like other beta-blockers, Lopresor SR should not be given in combination with antiarrhythmic agents of the

verapamil type because their concomitant use may result in bradycardia, hypotension or even cardiac arrest.

If it becomes necessary to discontinue treatment with a beta-blocker, one should withdraw the drug gradually i.e. over a period of 8–10 days, because abrupt interruption of the medication – particularly in cases of ischaemic heart disease – may be followed by an acute deterioration in the patient's condition.

Pregnancy: The administration of Lopresor SR during pregnancy as with other drugs is advised only if there are compelling reasons. If Lopresor SR is used during pregnancy and lactation special attention should be paid to the foetus, neonate and breast fed infant for undesirable effects of the drug's beta-blocking action (e.g. slowing of heart rate).

Side-effects: Gastro-intestinal upsets, sleep disturbances and exertional tiredness may occasionally occur. In most cases these effects have been transient or have disappeared after a reduction in dosage. In rare cases, feelings of coldness in the extremities may occur.

As with other beta-blockers excessive bradycardia may occasionally occur, bronchospasm and heart failure may occasionally be precipitated in susceptible patients.

Overdosage: The symptoms of overdosage will be marked bradycardia and possible hypotension.

Bradycardia may be overcome by the administration of intravenous atropine sulphate (0.25–2.0 mg) which will decrease vagal tone. If bradycardia persists, sympathomimetic drugs such as metaraminol or noradrenaline should be employed. These drugs have a pressor effect which may also help to overcome hypotension. The positive inotropic and chronotropic properties of glucagon may be useful when it is given in doses of 1–5 mg (maximum 10 mg).

Pharmaceutical precautions No special precautions.

Legal category POM.

Package quantities Lopresor SR packs of 28 tablets (2 × 14 calendar pack foils).

Further information Lopresor SR is a sustained release preparation of Lopresor (metoprolol tartrate) designed to release this selective beta-adrenergic receptor blocking drug so that maximal response is obtained within 4–6 hours while the pharmacological action is sustained for 24 hours. This formulation reduces peak serum concentration which, in turn, minimises unwanted side-effects of beta-blockade.

Lopresor SR is a cardioselective beta-adrenergic blocking agent. It has relatively greater blocking effects on β_1 receptors (i.e. those mediating adrenergic stimulation of heart rate and contractility and release of free fatty acids from fat stores) than on β_2 receptors which are chiefly involved in broncho- and vasodilation.

Lopresor SR therefore possesses the therapeutically desirable effect of shielding the heart and blood vessels from the harmful effects of extensive adrenergic challenge during stress or exercise with minimal interference with respiratory function or vascular tone.

In hypertension, Lopresor SR is effective during the first few days of treatment and reaches its full effect in fourteen days. No orthostatic hypotension or tendency has been observed even with fairly high doses.

Because of its cardioselectivity, Lopresor SR may be administered even to patients with obstructive respiratory disorders, provided that adequate precautions are taken.

Product licence number 0001/0081.

LOPRESORETIC*

Presentation Off-white, round, bi-convex film-coated tablets with slightly bevelled edges, approximately 10 mm diameter, with a breakline on one face and GEIGY impressed on the other. Each tablet contains metoprolol tartrate (active ingredient of Lopresor*) 100 mg and chlorthalidone BP (active ingredient of Hygroton*) 12.5 mg.

Uses Antihypertensive agent.

Principal therapeutic actions: Lopresor (metoprolol tartrate) is a beta-adrenergic receptor blocking agent which is relatively more selective for beta-1-receptors which mediate heart rate and force of contraction, free fatty acid release and renin production, than for beta-2-receptors which mediate bronchodilation and peripheral vascular dilation. Consequently Lopresor protects the heart and cardiovascular system from excessive sympathetic stimulation caused by either physical or emotional activity while having relatively little effect on the airways or on peripheral vascular responses. The attenuation of the effects of excessive sympathetic drive on the heart result in a fall in myocardial work and oxygen consumption. Systolic pressure is reduced and this is most noticeable in hypertensive subjects, in whom the diastolic pressure is also reduced significantly.

Hygroton (chlorthalidone BP) is a long acting diuretic which lowers both systolic and diastolic pressures in hypertensive patients. In general the higher the initial blood pressure, the greater the fall brought about by Hygroton. The addition of Hygroton enhances the antihypertensive effect of the selective beta-blocker thus resulting in a better control in a higher proportion of patients. This is probably the result of the two active ingredients having different sites of action, Lopresor acting on the heart and possibly also centrally while Hygroton reduces peripheral resistance.

Indications: In the treatment of mild and moderate hypertension.

Dosage and administration *Dosage:* Lopresoretic tablets should be administered orally. Initial starting dose, one tablet in the morning. However, in patients who have not been successfully controlled by a diuretic or beta-blocking drug used alone, a dose of two tablets in the morning would be appropriate. Most patients may be expected to respond within 14 days.

Occasionally the response may be unsatisfactory in which case it may be found beneficial to raise the dosage to 3-4 tablets given in single or divided doses and/or to add a vasodilator such as hydralazine at an initial dose of 25 mg twice daily, increasing as necessary.

Contra-indications, warnings, etc

Contra-indications: Atrioventricular block of second or third degree, uncontrolled heart failure, severe bradycardia, cardiogenic shock and marked renal insufficiency. Anti-diuretic effect has been reported following concomitant treatment with diuretics and lithium. As with all products which contain diuretics, Lopresoretic tablets are contra-indicated during lithium therapy.

Precautions: Metoprolol has proved safe in a large number of asthmatic patients, although it is a selective beta-blocker it is prudent to exercise care in the treatment of patients with chronic obstructive pulmonary disease. Therapy with a β_2 stimulant may become necessary or current therapy require adjustment.

As with other preparations containing beta-blockers, Lopresoretic tablets must not be used in patients with

untreated heart failure, but may be administered when the failure has been brought under control. Where heart failure appears during treatment with Lopresoretic the drug may be temporarily withdrawn until the failure has been controlled.

Lopresoretic may mask some of the symptoms of hypoglycaemia. Since treatment with a beta-blocker may affect carbohydrate metabolism, it may be necessary to adjust the dose of the hypoglycaemic agent in labile and insulin dependent diabetics. Chlorthalidone may also decrease glucose tolerance.

Hyperuricaemia may occasionally occur and acute attacks of gout may be precipitated. Where prolonged elevation of serum uric acid occurs the concurrent use of a uricosuric agent will reverse the hyperuricaemia without loss of therapeutic effect.

Lopresoretic tablets should be given cautiously to patients with metabolic acidosis.

Lopresoretic therapy should be brought to the attention of the anaesthetist prior to general anaesthesia. In a patient under beta-blockade, the anaesthetic selected should be one exhibiting as little negative inotropic activity as possible, (e.g. halothane/nitrous oxide).

If it becomes necessary to discontinue treatment with a beta-blocker one should withdraw the drug gradually i.e. over a period of 8-10 days, because abrupt interruption of the medication - particularly in cases of ischaemic heart disease - may be followed by an acute deterioration in the patient's condition.

Like other beta-blockers, Lopresoretic should not be given in combination with antiarrhythmic agents of the verapamil type because their concomitant use may result in bradycardia, hypotension or even cardiac arrest.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenoceptor blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuance of the beta-adrenoceptor blocking drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-blocker should be gradual.

Because of their chlorthalidone content, Lopresoretic tablets should be used with care in patients with some degree of renal impairment.

Pregnancy: The administration of Lopresoretic during pregnancy as with other drugs is advised only if there are compelling reasons. If Lopresoretic is used during pregnancy and lactation special attention should be paid to the foetus, neonate and breast fed infant for undesirable effects of the drug's beta-blocking action (e.g. slowing of the heart).

Side-effects: Gastro-intestinal upsets; sleep disturbances and exertional tiredness may occasionally occur. In most cases these effects have been transient or have disappeared after a reduction in dosage. In rare cases, feelings of coldness in the extremities may occur.

As with other beta-blockers excessive bradycardia may occasionally occur; bronchospasm and heart failure may occasionally be precipitated in susceptible patients.

Like other diuretics with a similar mode of action, chlorthalidone may cause latent gout or latent diabetes mellitus to become manifest. In a few cases, allergic skin reactions, mild anorexia, nausea, constipation and diarrhoea have been reported. There have been isolated reports of leucopenia, but these are rare.

Overdosage: The symptoms of overdosage will be marked bradycardia and possible hypotension. Bradycardia may be overcome by the administration of

intravenous atropine sulphate (0.25–2.0 mg) which will decrease vagal tone. If bradycardia persists – sympathomimetic drugs such as metaraminol or noradrenaline should be employed. These drugs have a pressor effect which may also help to overcome hypotension. The positive inotropic and chronotropic properties of glucagon may be useful when it is given in doses of 1–5 mg (max. 10 mg). Supportive treatment aimed at maintaining normal fluid and electrolyte balance is essential.

Pharmaceutical precautions Protect from moisture.

Legal category POM.

Package quantities Cartons of 56 tablets consisting of blister pack modules each containing 14 tablets (each carton represents 2–8 weeks treatment depending on the dose).

Further information Lopresoretic tablets simplify the management of hypertension since they combine two effective antihypertensive agents which act together in a complementary manner. In addition to the two modes of action already described, the Lopresor component prevents the increase in plasma renin which occurs as a result of diuretic therapy.

Lopresoretic tablets contain a selective beta-blocker and thus can be administered to patients with obstructive respiratory disease provided they have access to a beta-2-stimulant bronchodilator; being a selective agent, Lopresoretic is less likely to interfere with the action of beta-2-stimulants.

Product licence number 0001/0085.

MEDOMIN®

Presentation The active ingredient, Heptabarbitalone, is presented as: white, quarter-scored tablets approximately 11 mm diameter impressed 'Medomin' containing 200 mg heptabarbitalone.

Uses Heptabarbitalone is a barbiturate with a hypnotic action of the intermediate type; if taken in the proper therapeutic dose, it produces sleep for about 3 to 6 hours.

Hypnotic: Insomnia, oral premedication for major and minor surgery.

Dosage and administration Medomin is given orally in tablet form.

Hypnotic dosage: Adults: 1 or 2 tablets. For insomnia tablets should be taken with a warm drink half to one hour before retiring.

Contra-indications, warnings, etc

Contra-indications: Uncontrolled pain. Children and young adults. The elderly and the debilitated. Pregnancy and breast feeding. Patients with a history of alcohol or drug abuse. Porphyria.

Precautions: A reduction in dosage may be required in patients with renal or hepatic failure.

Barbiturates cause induction of liver enzymes so that the availability and blood levels of drugs given concurrently which are metabolised in the liver may be affected. These include the following: coumarin-type anticoagulants, systemic steroids (including oral contraceptives), phenytoin, griseofulvin, rifampicin, phenothiazines such as chlorpromazine, tricyclic antidepressants).

Side-effects: Adverse effects include drowsiness, seda-

tion, unsteadiness, vertigo and inco-ordination. Performance and alertness may be impaired during the first week of administration. Patients should be warned of the possible hazard when driving or operating machinery. These effects may be potentiated by alcohol.

Less frequent adverse reactions may include a "hangover" effect, paradoxical excitement, confusion, memory defects and skin rashes in patients who may be sensitive to this type of drug.

Accidental overdosage: Elimination of drug: Induction of vomiting, gastric lavage, and/or forced diuresis; reduce absorption of drug with activated charcoal or laxatives.

Respiratory depression: Maintenance of airway, if necessary by endotracheal intubation or tracheotomy; artificial respiration may be required. Antibiotics should be given if aspiration of vomit is suspected, or signs of bronchopneumonia are present.

Surveillance: Routine surveillance of respiration, ECG, blood pressure, body temperature, urine excretion, central venous pressure, and serum electrolytes; in severe cases, monitoring of arterial pH, pO₂, pCO₂, alkali reserve, and EEG is advised.

Pharmaceutical precautions Storage: Tablets – protect from heat and moisture.

Legal category POM.

Package quantities Tablets 200 mg: Blister packs of 100.

Further information Barbiturates have a high addiction potential. Long term use of high dosage for short periods may lead to tolerance and subsequently to physical and psychological dependence. Symptoms of dependence include confusion, defective judgement and loss of emotional control. Withdrawal symptoms occur following long-term normal use (and particularly following abuse) on rapid cessation of barbiturate treatment. Symptoms include nightmares, irritability and insomnia and, in severe cases, tremors, delirium, convulsions and death. Withdrawal symptoms have been reported in neonates following barbiturate treatment during pregnancy and labour.

Product licence number Tablets 0001/5014.

PARAZOLIDIN®

Presentation The active ingredients, Phenylbutazone BP and Paracetamol BP, are presented as: white, flat compressed tablets, approximately 13 mm diameter, scored on one side, impressed GEIGY on the other side. Containing Phenylbutazone BP 50 mg and Paracetamol BP 500 mg.

Uses Combined analgesic agent: Rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, secondary carcinoma (particularly in bone) and spondylitis.

Dosage and administration Parazolidin is given orally in tablet form.

Dosage: 1 or 2 tablets two or three times a day.

Contra-indications, warnings, etc

Contra-indications: Parazolidin should not be given in the presence of: oedema or hypertension where there is a danger of cardiac decompensation. Parazolidin is also

contra-indicated in the presence of renal and hepatic disease, including recent hepatitis.

History of gastro-intestinal ulceration, blood dyscrasia, drug rash or known sensitivity to pyrazoles.

Precautions: History of dyspepsia.

Since Parazolidin may potentiate the action of coumarin-type anticoagulants by displacement from plasma protein binding, frequent estimations of prothrombin levels should be undertaken when these drugs are administered concurrently. Similarly, Parazolidin potentiates certain oral hypoglycaemic agents and sulphonamides, the dosage of which may need reducing.

It is suggested that Parazolidin be used with caution in pregnant women, weighing the potential risks against the possible benefits.

Side-effects: Gastro-intestinal intolerance or bleeding due to Parazolidin may occur.

Drug rashes, oedema, haematemesis, salivary gland swelling, goitre and jaundice due to intrahepatic cholestasis or parenchymal hepatitis have also been reported.

Blood dyscrasias (agranulocytosis, thrombocytopenia, aplastic anaemia) may occur suddenly after a small dose or insidiously after prolonged therapy, particularly in the elderly. Blood counts should be monitored regularly both before and during therapy. Therapy should be stopped if symptoms suggestive of these complications arise (e.g. bruising, fever, sore throat and rash).

Isolated occurrences of an 'acute pulmonary syndrome' – marked by dyspnoea, fever, shadows in radiographs of the lungs, and sometimes also by eosinophilia – have been reported. Although a causal relationship has not been proven, the drug should be withdrawn at first signs of this potentially serious syndrome, for the treatment of which corticosteroids and supportive cardiotherapy may be necessary.

Adverse effects of phenylbutazone therapy should always be weighed against the severity of the patient's condition and the expected clinical effect.

Accidental overdosage: Overdosage may cause hepatic necrosis. There is no specific antidote to Parazolidin, and treatment is symptomatic. Immediate treatment consists of forced emesis to recover undigested tablets. This is followed by gastric lavage.

Pharmaceutical precautions *Storage:* Protect from heat and moisture.

Legal category POM.

Package quantities *Tablets:* Containers of 100 and 500.

Further information By combining the threefold long-acting anti-inflammatory and antipyretic activity of Butazolidin with the rapid analgesic activity of Paracetamol, Parazolidin enables lower than normal doses of either substance to be administered concurrently without loss of therapeutic effect and with a reduced risk of side-effects.

Product licence number 0001/5018.

PERTOFRAN®

Presentation The active ingredient, Desipramine Hydrochloride BP, is presented as: pale apricot-pink, sugar-coated tablets, bi-convex, 5.6mm diameter and imprinted GEIGY on one side. Containing 25 mg Desipramine Hydrochloride BP in each tablet.

Uses *Antidepressant:* Symptoms of depressive illness.

Dosage and administration Pertofran is given orally in tablet form.

Adult dosage: 1 × 25 mg tablet three times a day for the first three days, increasing to 2 tablets three or four times daily. It will often be possible for the daily dose to be given as a single dose at night.

Elderly: Patients over 60 years of age may respond to lower doses of Pertofran than those recommended, usually 25 mg daily initially. The initial dose should be increased with caution under close supervision.

Children: Not established.

Contra-indications, warnings, etc

Contra-indications: Recent myocardial infarction. Any degree of heart block or other cardiac arrhythmias. Mania. Severe liver disease. Narrow angle glaucoma. Retention of urine.

Precautions: The elderly are particularly liable to experience adverse reactions, especially agitation, confusion and postural hypotension. Avoid if possible in patients with a history of epilepsy or with symptoms of bladder neck obstruction e.g. prostatic hypertrophy. Patients posing a high suicide risk require close initial supervision. Tricyclic anti-depressants potentiate the central nervous depressant action of alcohol.

Anaesthetics given during tri/tetracyclic antidepressant therapy may increase the risk of arrhythmias and hypotension. If surgery is necessary, the anaesthetist should be informed that a patient is being so treated.

As improvement in depression may not occur during the first four weeks of treatment, patients should be closely monitored during this period.

Pertofran may initially impair alertness. Patients should be warned of the possible hazard when driving or operating machinery.

Cardiac arrhythmias and severe hypotension are likely to occur with high dosage or in deliberate overdosage. They may also occur in patients with pre-existing heart disease taking normal dosage.

Do not use during pregnancy, especially during the first and last trimesters, unless there are compelling reasons. There is no evidence as to drug safety in humans; there is evidence of harmful effects in pregnancy in animals, when given in exceptionally high doses.

Nursing mothers should be advised to cease breast feeding.

Drug interactions: Pertofran should not be given concurrently with, or within 2 weeks of cessation of therapy with monoamine oxidase inhibitors.

Pertofran may decrease the antihypertensive effect of guanethidine, debrisoquine, bethanidine and possibly clonidine. It would be advisable to review all antihypertensive therapy during treatment with tricyclic antidepressants.

Pertofran should not be given with sympathomimetic agents such as adrenaline, ephedrine, isoprenaline, noradrenaline, phenylephrine and phenylpropanolamine.

Barbiturates may decrease and neuroleptics and methylphenidate may increase respectively the plasma level of tricyclic antidepressants.

Side-effects: The following adverse effects, although not necessarily all reported with Pertofran, have occurred with other tricyclic antidepressants:

Atropine-like side effects including dry mouth, disturbances of accommodation, tachycardia, constipation

and hesitancy of micturition are common early in treatment, but usually lessen.

Serious adverse effects are rare; the following have been reported: Impaired liver function and jaundice, hypomania, epileptiform convulsions. Bone marrow depression, including leucopenia, eosinophilia and thrombocytopenia. Agranulocytosis has occasionally occurred in patients receiving tricyclic antidepressants. It is advisable to perform blood counts during treatment with tri/tetracyclic antidepressants, especially if the patient develops fever, sore throat or other signs of infection.

Other possible adverse effects include drowsiness, sweating, postural hypotension, tremor and skin rashes. Interference with sexual function may occur.

Psychotic manifestations, including mania and paranoid delusion, may be exacerbated during treatment with tricyclic antidepressants.

Although not indicative of addiction, withdrawal symptoms may occur on abrupt cessation of therapy and include insomnia, irritability and excessive perspiration.

Adverse effects such as withdrawal symptoms, respiratory depression and agitation have been reported in neonates whose mothers had taken Pertofran during the last trimester of pregnancy.

Accidental overdose: Major symptoms of overdose include coma, convulsions and cardiovascular disturbances. Gastric lavage should be performed immediately and patients removed to an intensive care unit where cardiac monitoring is possible. Although there is no specific antidote, slow intravenous injection of physostigmine has yielded particularly good results in the presence of central nervous disturbances (coma, myoclonia, athetoid movements); physostigmine may possibly also exert a favourable effect on cardiac arrhythmias. The single dose, which must be individually adapted to the patient's requirements and can, if necessary, be repeated several times, is 1–4 mg for adults and 0.5 mg for children.

Pharmaceutical precautions *Storage:* Protect from moisture.

Legal category POM.

Package quantities *Tablets 25 mg:* Containers of 100 and 1,000.

Further information Nil.

Product licence number 0001/5019.

SINTHROME®

Presentation The active ingredient, Nicoumalone BP, is presented as white, compressed, scored tablets, approx. 7 mm diameter, impressed GEIGY on one side containing 4 mg in each tablet.

Pink, compressed tablets, approx. 5 mm diameter, containing 1 mg in each tablet.

Uses Oral anticoagulant. Arterial thrombosis and embolism, venous thrombosis and embolism, thrombo-phlebitis. Myocardial infarction, coronary thrombosis. For prophylaxis whenever thromboembolic complications may be anticipated and particularly in rheumatic heart disease with atrial fibrillation.

Dosage and administration Sinthrome is given orally in tablet form.

Sinthrome is available as 1 mg and 4 mg tablets and

the use of both tablets in combination enables control of oral anticoagulant therapy with a single daily dose.

Initial therapy: If the prothrombin time is within the normal range, the following daily dosage schedule is suggested:

First day	8–12 mg
Second day	4–8 mg

Maintenance therapy: Maintenance dosage of Sinthrome varies from patient to patient and must be determined on the basis of regular laboratory estimations of the clotting time of the patient's blood as determined by Quick's one-stage test – prothrombin time. The daily maintenance dosage will vary also depending upon the intensity of treatment indicated and any other drugs that the patient may be taking. In general, however, this will lie between 1 mg and 8 mg daily. In practice the upper dosage limits are seldom required and only rarely need to be exceeded, when Sinthrome is the only drug administered (see 'Precautions').

The aim of therapy is to keep the prothrombin time between the limits of a predetermined therapeutic range. As an indication of the degree of anticoagulation, the prothrombin time itself is not of much help to the practising physician unless he knows also the range of prothrombin time which reflects a satisfactory response. This range varies between different laboratories according to the sensitivity of the thromboplastin used in the test.

A uniform system of testing and reporting has been proposed and is widely used. This is based on the use of a standardised thromboplastin, the British (Manchester) Comparative Thromboplastin (BCT). The control prothrombin time for this reagent is 12 seconds and the therapeutic range for adequate anticoagulation is 22–36 seconds. The ratio of patient's prothrombin time (using the BCT) to control is termed the British Ratio (BR), the therapeutic range for which is 1.8–3.0. A patient on Sinthrome, therefore, with a British Ratio of less than 1.8 would need an increase in dosage, whilst a BR over 3.0 would require a reduction in dosage.

Not all hospitals use the BCT and in these cases control prothrombin times and therapeutic ranges will possibly differ from those referred to above. If in doubt it is best to contact the laboratory concerned.

Sometimes the result may be expressed as percentage prothrombin activity or coagulation valency. This is an indication of the prothrombin content of the patient's blood relative to a normal control of 100%. In view of the variability of thromboplastin from different sources it is difficult to give precise therapeutic ranges using this system.

However, the usually accepted therapeutic range using Quick's one-stage test, expressed as a percentage activity and using a saline dilution curve, would be 25–20% if human brain thromboplastin is used.

The administration of daily requirements of Sinthrome and the taking of blood specimens for laboratory purposes should occur at the same time of day, but not after a heavy meal or a meal rich in fats.

Withdrawal of Sinthrome entails no additional risk of thromboembolism; hence, at the end of treatment, it is not necessary to give gradually diminishing doses.

Contra-indications, warnings, etc

Contra-indications: Sinthrome is contra-indicated in all haemorrhagic conditions, including peptic ulceration and occult risks implied by severe hypertension, sub-acute bacterial endocarditis and surgical procedures.

This is absolute in operations on the central nervous system. Sinthrome is also contra-indicated in severe liver disease. Similarly in pregnancy and parturition the use of Sinthrome is contra-indicated.

Precautions: Administration with other drugs.

1. Potentiation of anticoagulant effect: Sinthrome is transported in plasma, the major proportion being as an inactive complex with plasma proteins. Many drugs will compete with Sinthrome for these protein binding sites, the consequence being displacement of Sinthrome into the plasma and an increase in anticoagulant activity. This phenomenon has been reported with such commonly used drugs as clofibrate, indomethacin, oxyphenbutazone, paracetamol and phenylbutazone. In addition to this effect, aspirin and the salicylates have a direct anticoagulant action through an effect on platelet adhesiveness. Patients taking Sinthrome who also require treatment with these or any other drugs with similar affinity for protein-binding sites may need a reduction of their anticoagulant dosage.

Administration of broad-spectrum antibiotics may decrease the requirements for Sinthrome and potentiate its effects due to interference with the synthesis of vitamin K.

2. Inhibition of anticoagulant effect. Barbiturates, chloral hydrate, glutethimide, cardiac glycosides, carbamazepine and other drugs which are metabolised in the liver may increase the metabolism of Sinthrome by stimulation of liver microsomal enzyme systems. Diuretics can reduce anticoagulant activity by altering the concentration of plasma clotting factors. During combined therapy with these drugs it is likely that anticoagulant requirements will be increased, whilst cessation of treatment will necessitate a reduction in the dosage of Sinthrome.

Intramuscular injections during anticoagulant therapy may leave haematomata. Care is also necessary when subcutaneous injection is contemplated, but intravenous injections may be given without danger.

Side-effects: Sinthrome is well tolerated and side-effects such as nausea, loss of appetite, headache or giddiness are rarely encountered. Like other anticoagulants, Sinthrome may rarely cause skin necrosis, particularly after childbirth and during the menopause.

Accidental overdosage: Where slight bleeding occurs a temporary reduction or withdrawal of Sinthrome dosage will usually result in control being re-established. Transfusions of fresh whole blood are also effective. Where these measures are inadequate to control haemorrhage, the administration of vitamin K is the best measure for treating Sinthrome overdosage. However, this should normally be reserved for serious haemorrhages since, after administration of vitamin K, the patient remains resistant to anticoagulant therapy for some time.

Pharmaceutical precautions Sinthrome is light-sensitive. Store and dispense in the original or a dark container.

Legal category POM.

Package quantities Tablets 1 mg: Containers of 500 and 200.

Tablets 4 mg: Containers of 500 and 100.

Further information *Laboratory controls:* The patient's prothrombin time should be determined before anticoagulant therapy is begun. Should the initial level be abnormal, treatment should be instituted with caution.

During the early stages of anticoagulant therapy, or when any of the patient's drugs are changed (see Precautions), daily determination of prothrombin time should be made. The frequency of laboratory evaluation can be reduced when the patient's response to Sinthrome has been established.

Product licence numbers

Tablets 1 mg 0001/5021

Tablets 4 mg 0001/5022

STEROXIN[®]-HYDROCORTISONE

Presentation The active ingredients, Chlorquinaldol and Hydrocortisone BP, are presented as: yellowish-white soft cream, in a vanishing cream base, containing chlorquinaldol 3% and Hydrocortisone BP 1%.

Uses *Antibacterial, antifungal, anti-inflammatory:* Topical treatment of eczematous, mycotic and bacterial skin conditions in adults and children.

Infantile and adult eczema, allergic eczema, varicose eczema, neurodermatitis. Contact dermatitis due to cosmetics, chemicals, including detergents, clothing materials, plant secretion, seborrhoeic dermatitis, impetigo, folliculitis, sycosis barbae, otitis externa, varicose and indolent ulcers, ano-genital pruritus.

Dosage and administration

Method of application. Steroxin-Hydrocortisone Cream should be applied to the affected area of the skin two or three times a day. If desired a light dressing may be applied for protective purposes. The cream may leave a pale yellow stain on the skin and on clothing, but this is easily removed by washing with soap.

Contra-indications, warnings, etc Steroxin-Hydrocortisone Cream is not suitable for application to the eye or to mucous membranes, where it may give rise to some irritation.

Precautions: It has been shown that corticosteroids can be absorbed by eczematous skin. Long-term administration of Steroxin-Hydrocortisone to large areas should therefore, be avoided if possible regardless of whether occlusion is used. If such administration is unavoidable precautions similar to those taken with patients receiving small doses of oral steroids should be observed.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established, however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

In infants, long-term continuous topical therapy should be avoided. Adrenal suppression can occur even without occlusion.

Pharmaceutical precautions *Storage:* Protect from heat.

Dilutions: Diluents or other additives to this formulation are not recommended.

Legal category POM.

Package quantities Tubes of 20 g.

Further information Nil.

Product licence number 0001/5044.

SYMMETREL[®] CAPSULES

Presentation The active ingredient, amantadine hydrochloride, is presented as: brownish-red hard gelatin capsules, imprinted GEIGY in white on both cap and body, each containing 100 mg amantadine hydrochloride.

Uses Parkinson's disease. Herpes zoster. Prophylaxis and treatment of A₂, A/NJ/1/76, A/Moscow/77, A/Hong Kong/77, A/Brazil/11/78 and A/Alaska/78 influenza.

Note: *Herpes zoster:* It is recommended that the drug be given to elderly or debilitated patients in whom the physician suspects that a severe and painful rash could occur.

A₂ Influenza: It is suggested that Symmetrel be given to patients suffering from clinical influenza in whom complications might be expected to occur. In addition, Symmetrel is recommended prophylactically in cases particularly at risk, for example those with chronic respiratory disease or debilitating conditions, the elderly, those living in crowded conditions and for individuals in families where influenza has already been diagnosed, or those in essential services who are unvaccinated.

Dosage and administration *Parkinson's disease:* Initially one capsule daily for the first week, increasing to one capsule twice daily. In combination therapy, Symmetrel may be administered at these same doses. In many cases it will be possible after a few days to reduce the dosage of the other anti-Parkinson drug without loss of benefit.

Herpes zoster: Treatment should be started as soon as possible after the diagnosis has been made. The dosage is 1 capsule twice daily for 14 days. If post-herpetic pain persists after this period it is recommended that treatment be continued for a further 14 days.

Treatment of A₂ influenza: Adults: 1 capsule to be taken twice daily for five to seven days or at the discretion of the physician.

Prophylaxis of A₂ influenza: Adults: 1 capsule twice daily for as long as protection from influenza infection is required. In most instances this is expected to be for 7–10 days.

Treatment and prophylaxis in children: 10–15 years: 1 capsule every morning for the recommended period or at the discretion of the physician.

Below 10 years: As a reduced dosage is unavailable, it is not recommended that the drug be prescribed for this age group.

It is not recommended that the dosage be increased above that stated.

It may be found convenient to administer the drug at about 8 a.m. and 4 p.m.

Contra-indications, warnings, etc

Contra-indications: It is not recommended that Symmetrel be used to treat individuals who are subject to convulsions, or who have a history of gastric ulceration.

Symmetrel should not be used in patients with severe renal disease.

Although there are no specific contra-indications to the drug being administered to a person who has received a recent dose of influenza vaccine, such administration would be considered unnecessary.

Precautions: Symmetrel should be used with caution in patients with confusional or hallucinatory states.

As Symmetrel is excreted by the kidneys a cautious dosage scheme is recommended in the presence of impaired renal function. Care should be exercised when administering Symmetrel to patients with liver disease.

Patients who note central nervous system effects or blurring of vision should be advised to avoid situations where alertness is essential.

When employing Symmetrel in combination with other anti-Parkinson drugs, a watch should be kept for the latter's side-effects. Symmetrel may aggravate central nervous, gastro-intestinal or other side-effects provoked by anticholinergic drugs or L-dopa.

Although no incompatibilities with other drugs have become known, caution should be exercised if dextro-amphetamine or other central nervous stimulants are used during Symmetrel therapy.

Peripheral oedema thought to be due to an alteration in the responsiveness of peripheral vessels may occur in some patients during treatment with Symmetrel. This should be considered when the drug is prescribed for those with congestive heart failure.

Use in pregnancy: Symmetrel has not been studied in pregnant women. The use of this drug in women of child-bearing age should be undertaken only after weighing the possible risks to the foetus against benefit to the patient. Symmetrel has been reported to be embryotoxic and teratogenic in rats at 50 mg/kg/day, about 12 times the recommended human dose, but not at 37 mg/kg/day. Embryotoxic and teratogenic effects were not seen in rabbits which received up to 25 times the usual recommended adult human dose.

Side-effects: Symmetrel is well tolerated. Nevertheless, side-effects may occur in some patients. Livedo reticularis and peripheral oedema have been noted. In addition central nervous system effects such as nervousness, insomnia, dizziness and convulsions or psychic reactions such as hallucinations, or feeling of detachment have occurred. Skin rash has occurred rarely in patients sensitive to the drug.

Accidental overdose: There is no specific antidote to Symmetrel. Supportive therapeutic measures aimed at those symptoms arising from excessive central stimulation should be instituted.

Pharmaceutical precautions *Storage:* Protect from heat and light.

Legal category POM.

Package quantities *Capsules 100 mg:* Containers of 100.

Further information Symmetrel warrants serious consideration in the management of herpes zoster. This has been confirmed by a large double-blind study involving 100 patients which showed that Symmetrel can significantly reduce the proportion of patients experiencing pain of long duration.

Symmetrel has been shown to have an antiviral activity predominantly against A₂ influenza. When administered as a treatment to patients with clinical influenza, it results in a reduction of the duration of fever and symptoms of the infection. Used prophylactically, Symmetrel will provide rapid cover against influenza infection which will last for as long as therapy is continued.

The majority of studies have shown that Symmetrel does not interfere with normal antibody production.

Product licence number 0001/0006.

SYMMETREL[®] SYRUP

Presentation A clear, citrus flavoured syrup containing 50 mg/5 ml of the active ingredient amantadine hydrochloride.

Uses Parkinson's disease. Herpes zoster.

Note: *Herpes zoster:* It is recommended that the drug be given to elderly or debilitated patients in whom the physician suspects that a severe and painful rash could occur.

Dosage and administration *Parkinson's disease:* Initially 100 mg daily for the first week, increasing to 100 mg twice daily. In combination therapy, Symmetrel may be administered at these same doses. In many cases it will be possible after a few days to reduce the dosage of the other anti-Parkinson drug without loss of benefit.

Herpes zoster: The treatment should be started as soon as possible after the diagnosis has been made. The dosage is 100 mg Symmetrel twice daily for 14 days. If post-herpetic pain persists after this period it is recommended that treatment be continued for a further 14 days.

It is not recommended that the dosage be increased above that stated.

It may be found convenient to administer the drug at about 8 a.m. and 4 p.m.

Contra-indications, warnings, etc

Contra-indications: It is not recommended that Symmetrel be used to treat individuals who are subject to convulsions, or who have a history of gastric ulceration.

Symmetrel should not be used in patients with severe renal disease.

Precautions: Symmetrel should be used with caution in patients with confusional or hallucinatory states.

As Symmetrel is excreted by the kidneys a cautious dosage scheme is recommended in the presence of impaired renal function. Care should be exercised when administering Symmetrel to patients with liver disease.

Patients who note central nervous system effects or blurring of vision should be advised to avoid situations where alertness is essential.

When employing Symmetrel in combination with other anti-Parkinson drugs, a watch should be kept for the latter's side-effects. Symmetrel may aggravate central nervous, gastro-intestinal or other side-effects provoked by anticholinergic drugs or L-dopa.

Although no incompatibilities with other drugs have become known, caution should be exercised if dextroamphetamine or other central nervous stimulants are used during Symmetrel therapy.

Peripheral oedema thought to be due to an alteration in the responsiveness of peripheral vessels may occur in some patients during treatment with Symmetrel. This should be considered when the drug is prescribed for those with congestive heart failure.

Use in pregnancy: Symmetrel has not been studied in pregnant women. The use of this drug in women of child-bearing age should be undertaken only after weighing the possible risks to the foetus against benefit to the patient. Symmetrel has been reported to be embryotoxic and teratogenic in rats at 50 mg/kg/day, about 12 times the recommended human dose, but not at 37 mg/kg/day. Embryotoxic and teratogenic effects were not seen in rabbits which received up to 25 times the usual recommended adult human dose.

Side-effects: Symmetrel is well tolerated. Nevertheless,

side-effects may occur in some patients. Livedo reticularis and peripheral oedema have been noted. In addition central nervous system effects such as nervousness, insomnia, dizziness and convulsions or psychic reactions such as hallucinations, or feeling of detachment have occurred. Skin rash has occurred rarely in patients sensitive to the drug.

Accidental overdosage: There is no specific antidote to Symmetrel. Supportive therapeutic measures aimed at those symptoms arising from excessive central stimulation should be instituted.

Pharmaceutical precautions *Storage:* Protect from heat and light.

Legal category POM.

Package quantities 150 ml bottles.

Further information Symmetrel warrants serious consideration in the management of herpes zoster. This has been confirmed by a large double-blind study involving 100 patients which showed that Symmetrel can significantly reduce the proportion of patients experiencing pain of long duration.

Product licence number 0001/0067.

TANDACOTE[®]

Presentation The active ingredient Oxyphenbutazone BP is presented as: round, bi-convex, sugar-coated enteric tablets each containing 100 mg, pink in colour, of approximately 8.6 mm, and imprinted GEIGY on one side.

Uses Rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and acute gout.

Osteoarthritis of the spine and degenerative disc disease presenting as lumbago, sciatica or radiculitis.

Reiter's disease and other seronegative (non-rheumatoid) arthropathies.

Inflammation associated with certain ocular diseases including uveitis, scleritis, keratitis, and postoperative inflammation.

Prevention and treatment of severe postoperative inflammation and swelling, particularly in relation to facio-maxillary, ophthalmic, laryngeal and plastic surgery.

Swelling and pain due to *serious* sprains, strains fractures and contusions.

Bursitis or synovitis associated with recognised rheumatic disorders.

Moderate to extensive superficial thrombophlebitis.

Dosage and administration Tandacote is given orally in tablet form.

Adults: For the initial 48 hours, 400–600 mg daily in divided doses with meals. Maintenance doses should be reduced to the minimum amount that will provide continuous therapeutic control, usually 200–300 mg daily.

Note: In acute gout a maximum dosage of 800 mg daily may be necessary.

Paediatric: Dosage in the range 5–10 mg per kg, with emphasis on the lower end of the scale. The small 7-year-old and younger children should be given 1 × 100 mg tablet per day.

In children of average weight between 7–12 years o

age, 2 × 100 mg tablets in divided doses per day is sufficient.

Contra-indications, warnings, etc

Contra-indications: Tandacote is contra-indicated in the presence of oedema or hypertension where there is danger of cardiac decompensation.

Tandacote is also contra-indicated in the presence of renal and hepatic disease, including recent hepatitis.

History of gastro-intestinal ulceration, blood dyscrasia, drug rash or known sensitivity to pyrazoles.

Precautions: History of dyspepsia.

Since Tandacote may potentiate the action of coumarin-type anticoagulants by displacement from plasma protein binding, frequent estimations of prothrombin levels should be undertaken when these drugs are administered concurrently. Similarly, Tandacote potentiates certain oral hypoglycaemic agents and sulphonamides, the dosage of which may need reducing.

It is suggested that Tandacote be used with caution in pregnant women, weighing the potential risks against the possible benefits.

Side-effects: Gastro-intestinal intolerance or bleeding due to Tandacote may occur.

Drug rash, oedema, haematemesis, salivary gland swelling, goitre and jaundice due to intrahepatic cholestasis or parenchymal hepatitis have also been reported.

Blood dyscrasias (agranulocytosis, thrombocytopenia, aplastic anaemia) may occur suddenly after a small dose or insidiously after prolonged therapy, particularly in the elderly. Blood counts should be monitored regularly both before and during therapy. Therapy should be stopped if symptoms suggestive of these complications arise (e.g. bruising, fever, sore throat and rash).

Isolated occurrences of an 'acute pulmonary syndrome' – marked by dyspnoea, fever, shadows in radiographs of the lungs, and sometimes also by eosinophilia – have been reported. Although a causal relationship has not been proven, the drug should be withdrawn at first signs of this potentially serious syndrome, for the treatment of which corticosteroids and supportive cardiotherapy may be necessary.

Adverse effects of oxyphenbutazone therapy should always be weighed against the severity of the patient's condition and the expected clinical effect.

Accidental overdosage: There is no antidote to Tandacote and treatment is symptomatic. Immediate treatment consists of forced emesis to recover undigested tablets. This is followed by gastric lavage.

Pharmaceutical precautions *Storage:* Protect from heat and moisture.

Legal category POM.

Package quantities *Tablets 100 mg:* Containers of 100 and 500.

Further information Tandacote is formulated as an enteric sugar-coated tablet containing a core of 100 mg Tanderil and has proved consistently reliable and therapeutically effective. Tandacote has been subjected to both single and repeated dose studies which show that Tandacote produces blood levels of the same order as Tanderil sugar-coated tablets. The satisfactory long-term usage of potent antirheumatic drugs is all too frequently a compromise between therapeutic efficacy and undesirable side-effects, particularly distressing gastro-intestinal upsets. Whilst the administration of supplementary antacids can prove helpful in these patients, formulation

research and clinical evaluation clearly demonstrates that a reliable enteric coated tablet is designed to reduce the problems of direct gastric irritation associated with most antirheumatic drugs.

Product licence number 0001/0051.

TANDALGESIC*

Presentation The active ingredients, Oxyphenbutazone BP and Paracetamol BP, are presented as: white, scored, compressed tablets approximately 14.5 mm diameter, impressed GEIGY on one side and containing Oxyphenbutazone BP 50 mg and Paracetamol BP 500 mg in each tablet.

Uses *Combined analgesic agent:* Rheumatic diseases including: rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and spondylosis.

Dosage and administration Tandalgesic is given orally in tablet form.

Initially: 1 or 2 tablets three times daily, reducing to the minimum required to maintain therapeutic control.

Contra-indications, warnings, etc

Contra-indications: Tandalgesic is contra-indicated in the presence of oedema or hypertension where there is danger of cardiac decompensation.

Tandalgesic is also contra-indicated in the presence of renal and hepatic disease, including recent hepatitis.

History of gastro-intestinal ulceration, blood dyscrasia, drug rash or known sensitivity to pyrazoles.

Precautions: History of dyspepsia.

Since Tandalgesic may potentiate the action of coumarin-type anticoagulants by displacement from plasma protein binding, frequent estimations of prothrombin levels should be undertaken when these drugs are administered concurrently. Similarly, Tandalgesic potentiates certain oral hypoglycaemic agents and sulphonamides, the dosage of which may need reducing.

It is suggested that Tandalgesic be used with caution in pregnant women, weighing the potential risks against the possible benefits.

Side-effects: Gastro-intestinal intolerance or bleeding due to Tandalgesic may occur.

Drug rash, oedema, haematemesis, salivary gland swelling, goitre and jaundice due to intrahepatic cholestasis or parenchymal hepatitis have also been reported.

Blood dyscrasias (agranulocytosis, thrombocytopenia, aplastic anaemia) may occur suddenly after a small dose or insidiously after prolonged therapy, particularly in the elderly. Blood counts should be monitored regularly both before and during therapy. Therapy should be stopped if symptoms suggestive of these complications arise (e.g. bruising, fever, sore throat and rash).

Isolated occurrences of an 'acute pulmonary syndrome' – marked by dyspnoea, fever, shadows in radiographs of the lungs, and sometimes also by eosinophilia – have been reported. Although a causal relationship has not been proven, the drug should be withdrawn at first signs of this potentially serious syndrome, for the treatment of which corticosteroids and supportive cardiotherapy may be necessary.

Adverse effects of oxyphenbutazone therapy should always be weighed against the severity of the patient's condition and the expected clinical effect.

Accidental overdosage: Overdose can cause hepatic

necrosis. There is no specific antidote for Tandalgesic and treatment is symptomatic. Immediate treatment consists of forced emesis to recover undigested tablets. This is followed by gastric lavage.

Pharmaceutical precautions *Storage:* Tablets – protect from heat and moisture.

Legal category POM.

Package quantities *Tablets:* Containers of 100.

Further information During the past decade, an increasing bibliography of clinical papers has established Tanderil as a standard drug in the treatment of a wide range of painful rheumatic and traumatic inflammatory conditions.

The combination of 50 mg Tanderil and rapidly acting paracetamol 500 mg, therefore, provides an overall analgesic and antirheumatic effectiveness, and offers rapid pain relief for those patients who need more than a simple analgesic but do not yet require full doses of Tanderil.

Product licence number 0001/5025.

TANDERIL®

Presentation The active ingredient, Oxyphenbutazone BP, is presented as: coffee-coloured, sugar-coated tablets, bi-convex, approx. 8.6 mm diameter, and imprinted GEIGY on one side, containing 100 mg in each tablet.

Also cream-coloured, waxy suppositories, each containing Oxyphenbutazone BP 250 mg.

Uses Rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and acute gout.

Osteoarthritis of the spine and degenerative disc disease presenting as lumbago, sciatica or radiculitis.

Reiter's disease and other seronegative (non-rheumatoid) arthropathies.

Inflammation associated with certain ocular diseases, including uveitis, scleritis, keratitis, and post-operative inflammation.

Prevention and treatment of severe postoperative inflammation and swelling, particularly in relation to facio-maxillary, ophthalmic, laryngeal and plastic surgery.

Swelling and pain due to *serious* sprains, strains, fractures and contusions.

Bursitis or synovitis associated with recognised rheumatic disorders.

Moderate to extensive superficial thrombophlebitis.

Dosage and administration Tanderil is generally given orally in tablet form but can be administered rectally by suppository.

Oral dose (adult): For the initial 48 hours, 400–600 mg daily in divided doses with meals. Patients with sensitive stomachs should be given a sodium free antacid at the same time. Maintenance doses should be reduced to the minimum amount that will provide continuous therapeutic control, usually 200–300 mg daily.

Note: In acute gout a maximum dosage of 800 mg daily may be necessary.

Rectal dosage (adult): Suppositories of Tanderil (250 mg) have been found to be a therapeutically effective alternative or supplementary dosage form.

1 or 2 Tanderil suppositories (250 mg–500 mg) daily,

as a sole therapy achieves a clinical response similar to that obtained by oral maintenance therapy.

When a suppository is required on retiring to control night pain, the total daily dosage of tablets and suppositories should not exceed 650 mg initially, with subsequent reduction to the maximum combined maintenance dose (350 mg).

Paediatric: Dosage in the range 5–10 mg/kg, with emphasis on the lower end of the scale. The small 7-year-old and younger children should be given 1 × 100 mg tablet per day, in children of average weight between 7–12 years of age, 2 × 100 mg tablets in divided doses per day is sufficient.

Contra-indications, warnings, etc

Contra-indications: Tanderil is contra-indicated in the presence of oedema or hypertension where there is danger of cardiac decompensation.

Tanderil is also contra-indicated in the presence of renal and hepatic disease, including recent hepatitis.

History of gastro-intestinal ulceration, blood dyscrasia, drug rash or known sensitivity to pyrazoles.

Precautions: History of dyspepsia.

Since Tanderil may potentiate the action of coumarin-type anticoagulants by displacement from plasma protein binding, frequent estimation of prothrombin levels should be undertaken when these drugs are administered concurrently. Tanderil also potentiates certain oral hypoglycaemic agents and sulphonamides, the dosage of which may need reducing.

It is suggested that Tanderil be used with caution in pregnant women, weighing the potential risks against the possible benefits.

Side-effects: Gastro-intestinal intolerance or bleeding due to Tanderil may occur.

Drug rash, oedema, haematemeses, salivary gland swelling, goitre and jaundice due to intrahepatic cholestasis or parenchymal hepatitis have also been reported.

Blood dyscrasias (agranulocytosis, thrombocytopenia, aplastic anaemia) may occur suddenly after a small dose or insidiously after prolonged therapy, particularly in the elderly. Blood counts should be monitored regularly both before and during therapy. Therapy should be stopped if symptoms suggestive of these complications arise (e.g. bruising, fever, sore throat and rash).

Isolated occurrences of an 'acute pulmonary syndrome' – marked by dyspnoea, fever, shadows in radiographs of the lungs, and sometimes also by eosinophilia – have been reported. Although a causal relationship has not been proven, the drug should be withdrawn at first signs of this potentially serious syndrome, for the treatment of which corticosteroids and supportive cardiotherapy may be necessary.

Adverse effects of oxyphenbutazone therapy should always be weighed against the severity of the patient's condition and the expected clinical effect.

Accidental overdose: There is no specific antidote to Tanderil and treatment is symptomatic. Immediate treatment consists of forced emesis to recover undigested tablets. This is followed by gastric lavage.

Pharmaceutical precautions *Storage:* Tablets – protect from moisture. Suppositories – protect from heat.

Legal category POM.

Package quantities *Tablets 100 mg:* Containers of 100 and 1,000.

Suppositories 250 mg: Boxes of 5 and 50.

Further information Tanderil (Oxyphenbutazone BP) is a pyrazole compound. It is a potent non-hormonal antirheumatic agent with anti-inflammatory, analgesic and antipyretic properties, of proven efficacy for the treatment of a wide range of rheumatic or traumatic inflammatory conditions.

Product licence numbers

Tablets 0001/5024
Suppositories 0001/5045

TEGRETOL®

Presentation The active ingredient, Carbamazepine BP, is presented as: 100 mg white, compressed tablets, 7 mm diameter, impressed GEIGY on one side, breakline on the other.

200 mg white, scored, compressed tablets, 9 mm diameter impressed GEIGY on one side.

400 mg white, rod shaped, flat faced tablets with bevelled edges, 17 mm long, 5.5 mm wide and 5.3 mm thick, impressed GEIGY/GEIGY on one face with breakline. Other face impressed LR with breakline.

Syrup: White, with a flavour of caramel, containing 100 mg/5ml Carbamazepine BP.

Uses *Anticonvulsant and analgesic:* Epilepsy (grand mal and temporal lobe). Trigeminal neuralgia.

Dosage and administration Tegretol is given orally in either tablet or syrup form.

Epilepsy: It is advised that a gradually increasing dosage scheme is used and this should be adjusted to suit the needs of the individual patient.

Adults: Initially: 100–200 mg once or twice a day, followed by a slow increase until the best response is obtained, often 800–1,200 mg daily. In some instances, 1,600 mg daily may be necessary.

Children: Usual dosage 10–20 mg/kg bodyweight daily in divided doses.

Age up to 1 year: 1–2 × 100 mg tablets or 5–10 ml syrup per day.

1–5 years: 2–4 × 100 mg tablets or 10–20 ml syrup per day.

5–10 years: 2–3 × 200 mg tablets or 20–30 ml syrup per day.

10–15 years: 3–5 × 200 mg tablets or 30–50 ml syrup per day.

It may be helpful to monitor the plasma concentration of Tegretol to ensure adequate therapeutic levels. In most cases the optimum therapeutic plasma level for Tegretol ranges from 3–10 mcg/ml (13–42 mc moles/l).

Trigeminal neuralgia: The individual dosage requirements of Tegretol vary considerably, depending on the age and weight of the patient. It is recommended that the initial dose be small, particularly in the frail and elderly, and that 100 mg tablets or syrup are used in the first instance.

The dose may be increased gradually until a satisfactory clinical response is obtained, which in some instances necessitates 1,600 mg Tegretol daily. It has been found that in the majority of patients a dosage of 200 mg three or four times a day is sufficient to maintain a pain-free state. It is suggested that Tegretol is taken only during acute stage of the condition and not as a prophylactic measure.

Contra-indications, warnings, etc

Contra-indications: Previous drug sensitivity to Tegretol.

Because Tegretol depresses AV-conduction, it is inadvisable to administer this drug to patients with atrioventricular conduction abnormalities unless paced.

Precautions: Use in pregnancy: If pregnancy occurs in a woman receiving Tegretol, or if the problem of initiating treatment with Tegretol arises during pregnancy, the drug's potential benefits must be carefully weighed against its possible hazards for the unborn child. This applies particularly to the first 3 months of pregnancy.

Induction of hepatic enzymes in response to Tegretol may have the effect of diminishing the activity of certain drugs that are metabolised in the liver. In patients receiving oral anticoagulant medication, it may be necessary to adjust the dosage when Tegretol is prescribed.

Tegretol may also reduce the activity of those hormones contained in the combined oral contraceptive pill. This may present clinically as breakthrough bleeding or spotting. We would recommend that patients taking Tegretol and requiring oral contraception should receive a preparation containing not less than 50 mcg of oestrogen or use some alternative non-hormonal method of contraception.

Tegretol should not be administered with, or within two weeks of cessation of MAOI therapy.

In rats treated with carbamazepine for two years, the incidence of tumours of the liver was found to be increased. There is, however, no evidence to indicate that this observation has any significant bearing on the therapeutic use of the drug.

Note: In keeping with current opinion it is suggested that the level of serum folic acid is observed during anticonvulsant therapy.

Side-effects: Dizziness may occur, but this is much less likely to be noted if the gradually increasing dosage which has been recommended is followed.

Diplopia may occur and is usually dose dependent. Drowsiness, dry mouth, diarrhoea, nausea and vomiting have also occurred amongst some patients, but these symptoms are less frequent and seldom severe.

Hyponatraemia has been reported in a few patients on higher doses of Tegretol. Similarly oedema has occasionally been noted. Both are reversible upon reduction in dosage.

A generalised erythematous rash, in some cases severe, has been reported in about 3% of patients. This has been found to disappear leaving no sequelae on stopping therapy. Isolated occurrences of exfoliative dermatitis, leucopenia, thrombocytopenia, agranulocytosis, aplastic anaemia, cholestatic jaundice and acute renal failure have been reported.

It is suggested that blood count is checked at regular intervals during the early stages of treatment.

Accidental overdosage: There is no specific antidote. Signs of overdosage include somnolence increasing to unconsciousness, hyporeflexia and convulsions. Treatment recommended:

1. Simple aspiration of gastric contents.
2. Maintenance of airway, initially by means of pharyngeal airway. If necessary, pass endotracheal tube or perform a tracheotomy.
3. Routine temperature, pulse, respiration and blood pressure readings.
4. Administration of oxygen.
5. Curarisation and artificial ventilation have been successfully employed in one case of toxic overdosage which developed convulsions.

Pharmaceutical precautions *Storage:* Syrup – Protect from heat and light, keep container tightly closed.

Dilutions: Mucilage of Tragacanth BP is suitable when used in a 1 : 1 ratio with Tegretol Syrup.

After dilution the syrup should be used within 14 days.

Legal category POM.

Package quantities *Tablets 100 mg:* Containers of 100 and 500.

Tablets 200 mg: Containers of 100 and 500.

Tablets 400 mg: Containers of 100.

Syrup 100 mg/5 ml: Bottles of 300 ml.

Further information Nil.

Product licence numbers

Tablets 100 mg 0001/5027

Tablets 200 mg 0001/5028

Tablets 400 mg 0001/0088

Syrup 100 mg/5 ml 0001/0050

TOFRANIL*

Presentation The active ingredient, Imipramine Hydrochloride BP, is presented as: red-brown, sugar-coated tablets, bi-convex, 5.6 mm diameter, imprinted GEIGY on one side, each containing 25 mg.

Red-brown, sugar-coated, triangular-shaped tablets, 5.6 mm diameter, imprinted GEIGY on one side, each containing 10 mg.

Syrup – white, with a cream flavour, containing the equivalent to 25 mg/5 ml Imipramine Hydrochloride BP.

Uses *Antidepressant/anti-enuretic:* Endogenous depression, reactive depression, involutional depression. Relief of nocturnal enuresis in children. Supplementary to chronic rheumatic pain.

Dosage and administration Tofranil is given orally in tablet or syrup form.

Adults: 1 × 25 mg three times daily for the first three days increasing to 2 × 25 mg three or four times daily. It will often be possible for the daily dose of 75 mg or 150 mg to be given as a single dose, usually at night. In hospitalised patients, or in patients under close medical supervision, it is sometimes necessary to give doses up to 225 mg or more in cases of severe depression.

Chronic rheumatic pain: 1 × 25 mg three times daily, added to the existing treatment regimen. In patients over 60 years of age, 1 × 10 mg three times daily will usually provide an adequate therapeutic effect.

Elderly: Patients over 60 years of age may respond to lower doses of Tofranil than those recommended, usually 10 mg at night initially, increasing to 10–25 mg three times daily. The initial dose should be increased with caution and under close supervision.

Children (for nocturnal enuresis only)

6–7 years (weight 20–25 kg or 44–55 lbs) 25 mg

8–11 years (weight 25–35 kg or 55–77 lbs) 25–50 mg

Over 11 years (weight 35–54 kg or 77–119 lbs) 50–75 mg

The dose should be taken just before bedtime.

To ensure lasting improvement Tofranil should be continued for six to eight weeks after which time it should gradually be withdrawn. Should a relapse occur, a further course of treatment should not be started until a full physical examination has been made.

Contra-indications, warnings, etc

Contra-indications: Recent myocardial infarction. Any degree of heart block or other cardiac arrhythmias. Mania. Severe liver disease. Narrow angle glaucoma. Infants and children under 6 years. Retention of urine.

Precautions: The elderly are particularly liable to experience adverse reactions, especially agitation, confusion and postural hypotension (see Dosage). Behavioural changes may occur in children receiving Tofranil for the treatment of nocturnal enuresis. Avoid if possible in patients with a history of epilepsy or with symptoms of bladder neck obstruction e.g. prostatic hypertrophy. Patients posing a high suicide risk require close initial supervision. Tricyclic antidepressants potentiate the central nervous depressant action of alcohol.

Anaesthetics given during tri/tetracyclic antidepressant therapy may increase the risk of arrhythmias and hypotension. If surgery is necessary, the anaesthetist should be informed that a patient is being so treated.

Care should be taken in the treatment of nursing mothers with Tofranil, since there is evidence that small amounts of imipramine may be excreted in breast milk.

As improvement in depression may not occur during the first two to four weeks treatment, patients should be closely monitored during this period.

Tofranil may initially impair alertness. Patients should be warned of the possible hazard when driving or operating machinery.

Use in pregnancy: Do not use during pregnancy especially during the first and last trimesters, unless there are compelling reasons. There is no, or inadequate evidence of safety of the drug in human pregnancy; there is evidence of harmful effects in pregnancy in animals when given in exceptionally high doses.

Drug interactions: Tofranil should not be given concurrently with, or within 2 weeks of cessation of therapy with monoamine oxidase inhibitors.

Tofranil may decrease the antihypertensive effect of guanethidine, debrisoquine, bethanidine and possibly clonidine. It would be advisable to review all antihypertensive therapy during treatment with tricyclic antidepressants.

Tofranil should not be given with sympathomimetic agents such as adrenaline, ephedrine, isoprenaline, noradrenaline, phenylephrine and phenylpropanolamine.

Barbiturates may decrease and methylphenidate and neuroleptics may increase respectively the plasma level of Tofranil.

Side-effects: Atropine-like side-effects including dry mouth, disturbances of accommodation, tachycardia, constipation and hesitancy of micturition are common early in treatment, but usually lessen.

Other possible adverse effects include drowsiness, sweating, postural hypotension, tremor and skin rashes. Interference with sexual function may occur.

Serious adverse effects are rare; the following have been reported: Impaired liver function and jaundice, hypomania, epileptiform convulsions. Bone marrow depression, including leucopenia, eosinophilia and thrombocytopenia. Agranulocytosis has occasionally occurred in patients receiving tricyclic antidepressants. It is advisable to perform blood counts during treatment with tri/tetracyclic antidepressants, especially if the patient develops fever, sore throat or other signs of infection.

Cardiac arrhythmias and severe hypotension are likely to occur with high dosage or in deliberate overdosage.

They may also occur in patients with pre-existing heart disease taking normal dosage.

Psychotic manifestations, including mania and paranoid delusion, may be exacerbated during treatment with tricyclic antidepressants.

Although not indicative of addiction, withdrawal symptoms may occur on abrupt cessation of therapy and include insomnia, irritability and excessive perspiration.

Adverse effects such as withdrawal symptoms, respiratory depression and agitation have been reported in neonates whose mothers had taken Tofranil during the last trimester of pregnancy.

Accidental overdosage: Major symptoms of overdosage include coma, convulsions and cardiovascular disturbances. Gastric lavage should be performed immediately and patients removed to an intensive care unit where cardiac monitoring is possible. Treatment is symptomatic. Although there is no specific antidote, slow intravenous injection of physostigmine has yielded particularly good results in the presence of central nervous disturbances (coma, myoclonia, athetoid movements); physostigmine may possibly also exert a favourable effect on cardiac arrhythmias. The single dose, which must be adapted to the patient's requirements and can, if necessary, be repeated several times, is 1–4 mg for adults and 0.5 mg for children.

Pharmaceutical precautions *Storage:* Syrup – protect from heat; keep containers tightly closed. Tablets – protect from moisture.

Dilutions: Syrup – for dilutions down to 15 mg/5 ml, boiled distilled or de-ionised water can be used. For dilutions below 15 mg/5 ml, the recommended diluent is equal parts simple Syrup BP and freshly prepared Mucilage of Tragacanth BP. After dilution the solution should be used within a few days.

Legal category POM.

Package quantities *Tablets 25 mg:* Blister packs of 100.

Tablets 10 mg: Blister packs of 100.

Syrup 25 mg/5 ml: Bottles of 150 ml.

Further information Nil.

Product licence numbers

Tablets 25 mg 0001/5029

Tablets 10 mg 0001/5030

Syrup 25 mg/5 ml 0001/5032

VOLTAROL®

Presentation Tablets containing 25 mg diclofenac sodium, circular, slightly biconvex with bevelled edges, yellow enteric-coated, approximately 7 mm diameter, imprinted GEIGY on one side.

Tablets containing 50 mg diclofenac sodium, circular, slightly biconvex with bevelled edges, light brown enteric coated, approximately 8 mm diameter, imprinted GEIGY on one side.

Suppositories containing 100 mg diclofenac sodium in a waxy base, yellowish-white, torpedo shaped, weighing approximately 2.00 g.

Ampoules of clear glass containing 75 mg/3 ml diclofenac sodium.

Uses *Tablets and suppositories:* Rheumatoid arthritis; osteoarthritis; low back pain and other acute musculo-skeletal disorders such as periarthritis (especially frozen shoulder), tendinitis; tenosynovitis, bursitis, sprains,

strains and dislocations; ankylosing spondylitis; acute gout; control of pain and inflammation in orthopaedic, dental and other minor surgery.

Ampoules: Acute exacerbation of rheumatoid arthritis and osteoarthritis; acute back pain; acute gout; post operative pain.

Mode of action: Voltarol is a non-steroidal agent with marked analgesic/anti-inflammatory and antipyretic properties.

Dosage and administration *Tablets:* A total of 75–150 mg daily given in two or three divided doses.

Suppositories: One suppository daily, usually administered at night. In more severe cases, combined therapy with tablets is recommended. The daily dose should not exceed 150 mg.

Ampoules: 1 × 75 mg ampoule once or twice daily intramuscularly by deep intragluteal injection into the upper outer quadrant. Following a satisfactory response to intramuscular injection, changeover to oral therapy may be initiated. Voltarol should *not* be administered by intravenous injection.

Dosage in children has not yet been established.

Contra-indications, warnings, etc *Side-effects:* Initially, some patients may complain of epigastric pain, nausea and diarrhoea, headache and slight dizziness. These side-effects are often transient, disappearing with continuation of medication.

Occasionally skin rash, peripheral oedema and abnormalities of serum transaminases have been reported.

Very rarely peptic ulcer and haematemesis or melaena have been reported, mainly in patients with a history of such disorders, or who were receiving concomitant antirheumatic medication.

Suppository: local reactions include itching, burning and increased frequency of bowel movement.

Ampoule: local reactions may include pain or a burning sensation.

Precautions: Voltarol should not be prescribed during pregnancy, unless there are compelling reasons for doing so.

Patients with a history of peptic ulcer, haematemesis or melaena, or bleeding diathesis or with severe hepatic or renal insufficiency, should be kept under close surveillance.

Voltarol has been reported to depress salicylate levels and vice versa; the clinical relevance of this phenomenon is not yet clear.

Voltarol suppositories should be used only with caution in patients with painful or irritable ano-rectal conditions.

Contra-indications: Peptic ulcer.

Voltarol is contra-indicated in asthmatic patients in whom attacks of asthma, urticaria or acute rhinitis are precipitated by aspirin or other non-steroidal anti-inflammatory agents with prostaglandin synthetase inhibiting activity.

Treatment of overdosage: There is no known antidote to Voltarol and the treatment is symptomatic. Immediate treatment consists of forced emesis to recover undigested tablets.

Pharmaceutical precautions *Storage:* Tablets – protect from heat and moisture.

Suppositories – protect from heat.

Ampoules – protect from heat and light.

Legal category POM.

Package quantities *Tablets:* Packs of 100.

Suppositories: Packs of 10.

Ampoules: packs of 10.

Further information Pharmacodynamic studies have shown no potentiation of oral hypoglycaemic and anticoagulant drugs.

Product licence numbers

Tablets 25 mg 0001/0036

Tablets 50 mg 0001/0082

Suppositories 100 mg 0001/0083

Ampoules 75 mg/3ml 0001/0091

**Trade Mark*



AMINOPLEX* 5

Presentation A solution of synthetic L-form amino acids in combination with calorie supplement. Sterile and pyrogen-free.

Active ingredients per litre: Synthetic-L-form amino acids:

L-Isoleucine	1.53 g
L-Leucine	2.33 g
L-Lysine HCl	2.74 g*
L-Methionine	1.93 g
L-Phenylalanine	2.77 g
L-Threonine	1.29 g
L-Tryptophan	0.56 g
L-Valine	1.80 g
L-Arginine	3.70 g
L-Histidine	0.89 g
L-Alanine	4.03 g
L-Glutamic acid	0.80 g
Glycine	1.77 g
L-Proline	4.83 g
L-Ornithine-L-Aspartate	0.80 g
L-Serine	0.97 g

*2.19 g as free base.

Calorie source:

Sorbitol	125 g
Ethanol	50 g

Electrolytes:

Sodium	35 mmol
Potassium	28 mmol
Magnesium	4 mmol
Chloride	43 mmol
Acetate	28 mmol

Additional nutrients:

L-Malic acid	1.85 g
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Providing: 5 g/l of utilisable nitrogen, 4.2 MJ (1000 kcal). Total energy content, 3.6 MJ (868 kcal) non-nitrogen energy content.

Hypertonic solution pH 7.4 ± 0.2

Osmolality approximately 2415 mosmol/kg.

Uses For intravenous feeding, providing in a utilisable form, basic body requirements for amino acids, calories and certain electrolytes in one solution. This provides a simple regime for short-term total intravenous feeding, or alternatively a basis for more complex nutritional programmes tailored to specific clinical requirements.

Indications are clinical situations when oral feeding is impossible or contra-indicated. Alternatively Aminoplex 5 infusion would be appropriate pre- or post-operatively or in gastro-intestinal disturbances such as malabsorptive states, where adequate nutrition cannot be achieved orally.

Dosage and administration *Adult Dose (70 kg bodyweight):* 1000–3000 ml in 24 hours by central intravenous injection.

Infusion Rate: Maximum 40ml/kg/day.

Children's dosage at physicians' discretion.

Infusion rate should be tailored to patient body weight and should be commenced slowly at 20 ml/kg/day on the first day. For the second day and thereafter the infusion rate may be increased to a maximum of 40 ml/kg/day; the aim should be to maintain a constant infusion rate over the full 24 hours of each day.

Utilisable nitrogen is provided as synthetic L-form amino acids, 1 g of nitrogen being administered with each 175 non-nitrogen kcal. In cases with greatly increased requirements, e.g. sepsis or complications of surgery where glucose may be a more appropriate energy source, patients may benefit from an alternative regimen of Aminoplex 12 plus GluCoPLEX (with or without insulin).

Contra-indications, warnings, etc Before commencing infusion with Aminoplex 5, it is important to exclude conditions which may promote the risk of acidosis; for this reason, certain patient selection criteria should be applied during regimen planning – these are:–

- Adequate circulating volume.
- Adequate liver function.
- Adequate renal function.
- Absence of acidosis or hypoxaemia.

Patients not conforming to these criteria may have elevated lactate levels; for patients in this category or where the requirement for nitrogen and calories cannot be met within the maximum recommended infusion rate of 40 ml/kg/day, a regimen of Aminoplex 12 and GluCoPLEX will be more appropriate.

Depending on the patients clinical state and electrolyte balance, there may be a need for supplementary electrolyte replacement based on biochemical monitoring. Routine supplementation with vitamins and trace elements should also be undertaken as and when necessary. Of special importance is folic acid as amino acid mixtures may precipitate acute folate deficiency; accordingly folic acid should be given daily together with B vitamins. As Aminoplex 5 contains ethanol and sorbitol, care should be taken when considering the administration of drugs which interfere with their pathways of metabolism.

Pharmaceutical precautions Check that the solution is clear, and the container undamaged. Discard if not fully used at one injection.

Store below 25°C.

Keep away from light.

Data on compatibility and levels of permissible additions of vitamins and trace elements are available from the manufacturers.

The addition of drugs to amino acid solutions should be avoided.

Legal category POM.

Package quantities Glass bottles of 1000 ml.

Further information Due to optical sensitivity of the ingredients, some colour variation of the solution may be anticipated.

Product licence number 0184/0036.

AMINOPLEX* 12

Presentation A concentrated solution of synthetic L-form amino acids. Sterile and pyrogen-free.

Active ingredients per litre: Synthetic L-form amino acids:

L-Isoleucine	3.80 g
L-Leucine	5.80 g
L-Lysine HCl*	6.80 g
L-Methionine	4.80 g
L-Phenylalanine	6.88 g
L-Threonine	3.20 g
L-Tryptophan	1.40 g
L-Valine	4.48 g
L-Arginine	9.20 g
L-Histidine	2.20 g
L-Alanine	10.00 g
L-Glutamic acid	2.00 g
Glycine	4.40 g
L-Proline	12.00 g
L-Ornithine-L-Aspartate	2.00 g
L-Serine	2.40 g
(*5.44 g as base)	

Electrolytes:

Sodium	35 mmol
Potassium	30 mmol
Magnesium	2.5 mmol
Chloride	67 mmol
Acetate	5 mmol

Additional nutrients: L-Malic acid 4.6 g.

Providing: 12.44 g/l of utilisable nitrogen. Total energy content 315 kcal (1.3MJ).

Hypertonic solution pH 7.4 ± 0.2

Osmolality approximately 830 mosmol/kg.

Uses A synthetic L-form amino acid and electrolyte mixture for intravenous administration in intravenous feeding when a high level intake of protein amino acids is required in low fluid volume and also situations where flexibility of choice of calorific substrate is preferred.

In cases with greatly increased requirements, eg. sepsis or complications of surgery and trauma, glucose is considered the appropriate energy source, and patients may benefit from a regimen of Aminoplex 12 plus GluCoPLEX (with or without insulin). Administration of Aminoplex 12 should always be accompanied by concurrent administration of a suitable energy source, for example, GluCoPLEX.

Dosage and administration *Adult Dose (70 kg bodyweight):* 500–2000 ml in 24 hours by central intravenous injection.

Infusion Rate: Maximum 40–50 drops per minute.

Children's dosage at physicians' discretion.

Contra-indications, warnings, etc Aminoplex 12 is contra-indicated in irreversible liver damage.

Moderate liver damage and uraemic states where facilities for dialysis exist are not contra-indications for the use of Aminoplex 12.

Amino acid mixtures may precipitate acute folate deficiency and folic acid should be given daily. Vitamin

B₁₂ status should be checked and prophylaxis given if necessary.

Pharmaceutical precautions Check that the solution is clear, and the container undamaged. Discard if not fully used at one injection.

Store below 25°C.

Keep away from light.

Data on compatibility and levels of permissible additions of vitamins and trace elements are available from the manufacturers.

The addition of drugs to amino acid solutions should be avoided.

Legal category POM.

Package quantities Glass bottles of 500 ml and 1000 ml.

Further information Due to optical sensitivity of the ingredients, some colour variation of the solution may be anticipated.

Product licence number 0184/0030.

AMINOPLEX* 14

Presentation A concentrated solution of synthetic L-form amino acids. Sterile and pyrogen-free.

Active ingredients per litre: Synthetic L-form amino acids:

L-Isoleucine	3.20 g
L-Leucine	4.40 g
L-Lysine HCl	8.49 g
L-Methionine	6.40 g
L-Phenylalanine	4.40 g
L-Threonine	3.20 g
L-Tryptophan	1.60 g
L-Valine	5.20 g
L-Arginine	9.20 g
L-Histidine	2.80 g
L-Alanine	14.80 g
Glycine	12.00 g
L-Proline	4.00 g
L-Ornithine-L-Aspartate	2.00 g

Electrolytes:

Sodium	35 mmol
Potassium	30 mmol
Chloride	79 mmol

Additional nutrients:

Vitamin B ₆ HCl	0.03 g
Nicotinamide	0.05 g
L-Malic acid	5.36 g

Providing: 13.4 g/l of utilisable nitrogen. Total energy content 340 kcal (1.4MJ).

Hypertonic solution pH 7.4 ± 0.2

Osmolality approximately 875 mosmol/kg.

Uses A synthetic L-form amino acid and electrolyte mixture for intravenous administration in intravenous feeding when a high level intake of protein amino acids is required in low fluid volume and also situations where flexibility of choice of calorific substrate is preferred.

In cases with greatly increased requirements, eg. sepsis or complications of surgery and trauma, glucose is considered the appropriate energy source, and patients may benefit from a regimen of Aminoplex 14 plus GluCoPLEX (with or without insulin). Administration of Aminoplex 14 should always be accompanied by

concurrent administration of a suitable energy source, for example, GluComplex.

Dosage and administration *Adult Dose (70 kg bodyweight):* 500–2000 ml in 24 hours by central intravenous injection.

Infusion Rate: Maximum 40–50 drops per minute. Children's dosage at physicians' discretion.

Contra-indications, warnings, etc Aminoplex 14 is contra-indicated in irreversible liver damage.

Moderate liver damage and uraemic states where facilities exist for dialysis are not contra-indications for the use of Aminoplex 14. Amino acid mixtures may precipitate acute folate deficiency and folic acid should be given daily. Vitamin B₁₂ status should be checked and prophylaxis given if necessary.

Pharmaceutical precautions Check that solution is clear. Discard if not fully used at one injection.

Store below 25°C.

Keep away from light.

The addition of drugs to amino-acid solutions should be avoided.

Legal category POM.

Package quantities Glass bottles of 500 ml, 10 bottles per box.

Further information Due to optical sensitivity of the ingredients some colour variation of the solution may be anticipated.

Product licence number 0184/5002.

AMINUTRIN*

Presentation A pale yellow powder with a slight odour. Contains amino acids.

Active ingredients %: Typical Analysis per 100 g.

L-Isoleucine	5.00 g
L-Leucine	9.00 g
L-Lysine	8.20 g
L-Methionine	4.30 g
L-Phenylalanine	7.30 g
L-Threonine	3.80 g
L-Tryptophan	1.40 g
L-Valine	5.90 g
L-Arginine	0.90 g
L-Histidine	2.40 g
L-Alanine	3.30 g
L-Glutamic acid	23.10 g
Glycine	1.90 g
L-Proline	12.00 g
L-Aspartic acid	6.60 g
L-Serine	4.60 g
L-Tyrosine	0.30 g

One 15 g sachet of Aminutrin provides 1.8 g of available Nitrogen equivalent to 11.7 g Protein.

Uses Aminutrin is used to provide the protein basis of a diet in order to maintain a good state of nutrition for patients who are unable or unwilling to take conventional diets. When used with a suitable calorie source (e.g. Calonutrin), Aminutrin is ideal for tube-feeding.

Clinical indications being—trauma, burns, unconscious patients, anorexia nervosa, impaired mastication due to maxillo-facial injury, Crohn's disease, ulcerative

colitis, diverticulitis, malabsorption syndromes (i.e. coeliac disease, sprue, genetic disorders, intestinal malfunction), nutritional provision in pre- or post-surgery, low bulk feeding in patients where intestinal surgery is a factor, and where preparation for X-ray is imminent, short bowel syndrome and intestinal fistulae, Geriatrics – inability to take a normal diet.

Dosage and administration 30–75 g per day (two to five 15 g sachets). This product is a protein-based food and upper restriction on intake is therefore inappropriate. Aminutrin should be given with the correct quantity of carbohydrate calories (Calonutrin) for maximum utilisation. As a guide the calorie to nitrogen ratio should be about 200:1 kcal/g (or 15 g Aminutrin to 100 g Calonutrin).

Tube and oral feeding: For oral feeding Aminutrin is best given as an addition to consommé beef soup, 1 sachet per portion. Other recipes for oral use are contained in a recipe book obtainable from the manufacturers.

Contra-indications, warnings, etc With all tube feeding regimes, careful attention must be paid to fluid and electrolyte balance as these may need to be corrected. Vitamin supplements will be required, and will depend on the needs of the patient.

Not for parenteral administration.

Accidental Overdosage: No instance of adverse reaction to an overdosage of Aminutrin has been recorded and no specific measures are indicated.

Pharmaceutical precautions Solutions of Aminutrin should not be boiled. Store below 25°C.

Legal category GSL.

Package quantities 10 × 15 g vacuum-sealed sachets in each carton. A package insert leaflet is included, with instructions and suggested diet regimes.

Further information Nil.

Product licence number 0184/0026.

ANAFLEX* AEROSOL

Presentation Antibacterial and antifungal spray containing Polynoxylin 2% for the control of localised infection by external application.

Uses Anaflex Aerosol is indicated for the treatment of athlete's foot, nappy rash, pressure sores, pruritus ani, pruritus vulvae, boils, infective dermatitis, intertrigo, minor wounds.

It is of benefit for colostomy and ileostomy control and for general use in casualty.

Dosage and administration Apply freely to the site of infection or of potential infection.

Contra-indications, warnings, etc For external application only. Caution when spraying near the eyes. Not for intubation nor inhalation.

Pharmaceutical precautions The aerosol can should be stored away from direct heat. The container should not be punctured or destroyed by burning, even when empty.

Legal category P.

Package quantities Aerosol canisters of 100 g.

Further information Contains talc.

Product licence number 0184/5008.

ANAFLEX* CREAM

Presentation A smooth white water-miscible cream with a pleasant odour containing 10% Polynoxylin.

Uses An antibacterial and antifungal preparation for use in a wide variety of dermatological conditions including athlete's foot, nappy rash, pressure sores, boils, stasis ulcers, pruritus ani, pruritus vulvae.

The product has proved of value in promoting wound healing and for the control of tissue reaction following radiotherapy.

Anaflex Cream is indicated also for the treatment of a wide range of aural and nasal infections including otitis externa.

Dosage and administration By application to the affected site once or twice daily.

For the treatment of infected ears the cream should be applied daily by means of a $\frac{1}{2}$ -inch ribbon gauze wick.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Store below 25°C.

Legal category P.

Package quantities Tubes of 50 g.

Further information Anaflex cream may be used in conjunction with Anaflex Paste in the treatment of stasis ulcers.

Product licence number 0184/5006.

ANAFLEX* LOZENGES

Presentation Flat, white, circular lozenges with a bevelled edge and embossed 'GEISTLICH' on each face. Each lozenge contains 30 mg Polynoxylin in a citrus-flavoured base.

Uses An antibacterial, antifungal preparation having an anti-inflammatory action and ideally suited for the treatment of mouth and throat infections in tonsillitis, oral thrush, mouth ulcers.

Dosage and administration In most conditions 6–10 lozenges per day will be found suitable. Minor throat infections usually respond in two to three days. More difficult infections (eg Candida) will take longer to respond and treatment can be continued if necessary for four to six weeks.

The lozenges do not contain local anaesthetic and sensitisation will not occur when given over a period of time.

Contra-indications, warnings, etc *Accidental overdose:* No instance of adverse reaction to an overdose of Anaflex Lozenges has been recorded and no specific measures are indicated.

Pharmaceutical precautions Store below 25°C.

Legal category P.

Package quantities Containers of 50 lozenges.

Further information Nil.

Product licence number 0184/5007.

ANAFLEX* PASTE

Presentation A smooth white paste containing Polynoxylin 10%.

Uses Anaflex Paste is beneficial for the control of external infections of bacterial and fungal origin in body areas where moisture is present.

It is indicated for use in athlete's foot, nappy rash, intertrigo, colostomy and ileostomy control, infective dermatitis, boils and stasis ulcers.

Dosage and administration Application to the area for treatment once or twice daily.

Colostomy and ileostomy control: Anaflex Paste gently massaged into the surrounding area will control and effectively treat excoriated tissue present. It will be noted that a colostomy bag will adhere to a surface treated with Anaflex Paste.

Stasis ulcers: Anaflex Cream may be applied direct to the ulcer. Any surrounding eczema will benefit by the application of Anaflex Paste.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Store below 25°C.

Legal category P.

Package quantities Tubes of 20 g.

Further information Anaflex Paste may be used in conjunction with Anaflex Cream in the treatment of stasis ulcers.

Product licence number 0184/5005.

ANAFLEX* POWDER

Presentation A white powder with antibacterial, antifungal and anti-inflammatory properties containing Polynoxylin 10%.

Uses For the control of infection on the body surface including athlete's foot, nappy rash, pressure sores, minor wounds, stasis ulcers and in casualty.

Anaflex Powder is indicated also for the treatment of a wide range of aural and nasal infections including otitis externa.

Dosage and administration Apply freely to infected area or area of potential infection by means of the sprinkler pack.

Contra-indications, warnings, etc For external application only. Exclude perforated ear drum.

Pharmaceutical precautions Store below 25°C.

Legal category P.

Package quantities Sprinkler pack of 30 g.

Further information Contains talc.

Product licence number 0184/5003.

CALONUTRIN*

Presentation White, odourless, free-flowing powder containing glucose, maltose and polysaccharides.

Each 100 g sachet provides 1.72 MJ (410 kcal)

Uses Generally in any condition where calories are needed and high tolerance is essential in tube and oral feeding.

Clinical indications being—nutrition in pre- and post-surgical situations, burns, coma, coeliac disease, sprue, Crohn's disease, etc. ulcerative colitis, cystic fibrosis, renal failure (uraemia), hepatic failure, cirrhosis of the liver, anorexia nervosa, dysphagia and geriatric malnutrition, hypoglycaemia, convalescence, intolerance conditions, i.e. fat and lactose intolerance.

Dosage and administration Because Calnutrin provides calories alone it should be given in conjunction with a protein/amino acid tube or oral food, such as Aminutrin.

Exact methods of use of the combined diet will be found in every pack of Aminutrin.

In cases where extra calories are required Calnutrin may be given as a drink using one part Calnutrin to three parts fluid (1 sachet 100 g Calnutrin to 300 ml fluid) in fruit drinks, tea, coffee or milk. It may, in place of sugar, also be used in cooking, to prepare cakes, pastry, etc.

Contra-indications, warnings, etc When used in the diabetic the usual precautions for carbohydrate intake must be considered. Not for parenteral administration.

Pharmaceutical precautions Store below 25°C protected from moisture.

Legal category GSL.

Package quantities Boxes of 10 sachets of 100 g.

Further information The electrolyte content is low; each 100 g of Calnutrin containing: Sodium 4 mmol, Potassium 0.3 mmol.

Product licence number 0184/0025.

GLUCOPLEX* 1000

Presentation A clear solution of 24% glucose premixed with electrolytes and trace elements. Sterile and pyrogen-free.

Active ingredients per litre:

Sodium	50.0 mmol
Potassium	30.0 mmol
Magnesium	2.5 mmol
Zinc	45.6 mcmol
Dihydrogen phosphate	18.0 mmol
Chloride	67.0 mmol
Anhydrous glucose	240.0 g

Providing: 4.2 MJ (1000 kcal) per litre.

Hypertonic solution

Osmolality approximately 1750 mosmol/kg.

Uses A solution of glucose calories, electrolytes and trace elements for use in intravenous feeding; it is intended for use in combination with a nitrogen source, for example, Aminoplex 12.

Dosage and administration *Adult Dose* (70 kg bodyweight): 1000–3000 ml in 24 hours by intravenous injection.

Infusion Rate: maximum 50 drops per minute.

Children's dosage at physicians' discretion.

Contra-indications, warnings, etc Special precautions to be taken in diabetes mellitus, diabetes insipidus, hyperosmotic coma, hyperkalaemia, untreated shock, renal failure, water intoxication and patients with glucose/galactose malabsorption syndrome.

Hypertonic glucose may induce thrombophlebitis especially when infused into peripheral veins. Rapid infusion may invoke hyperglycaemia, hyperosmolar states, osmotic diuresis and resultant dehydration if used in inappropriately high doses or in patients with impaired glucose metabolism. Because Glucoplex contains potassium, hyperkalaemia may be exacerbated or induced on rapid infusion. If glucose solutions are given at a rate which exceeds their metabolism a hyper-osmolar condition with a rising serum sodium may occur. In such cases there may be hypernatraemia and a rise in the MCV which must be differentiated from iatrogenic sodium overload. Alternatively the respiratory quotient (RQ) may rise above one giving a high CO₂ production. These complications are more common in severely ill patients. The appropriate glucose load for the patient may be judged from patient clinical state, biochemical response to glucose or by assessment of resting metabolic expenditure.

Pharmaceutical precautions Check that the solution is clear and the container undamaged. Discard if not fully used at one injection. Store below 25°C. Keep away from light.

Data on compatibility and levels of permissible additions of vitamins and trace elements are available from the manufacturers.

Legal category POM.

Package quantities Clear glass bottles of 500 ml and 1000 ml.

Further information Nil.

Product licence number 0184/0032.

GLUCOPLEX* 1600

Presentation A clear solution of 40% glucose premixed with electrolytes and trace elements. Sterile and pyrogen-free.

Active ingredients per litre:

Sodium	50.0 mmol
Potassium	30.0 mmol
Magnesium	2.5 mmol
Zinc	45.6 mcmol
Dihydrogen phosphate	18.0 mmol
Chloride	67.0 mmol
Anhydrous glucose	400.0 g

Providing: 6.72 MJ (1600 kcal) per litre.

Hypertonic solution

Osmolality approximately 2900 mosmol/kg.

Uses A solution of glucose calories, electrolytes and trace elements for use in intravenous feeding; it is intended for use in combination with a suitable nitrogen source, for example, Aminoplex 12.

Dosage and administration *Adult Dose* (70 kg bodyweight) 1000–3000 ml in 24 hours by intravenous injection.

Infusion Rate: maximum 50 drops per minute.

Children's dosage at physicians' discretion.

Contra-indications, warnings, etc Special precautions to be taken in diabetes mellitus, diabetes insipidus, hyperosmotic coma, hyperkalaemia, untreated shock, renal failure, water intoxication and patients with glucose/galactose malabsorption syndrome.

Hypertonic glucose may induce thrombophlebitis

especially when infused into peripheral veins. Rapid infusion may invoke hyperglycaemia, hyperosmolar states, osmotic diuresis and resultant dehydration if used in inappropriately high doses or in patients with impaired glucose metabolism. Because GlucoPlex contains potassium, hyperkalaemia may be exacerbated or induced on rapid infusion. If glucose solutions are given at a rate which exceeds their metabolism a hyper-osmolar condition with a rising serum sodium may occur. In such cases there may be hypernatraemia and a rise in the MCV which must be differentiated from iatrogenic sodium overload. Alternatively the respiratory quotient (RQ) may rise above one giving a high CO₂ production. These complications are more common in severely ill patients. The appropriate glucose load for the patient may be judged from patient clinical state, biochemical response to glucose or by assessment of resting metabolic expenditure.

Pharmaceutical precautions Check that the solution is clear and the container undamaged. Discard if not fully used at one injection. Store below 25°C. Keep away from light.

Data on compatibility and levels of permissible additions of vitamins and trace elements are available from the manufacturers.

Legal category POM.

Package quantities Clear glass bottles of 500 ml and 1000 ml.

Further information Nil.

Product licence number 0184/0033.

KAY-CEE-L* SYRUP

Presentation A clear red cherry flavoured sugar-free syrup containing Potassium Chloride BP 7.50% w/v providing Potassium – 1 mmol per ml.

Uses Indicated in all situations where oral potassium supplementation is required. Typical examples—diuretic therapy, Cushing's syndrome, megaloblastic anaemia, diabetic ketosis; during intensive steroid, corticotrophin and carbenoxolone therapy. Primary aldosteronism, metabolic alkalosis.

Dosage and administration *Adults:* 10–50 ml per day at clinician's discretion.

Children: At clinician's discretion.

Doses should be given in divided amounts, after food.

Contra-indications, warnings, etc Impaired renal function, dehydration, and hyperkalaemia.

High doses taken inadvertently will act as an emetic.

Pharmaceutical precautions Store below 25°C.

Legal category P.

Package quantities Bottles of 500 ml.

Further information Potassium chloride in an oral syrup form has recently been cited as potentially more effective than tablets because of its rapid absorption from the stomach. The syrup is also without risk of causing small bowel haemorrhage, ulceration, and stricture formation. It is important to recognise the use of the chloride salt of potassium, due to the effect of the chloride moiety in controlling metabolic alkalosis. Contains Sorbitol.

Product licence number 0184/0031.

LAEVUFLEX* 20

Presentation A colourless solution containing laevulose. Sterile and pyrogen free.

Active ingredients per litre:

Laevulose BP 200 g

Providing: 3.4 MJ (820 kcal)

Hypertonic solution

Osmolality approximately 1330 mosmol/kg

Uses As a calorie source for parenteral administration.

Dosage and administration *Adult Dose* (70 kg bodyweight) 500–2000 ml in 24 hours by intravenous injection.

Infusion Rate: Maximum 50 drops per minute.

Children's dosage at physicians' discretion.

Contra-indications, warnings, etc Administration to patients with familial laevulose intolerance may result in hypoglycaemia.

Before commencing infusion with Laevuflex 20, it is important to exclude conditions which may promote the risk of acidosis; for this reason, certain patient selection criteria should be applied during regimen planning – these are:–

- Adequate circulation volume.
- Absence of impaired liver function.
- Adequate renal function.
- Absence of acidosis.
- Adequate pulmonary function.

If the patient does not fulfil these selection criteria, a regimen based on a glucose calorie source, for instance GlucoPlex, will be more appropriate.

Pharmaceutical precautions Store below 25°C. Keep away from light. Check solution is clear: discard if not fully used at one injection.

Legal category POM.

Package quantities Glass bottles of 500 ml, 10 bottles per box.

Further information Nil.

Product licence number 0184/5001.

NOXYFLEX* 'S'

Presentation A white crystalline powder containing 2.5 g Noxythiolin.

Uses Noxythiolin has a wide spectrum of antifungal and antibacterial activity for the prevention and eradication of infection from the body surface and specified accessible cavities. Intraperitoneally, it is an effective anti-endotoxin and anti-adhesion agent.

Dosage and administration The solution is most commonly used at concentrations of 1, 2.5 and occasionally 5%. For prophylactic use a 1% solution is frequently employed; for therapeutic use a 2.5% solution is normally administered.

Ensure contact of the solution on the body surface or in specified cavities for at least 30 minutes. The period of treatment should not normally extend beyond 72 hours, or five days where otherwise stated above.

Gynaecology: Intermittent catheterisation: Use 100 ml of 1% solution at each catheterisation as prophylaxis; for treatment, use a 2.5% solution.

Indwelling catheters: Use 100 ml of 1% solution twice daily as prophylaxis; for treatment, use a 2.5% solution.

Urology and surgery: Catheterisation: 100 ml of 1% solution once or twice daily as prophylaxis. 100 ml of 2.5% solution once or twice daily as a treatment.

Peritonitis: 100 ml of a 2.5% Solution instilled into the peritoneum before closure.

Empyema: 100 ml of a 1% Solution daily for a minimum of five days, leaving the intercostal drain clamped for a period of 30 minutes.

Infected wounds and fistulae: Irrigate with a 1% Solution twice daily for five days.

Burns: 1% Solution as a wet dressing twice daily.

Abscess cavities: 2.5% Solution administered via polythene tube, twice daily for five days.

Radiotherapy (Ca Bladder): 50 ml of 2.5% Solution administered via catheter during planning.

Contra-indications, warnings, etc Noxyflex 'S' can be used concurrently with the administration of systemic drugs. The use of Noxyflex 'S' in conjunction with other pharmaceutical agents for combined irrigation/instillation therapy is not recommended and solution preparation should be carried out as stated under 'Pharmaceutical preparation'. The normal daily usage of Noxyflex 'S' in adults should not exceed 10 g for either accumulative (ie. repeated) instillation regimens or continuous irrigation regimens. Solutions are not intended for intravenous use.

Pharmaceutical precautions *Storage of powder:* The powder vials should be kept in a cool place.

Storage of Solution: Solution should be kept at 2–10°C and used within 7 days. Containers of prepared solution are intended for single use only.

Solution Preparation: The powder should be dissolved completely in a sufficient quantity of Water for Injections BP or Sodium Chloride Intravenous Infusion BP (0.9 per cent w/v) by an aseptic technique. Slight difficulty may be experienced in preparing solutions.

To make a 2.5% solution: Add contents of one vial (2.5 g) to 100 ml of Water for Injections BP or Sodium Chloride Intravenous Infusion BP (0.9 per cent w/v) and shake for a half to two minutes. **Do not heat.**

To make a 1% solution: Add contents of one vial (2.5 g) to 250 ml of Water for Injections BP or Sodium Chloride Intravenous Infusion BP (0.9 per cent w/v) and shake for a half to two minutes. **Do not heat.**

Legal category POM.

Package quantities Vials containing 2.5 g. Boxes of 10 vials.

Further information Where desirable, the discretionary use of a suitable local anaesthetic may be used. Noxyflex (ie with amethocaine hydrochloride) may therefore be more appropriate for urological use, or when a degree of pain might be expected.

Product licence number 0184/5012

NOXYFLEX*

Presentation A white crystalline powder containing 2.5 g Noxythiolin and 10 mg Amethocaine Hydrochloride BP.

Uses Noxythiolin has a wide spectrum of antifungal and antibacterial activity. It is intended for the prevention and eradication of infection from the body surface and

specified accessible cavities, particularly for urological use, or when a degree of pain might be expected.

Dosage and administration The solution is most commonly used at concentrations of 1, 2.5 and occasionally 5%. For prophylactic use a 1% solution is frequently employed; for therapeutic use, a 2.5% solution is normally administered. Ensure contact of the solution on the body surface or in specified cavities for at least 30 minutes. The period of treatment should not normally extend beyond 72 hours, or five days where otherwise stated above.

Gynaecology: Intermittent catheterisation: Use 100 ml of 1% solution at each catheterisation as prophylaxis; for treatment, use a 2.5% solution.

Indwelling catheters: Use 100 ml of 1% solution twice daily as prophylaxis; for treatment, use a 2.5% solution.

Urology and surgery: Catheterisation: 100 ml of 1% solution once or twice daily as prophylaxis. 100 ml of 2.5% solution once or twice daily as a treatment.

Infected wounds and fistulae: Irrigate with 1% Solution twice daily for five days.

Burns: 1% Solution as a wet dressing, twice daily.

Abscess cavities: 2.5% Solution via polythene tube, twice daily for five days.

Radiotherapy (Ca Bladder): 50 ml of 2.5% Solution administered via catheter during planning.

Contra-indications, warnings, etc Noxyflex can be used concurrently with the administration of systemic drugs. The use of Noxyflex in conjunction with other pharmaceutical agents for combined irrigation/instillation therapy is not recommended and solution preparation should be carried out as stated under 'Pharmaceutical preparation'. The normal daily usage of Noxyflex in adults should not exceed 10 g for either accumulative (ie. repeated) instillation regimens or continuous irrigation regimens. Solutions are not intended for intravenous use.

Pharmaceutical precautions *Storage of powder:* The powder vials should be kept in a cool place.

Storage of Solution: Solution should be kept at 2–10°C and used within 7 days. Containers of prepared solution are intended for single use only.

Solution Preparation: The powder should be dissolved completely in a sufficient quantity of Water for Injections BP or Sodium Chloride Intravenous Infusion BP (0.9 per cent w/v) by an aseptic technique. Slight difficulty may be experienced in preparing solutions.

To make a 2.5% solution: Add contents of one vial (2.5 g) to 100 ml of Water for Injections BP or Sodium Chloride Intravenous Infusion BP (0.9 per cent w/v) and shake for a half to two minutes. **Do not heat.**

To make a 1% solution: Add contents of one vial (2.5 g) to 250 ml of Water for Injections BP or Sodium Chloride Intravenous Infusion BP (0.9 per cent w/v) and shake for a half to two minutes. **Do not heat.**

Legal category POM.

Package quantities Vials containing 2.5 g. Boxes of 10 vials.

Further information In those situations where the inclusion of local anaesthetic is undesirable or unnecessary, Noxyflex 'S' should be used.

Product licence number 0184/5013.

* *Trade Mark*

ALTHESIN*

Presentation Althesin is a clear, colourless, ready-prepared solution that is isotonic with blood. Each millilitre of Althesin contains 9 mg alphaxalone (3 α -hydroxy-5 α -pregnane-11, 20-dione) and 3 mg alphadolone acetate (21-acetoxy-3 α -hydroxy-5 α -pregnane-11, 20-dione).

The latter steroid has about one-half the anaesthetic activity of the former, and is included to improve the solubility of alphaxalone. The aqueous vehicle contains 20% of a polyoxyethylated castor oil (a surfactant) and is rendered isotonic with sodium chloride.

Uses Induction of anaesthesia. Maintenance of anaesthesia. Experience is insufficient at present to advocate use of Althesin in infants under 1 year and for maintenance of anaesthesia in obstetrics.

Dosage and administration As usual, it is recommended that patients should fast before receiving Althesin.

Induction of anaesthesia: For adults, undiluted Althesin should be administered intravenously allowing at least 20 seconds per millilitre of injection. The induction dose for adults of average size is between 1.5 and 3.5 ml requiring between 30 and 70 seconds to administer. Alternatively, the induction dose may be calculated on the basis of 0.025–0.05 ml (25–50 microlitres) per kg body weight.

Children tend to require proportionately higher doses than adults within the 0.05 to 0.075 ml/kg body weight range, and younger children may need 0.075 ml/kg. The approximate duration of anaesthesia after a dose of 0.05 ml/kg is seven minutes, and 11 minutes after 0.075 ml/kg. Althesin has negligible analgesic activity. Althesin is pharmacologically compatible with the muscle relaxants, premedicant drugs, and inhalation anaesthetics in current clinical use.

Maintenance of anaesthesia: For short procedures, incremental doses of undiluted Althesin may be given. In dilatation and curettage, for example, after induction of anaesthesia by slow injection of Althesin, additional doses of 0.5–1 ml, according to the weight and response of the patient, may be given for swabbing the perineum and manipulating the cervix.

For longer procedures, intravenous infusion of diluted Althesin is usually preferred. The dosage normally totals 10–20 ml Althesin per hour. A convenient strength for infusion is 10% by volume of Althesin in Sodium Chloride Injection or 5% Dextrose Injection.

Althesin does not provide sufficient analgesia for operations involving painful stimuli, and this should be provided by the premedication, intravenous analgesics such as pethidine in small increments, or by local or regional anaesthetic techniques. Analgesia may also be provided by nitrous oxide.

Muscle relaxants may be used, and the patient ventilated with oxygen-enriched air. In paralysed

patients the level of anaesthesia is assessed by observing autonomic activity.

As with volatile anaesthetics, some prolongation of recovery time may occur with maintenance techniques, particularly when several doses of analgesics have been given. Oxygen is often added to the inspired air when using infusions or repeated doses of Althesin, particularly when opiate analgesics have been given and the patient is breathing spontaneously.

Contra-indications, warnings, etc

Contra-indications: Previous adverse reactions to Althesin.

Its use in patients with liver disease may be considered, although evidence at present is insufficient to advocate use in patients with complete liver failure.

Precautions: Like other anaesthetics, Althesin should be used only in the presence of an experienced anaesthetist, and resuscitative equipment should be immediately available.

The risk of severe reactions (see below) may be higher in patients with a personal or family history of atopy or those who have recently had a prior exposure to Althesin or to another Cremophor* (BASF-Germany) containing agent.

Since Althesin produces relaxation of the jaw muscles, the jaw requires support to prevent obstruction of the airway. Concurrent use of other depressants of the central nervous system may retard recovery of full consciousness, and recovery from anaesthesia should, as always, be assessed carefully before allowing out-patients to go home or resume normal activities.

Animal experiments show no evidence of teratogenicity, but Althesin should be used with caution in pregnancy.

Side-effects: Minor side-effects may include a transient flush and muscle twitching, the latter occurring more often in patients given hyoscine alone as premedication. There is a possibility of generalised convulsions, and of cardiac arrhythmias in patients concomitantly treated with muscle relaxants. Short periods of coughing, hiccoughing, salivation, laryngospasm or shivering may occur, particularly in association with light anaesthesia or rapid injection. Mild euphoria or depression during recovery from Althesin anaesthesia sometimes occurs. Post-operative nausea and vomiting are infrequent.

There have been occasional reports of more severe reactions. Bronchospasm and/or a marked drop in blood pressure may be accompanied by a generalised flushing of deep red or purplish colour, and followed by some oedema of lips and eyelids. Such reactions may require treatment with pure oxygen, intravenous corticosteroids and plasma expanders.

Overdosage: If serious respiratory depression occurs, respiration should be supported mechanically. The margin of safety is wide, and 0.2 ml/kg, or eight times the minimum recommended sleep dose, has been given as a single dose without serious effects.

Pharmaceutical precautions Do not refrigerate, as this may precipitate the steroids, which are difficult to re-solubilise. Protect from light. Do not shake, as this may cause frothing.

Legal category POM.

Package quantities Ceramically printed 5 or 10 ml ampoules in boxes of 10 ampoules.

Further information Althesin does not appear to be retained in the tissues, and is rapidly inactivated by the liver. As a result, there is considerably less cumulation than with the barbiturates. Recovery from a single dose is therefore rapid, and in maintenance anaesthesia the dosage requirements remain relatively constant, and recovery is progressive. Because of the great capacity of the liver to metabolise the constituents of Althesin, this agent may be considered for induction and maintenance of anaesthesia in patients with chronic liver disease.

Althesin is practically non-irritant, so that leakage outside the vein is unlikely to damage surrounding tissue.

Maintenance anaesthesia with Althesin (together with analgesics) can enable volatile agents to be avoided, and the atmosphere kept free of contamination by anaesthetics.

Product licence number 0004/0189.

BETNELAN* TABLETS

Presentation Small white tablets engraved 'Betnelan Glaxo' on one side and scored on the reverse. Each tablet contains 0.5 mg betamethasone.

The product complies with the specification for Betamethasone Tablets BP.

Uses Betamethasone is a glucocorticosteroid which is about eight to ten times as active as prednisolone on a weight-for-weight basis.

A wide variety of diseases may sometimes require corticosteroid therapy. Some of the principal indications are: asthma, severe allergic disturbances, leukaemia, rheumatoid arthritis, collagen diseases and various inflammatory skin diseases. Other indications are the ephrotic syndrome, ulcerative colitis, regional ileitis (Crohn's disease), pemphigus, sarcoidosis (especially with hypercalcaemia), rheumatic carditis, ankylosing spondylitis and various blood dyscrasias, including selected cases of haemolytic anaemia, agranulocytosis and thrombocytopenic purpura.

Dosage and administration The lowest dosage that will produce an acceptable result should be used; when it is possible to reduce the dosage, this must be accomplished by stages. During prolonged therapy, dosage may need to be increased temporarily during periods of stress or in exacerbations of illness.

Adults: The dose used will depend upon the disease, its severity and the clinical response obtained. The following regimens are for guidance only. Divided dosage is usually employed.

Short-term treatment: 2–3 mg daily for the first few days, subsequently reducing the daily dosage by 0.25 or 0.5 mg every two to five days, depending upon the response.

Rheumatoid arthritis: 0.5–2 mg daily. For maintenance therapy the lowest effective dosage is used.

Most other conditions: 1.5–5.0 mg daily for one to three weeks, then reducing to the minimum effective dosage.

Larger doses may be needed for collagen diseases and ulcerative colitis.

Children: Fractions of the adult dosage may be used (e.g. 75% at 12 years, 50% at seven years and 25% at 1 year), but clinical factors must be given due weight.

Contra-indications, warnings, etc

Contra-indications: Systemic infections, unless specific anti-infective therapy is employed.

Precautions: Administration of corticosteroids may impair the ability to resist and counteract infection; in addition clinical signs and symptoms of infection are suppressed.

Corticosteroid treatment is unlikely to reduce the response of the pituitary-adrenal axis to stress, and relative insufficiency may persist for up to a year after withdrawal of prolonged therapy.

In pregnant animals, systemic administration of corticosteroids can cause abnormalities of fetal development. The relevance of this finding to humans has not been established.

Corticosteroids may worsen diabetes.

Side-effects: Prolonged treatment with corticosteroids in high dosage is occasionally associated with subcapsular cataract or glaucoma, in addition, any of the features of hypercorticism, such as osteoporosis, may occur. Aseptic osteonecrosis, particularly of the femoral head, may occur after prolonged corticosteroid therapy, or after repeated short courses involving high dosage. Peptic ulceration may develop, or be aggravated. In children, prolonged therapy may retard growth.

Overdosage: Treatment is unlikely to be needed in cases of acute overdosage.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Bottles of 100 or 500 tablets.

Further information Betnelan does not normally cause retention of salt and water, and the risk of inducing oedema and hypertension is almost negligible.

Product licence number 0004/5134.

BETNESOL* EYE, EAR AND NOSE PREPARATIONS

Presentation Betnesol Drops contain betamethasone sodium phosphate 0.1% w/v, and benzalkonium chloride 0.02% w/v in a clear and colourless aqueous solution that is sterile until the bottle is opened. This product complies with the BPC and BNF specification for Betamethasone Eye Drops.

Betnesol Eye Ointment contains betamethasone sodium phosphate 0.1% w/w in a bland, soft paraffin base of white, translucent appearance. Sterile until opened.

Uses Non-infected inflammatory conditions of the eye, ear or nose.

Dosage and administration **Eyes:** 1 or 2 drops instilled into the eye every one or two hours until control is achieved, when the frequency may be reduced. An extrusion of the ointment about $\frac{1}{2}$ inch long may be introduced beneath the lower lid two or three times daily and/or at night.

Ears: 2 or 3 drops instilled into the ear every two or three

hours until control is achieved, when the frequency may be reduced.

Nose: 2 or 3 drops instilled into each nostril two or three times daily.

Contra-indications, warnings, etc

Contra-indications: Viral, fungal, tuberculous or purulent conditions. Hypersensitivity to any component of the preparation. Use in the eye is contra-indicated if glaucoma is present.

Betnesol Eye Drops contain benzalkonium chloride as a preservative and therefore should not be used to treat patients who wear soft contact lenses.

Precautions: Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Side-effects: Eye drops containing corticosteroids cause a serious rise in intra-ocular pressure in a small percentage of the population, including most of those with a family history of glaucoma. A milder rise may be experienced by a larger proportion of subjects if treatment is continued for longer than a few weeks. Thinning of the cornea leading to perforation, has occurred with use of topical corticosteroids. Cataract is reported to have occurred after unduly prolonged treatment with topical corticosteroids.

Pharmaceutical precautions It is desirable that the contents should not be used more than four weeks after first opening the bottle or tube.

Legal category POM.

Package quantities *Betnesol Drops:* Plastic dropper bottles containing 5 ml or 10 ml.

Betnesol Eye Ointment: Narrow-nozzle tubes containing 3 g.

Further information Nil.

Product licence numbers

Betnesol Drops 0004/5135
Betnesol Eye Ointment 0004/5137

BETNESOL* INJECTION

Presentation Each ampoule of ready-prepared Betnesol Injection contains 4 mg betamethasone as the sodium phosphate ester in 1 ml of sterile aqueous solution. The injection is clear and colourless or pale yellow, and complies with the specification for Betamethasone Sodium Phosphate Injection BP.

Uses Betamethasone is a glucocorticosteroid which is about eight to ten times as active as prednisolone on a weight-for-weight basis. It may be indicated in the following conditions:

Status asthmaticus and acute allergic reactions, in anaphylactic reaction to drugs. Betnesol Injection supplements the action of adrenaline.

Severe shock arising from surgical or accidental trauma or overwhelming infection.

Adrenal crisis precipitated by abnormal stress in Addison's disease, Simmonds' disease, following adrenalectomy, and when adrenocortical function has been suppressed by prolonged corticosteroid therapy.

Soft tissue lesions such as tennis elbow and periarthritis of the shoulder joint (by local injection).

N.B. Betnesol Injection does not replace other forms of therapy for the treatment of shock and status asthmaticus.

Dosage and administration *Systemic therapy in adults:* 4–20 mg betamethasone (1–5 ml) administered by intravenous injection over half to one minute. This dose can be repeated three or four times in 24 hours, or as required, depending upon the condition being treated and the patient's response. Alternatively, Betnesol Injection may be given in an intravenous infusion. The same dose can be given by intramuscular injection, but the response is likely to be less rapid, especially in shock.

Systemic therapy in children: Infants up to 1 year may be given 1 mg betamethasone intravenously; children aged 1–5 years, 2 mg; 6–12 years, 4 mg (1 ml).

Other routes: Local injections of 4–8 mg Betnesol may be used when treating soft tissue lesions in adults; children may require smaller doses.

Betnesol Injection has also been administered subconjunctivally as a single injection of 0.5–1 ml.

Intrathecal use is not recommended.

Contra-indications, warnings, etc

Contra-indications: Systemic infections, unless specific anti-infective therapy is employed. Hypersensitivity to any component of the injection.

Betnesol Injection should not be injected directly into tendons.

Precautions: Administration of corticosteroids may impair the ability to resist and counteract infection; in addition clinical signs and symptoms of infection are suppressed.

In pregnant animals, systemic administration of corticosteroids can cause abnormalities of fetal development. The relevance of this finding to humans has not been established.

Side-effects: In the short term, high dosage of betamethasone involves little risk of adverse reactions except that peptic ulceration may occur, or be aggravated. With continued use, signs of hypercorticism may become apparent.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities 1 ml ampoules in box of 5.

Further information Nil.

Product licence number 0004/5139.

BETNESOL* TABLETS

Presentation Small, soluble pink tablets engraved 'Betnesol Glaxo' on one side and scored on the reverse. Each tablet contains 0.5 mg betamethasone as the sodium phosphate ester.

The tablets comply with the specification for Betamethasone Sodium Phosphate Tablets BP, BNF.

Uses Betamethasone is a glucocorticosteroid which is about eight to ten times as active as prednisolone on a weight-for-weight basis.

Betamethasone sodium phosphate is very soluble in water, and is therefore less likely to cause local gastric irritation than corticosteroids which are only slightly soluble. This is important when high dosages are required, as in immunosuppressive therapy.

Betnesol does not normally cause retention of salt and

water, and the risk of inducing oedema and hypertension is almost negligible.

A wide variety of diseases may sometimes require corticosteroid therapy. Some of the principal indications are: asthma, severe allergic disturbances, leukaemia, rheumatoid arthritis, collagen diseases, and various inflammatory skin diseases. Other indications are the nephrotic syndrome, ulcerative colitis, regional ileitis (Crohn's disease), pemphigus, sarcoidosis (especially with hypercalcaemia), rheumatic carditis, ankylosing spondylitis, and various blood dyscrasias, including selected cases of haemolytic anaemia, agranulocytosis and thrombo-cytopenic purpura.

Dosage and administration Betnesol Tablets are best taken dissolved in water, but they can be swallowed whole without difficulty. The lowest dosage that will produce an acceptable result should be used; when it is possible to reduce the dosage, this must be accomplished by stages. During prolonged therapy, dosage may need to be increased temporarily during periods of stress or in exacerbations of illness.

Adults: The dose used will depend upon the disease, its severity and the clinical response obtained. The following regimens are for guidance only. Divided dosage is usually employed.

Short-term treatment: 2–3 mg daily for the first few days, subsequently reducing the daily dosage by 0.25 or 0.5 mg every two to five days, depending upon the response.

Rheumatoid arthritis: 0.5–2 mg daily. For maintenance therapy the lowest effective dosage is used.

Most other conditions: 1.5–5 mg daily for one to three weeks, then reducing to the minimum effective dosage.

Larger doses may be needed for collagen diseases and ulcerative colitis.

Children: Fractions of the adult dosage may be used (e.g. 75% at 12 years, 50% at seven years and 25% at 1 year), but clinical factors must be given due weight.

Contra-indications, warnings, etc

Contra-indications: Systemic infections, unless specific anti-infective therapy is employed. Hypersensitivity to any component of the tablets.

Precautions: Administration of corticosteroids may impair the ability to resist and counteract infection; in addition clinical signs and symptoms of infection are suppressed.

Corticosteroid treatment is likely to reduce the response of the pituitary-adrenal axis to stress, and relative insufficiency may persist for up to a year after withdrawal of prolonged therapy.

In pregnant animals, systemic administration of corticosteroids can cause abnormalities of fetal development. The relevance of this finding to humans has not been established.

Corticosteroids may worsen diabetes.

Side-effects: Prolonged treatment with corticosteroids in high dosage is occasionally associated with subcapsular cataract or glaucoma, in addition, any of the features of hypercorticism, such as osteoporosis, may occur. Aseptic osteonecrosis, particularly of the femoral head, may occur after prolonged corticosteroid therapy, or after repeated short courses involving high dosage. Peptic ulceration may develop, or be aggravated. In children, prolonged therapy may retard growth.

Overdosage: Treatment is unlikely to be needed in cases of acute overdosage.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities The tablets are strip-packed in cartons of 100.

Further information Betnesol Tablets do not contain carbohydrates.

Product licence number 0004/5140.

BETNESOL*-N EYE, EAR AND NOSE PREPARATIONS

Presentation Betnesol-N Drops contain betamethasone sodium phosphate 0.1% w/v, neomycin sulphate 0.5% w/v and thiomersal 0.005% w/v in a clear and colourless aqueous solution. Sterile until opened.

Betnesol-N Eye Ointment contains betamethasone sodium phosphate 0.1% w/w and neomycin sulphate 0.5% w/w in a bland, soft paraffin base of white translucent appearance. Sterile until opened.

Uses Betamethasone has topical corticosteroid activity. The presence of neomycin should prevent the development of bacterial infection.

Eye: Non-infected inflammatory conditions where development of bacterial infection is likely.

Ear: Otitis externa and other inflammatory conditions where bacterial infection is present or suspected (see 'Contra-indications').

Nose: Allergic rhinitis and other inflammatory conditions.

Dosage and administration **Eyes:** 1 or 2 drops instilled into the eye every one or two hours until control is achieved, when the frequency may be reduced. An extrusion of the ointment about $\frac{1}{4}$ inch long may be introduced beneath the lower lid two or three times daily and/or at night.

Ears: 2 or 3 drops instilled into the ear every two or three hours until control is achieved, when the frequency can be reduced.

Nose: 2 or 3 drops instilled into each nostril two or three times daily.

Contra-indications, warnings, etc

Contra-indications: Viral, fungal or tuberculous conditions; use in the eye is contra-indicated if purulent infection or glaucoma is present.

Hypersensitivity to any component of the preparations.

Preparations containing neomycin should not be used for treating otitis externa when the ear drum is perforated, because of the risk of ototoxicity.

Precautions: Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Side-effects: Eye drops containing corticosteroids cause a serious rise in intra-ocular pressure in a small percentage of the population, including most of those with a family history of glaucoma. A milder rise may be experienced by a larger proportion of subjects if treatment is continued for longer than a few weeks. Thinning of the cornea leading to perforation has occurred with use of topical corticosteroids. Cataract is reported to have occurred after unduly prolonged treatment of eye conditions with topical corticosteroids.

Pharmaceutical precautions It is desirable that the contents should not be used more than four weeks after first opening the bottle or tube.

Legal category POM.

Package quantities *Betnesol-N Drops*: Plastic drop-per bottles containing 5 ml or 10 ml.

Betnesol-N Eye Ointment: Tubes containing 3 g.

Further information Nil.

Product licence numbers

Betnesol-N Drops 0004/5136

Betnesol-N Eye Ointment 0004/5138

BETNOVATE* RECTAL PREPARATIONS

Presentation Betnovate Rectal Ointment is a white, translucent preparation containing 0.05% w/w betamethasone valerate, 0.1% w/w phenylephrine hydrochloride, and 2.5% w/w lignocaine hydrochloride.

Betnovate Compound Suppositories are white and opaque, and each contains 0.5 mg betamethasone valerate, 2 mg phenylephrine hydrochloride and 40 mg lignocaine hydrochloride.

Uses The clinical effectiveness of the Betnovate rectal preparations is attributable to the marked local anti-inflammatory property of the corticosteroid betamethasone valerate, the analgesic effect of lignocaine, and the vasoconstrictor effect of phenylephrine.

Betnovate Rectal Ointment or Suppositories are indicated for: pain and bleeding associated with anal fissures and internal or external haemorrhoids; post-haemorrhoidectomy pain; minor degrees of proctitis.

Dosage and administration *Ointment*: Apply a small amount of ointment two or three times a day initially, using the applicator if internal administration is required. When inflammation is subsiding, once-daily application is sufficient in most cases. One tube should provide treatment for at least a week.

Suppositories: Insert a suppository night and morning after defaecation.

Contra-indications, warnings, etc

Contra-indications: Corticosteroids should not be used in the presence of infection unless effective chemotherapy is also employed. Hypersensitivity to any component of the preparations.

Precautions: Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Side-effects: As with all topical corticosteroids, if the Betnovate preparations are used for prolonged periods, the consequences of systemic absorption should be considered, especially in children.

Prolonged and intensive treatment with active corticosteroid preparations may cause local atrophic changes in the skin.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities *Betnovate Compound Suppositories*: Box of 10.

Betnovate Rectal Ointment: Tube of 25 g with applicator nozzle.

Further information Nil.

Product licence numbers

Betnovate Compound Suppositories 0004/5129

Betnovate Rectal Ointment 0004/5128

BETNOVATE* SCALP APPLICATION

Presentation Betnovate Scalp Application is a transparent, slightly gelled solution containing 0.1% w/w betamethasone as valerate. The vehicle contains 50% of isopropyl alcohol, which has antibacterial activity. This preparation complies with the specification for Betamethasone Scalp Application, BPC, BNF.

Uses Steroid-responsive dermatoses of the scalp, such as psoriasis, seborrhoea capitis and the inflammation associated with severe dandruff.

Dosage and administration A small quantity of Betnovate Scalp Application should be applied to the scalp night and morning until improvement is noticeable. It may then be possible to sustain improvement by applying once a day, or less frequently.

Contra-indications, warnings, etc

Contra-indications: Infections of the scalp. Hypersensitivity to the preparation.

Precautions: Care must be taken to keep the preparation away from the eyes. Do not use near a naked flame.

Long-term continuous topical therapy should be avoided where possible, particularly in infants and children, as adrenal suppression can occur even without occlusion.

Development of secondary infection requires withdrawal of topical corticosteroid therapy and commencement of appropriate systemic antimicrobial therapy.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Side-effects: Betnovate preparations are usually well tolerated, but if signs of hypersensitivity appear, application should be stopped immediately.

As with other topical corticosteroids, when extensive areas are treated, sufficient systemic absorption may occur to produce the features of hypercorticism. This effect is more likely to result in infants and children, and if occlusive dressings are used, or if treatment is prolonged. Local atrophy may occur after prolonged treatment under occlusion.

In rare instances, treatment of psoriasis with corticosteroids (or its withdrawal) is thought to have provoked the pustular form of the disease.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Plastic squeeze bottles of 30 and 100 ml.

Further information The least potent corticosteroid which will control the disease should be selected. The viscosity of the scalp application has been adjusted so that the preparation spreads easily without being too

fluid. The specially-designed bottle and nozzle allow easy application direct to the scalp through the hair.

Product licence number 0004/5133.

BETNOVATE* SKIN PREPARATIONS

Presentation The Betnovate skin preparations contain 0.1% betamethasone as the valerate ester. The Betnovate R.D. (Ready Diluted) skin preparations contain 0.025% betamethasone as the valerate ester.

Betnovate Cream is a smooth, white, water-miscible preparation. It complies with the specifications for Betamethasone Valerate Cream BPC, BNF. Betnovate Ointment is a white preparation based on soft paraffin. It complies with the specification for Betamethasone Valerate Ointment BPC, BNF. Betnovate Lotion is a white, translucent, aqueous fluid. It complies with the specification for Betamethasone Lotion BPC, BNF. Betnovate R.D. Cream and Ointment are ready-diluted 1 in 4 preparations.

Uses Betamethasone valerate is an active topical corticosteroid which produces a rapid response in those inflammatory dermatoses that are normally responsive to topical corticosteroid therapy, and is often effective in the less responsive conditions such as psoriasis.

Betnovate preparations are indicated for the treatment of: eczema, including atopic, infantile, discoid and stasis; eczemas, prurigo, psoriasis, neuro-dermatoses, including ichen simplex, lichen planus, seborrhoeic dermatitis, tinea, contact sensitivity reactions, discoid lupus erythematosus, generalised erythroderma.

Betnovate can also be used in the management of insect bites, sunburn, prickly heat, and otitis externa.

Betnovate R.D. preparations are indicated for maintenance treatment when control has been achieved with Betnovate.

Dosage and administration A small quantity of Betnovate should be applied to the affected area two or three times daily until improvement occurs. It may then be possible to maintain improvement by applying once a day, or even less often, or by using the appropriate ready-diluted (1 in 4) preparation Betnovate R.D.

Betnovate and Betnovate R.D. Creams are especially appropriate for moist or weeping surfaces and Betnovate and Betnovate R.D. Ointments for dry, lichenified or scaly lesions, but this is not invariably so. Betnovate Lotion is particularly suitable when a minimal application over a large area is required.

In the more resistant lesions, such as the thickened plaques of psoriasis on elbows and knees, the effect of Betnovate can be enhanced, if necessary, by occluding the treatment area with polythene film. Overnight occlusion only is usually adequate to bring about a satisfactory response in such lesions; thereafter, improvement can usually be maintained by regular application without occlusion.

Contra-indications, warnings, etc

Contra-indications: Rosacea, acne and peri-oral dermatitis.

Skin lesions caused by infection with viruses (e.g., herpes simplex, chickenpox), fungi (e.g., candidiasis; tinea) or bacteria (e.g., impetigo).

Hypersensitivity to the preparation.

Precautions: Long-term continuous topical therapy should be avoided where possible, particularly in infants and children, as adrenal suppression can occur even

without occlusion. The face, more than other areas of the body, may exhibit atrophic changes after prolonged treatment with potent topical corticosteroids. This must be borne in mind when treating such conditions as psoriasis, discoid lupus erythematosus and severe eczema. If applied to the eyelids, care is needed to ensure that the preparation does not enter the eye, as glaucoma might result.

Appropriate antimicrobial therapy should be used whenever treating inflammatory lesions which have become infected. Any spread of infection requires withdrawal of topical corticosteroid therapy and systemic administration of antimicrobial agents. Bacterial infection is encouraged by the warm, moist conditions induced by occlusive dressings, and so the skin should be cleansed before a fresh dressing is applied.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e., in large amounts or for prolonged periods.

Side-effects: Prolonged and intensive treatment with highly active corticosteroid preparations may cause local atrophic changes in the skin such as striae, thinning and dilatation of the superficial blood vessels, particularly when occlusive dressings are used or when skin folds are involved.

As with other topical corticosteroids, prolonged use of large amounts, or treatment of extensive areas, can result in sufficient systemic absorption to produce the features of hypercorticism. This effect is more likely to occur in infants and children, and if occlusive dressings are used. In infants, the napkin may act as an occlusive dressing.

In rare instances, treatment of psoriasis with corticosteroids (or its withdrawal) is thought to have provoked the pustular form of the disease.

The Betnovate and Betnovate R.D. preparations are usually well tolerated, but if signs of hypersensitivity appear, application should stop immediately.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Betnovate Cream and Ointment are supplied in 15, 30 and 100 g tubes.

Betnovate R.D. Cream and Ointment are supplied in 100 g tubes.

Betnovate Lotion is supplied in 20 ml bottles.

Further information The least potent corticosteroid which will control the disease should be selected. None of these preparations contain lanolin. Betnovate Cream and Ointment and the corresponding R.D. preparations, do not contain parabens.

Product licence numbers

Betnovate Cream	0004/5121
Betnovate Ointment	0004/5124
Betnovate R.D. Cream	0004/0277
Betnovate R.D. Ointment	0004/0278
Betnovate Lotion	0004/5130

BETNOVATE*-C SKIN PREPARATIONS

Presentation The Betnovate-C skin preparations contain 0.1% betamethasone as the valerate ester and 3% clioquinol.

Betnovate-C Cream is a smooth, straw-coloured water-miscible cream.

Betnovate-C Ointment is a white or pale straw-coloured paraffin-based ointment.

Uses Betamethasone valerate is an active topical corticosteroid which produces a rapid response in those inflammatory dermatoses that are normally responsive to topical corticosteroid therapy, and is often effective in the less responsive conditions such as psoriasis.

Clioquinol is an anti-infective agent which has both antibacterial and anticandidal activity.

Betnovate-C preparations are indicated for the treatment of the following conditions where secondary bacterial and/or fungal infection is present, suspected, or likely to occur: eczema, including atopic, infantile, discoid and stasis eczemas, and prurigo; psoriasis; neurodermatoses, including lichen simplex; lichen planus; seborrhoeic dermatitis; intertrigo; contact sensitivity reactions; discoid lupus erythematosus; generalised erythroderma.

Betnovate-C can also be used in the management of insect bites, sunburn, prickly heat, anal and vulval pruritus, and otitis externa.

Dosage and administration A small quantity should be applied gently to the affected area two or three times daily until improvement occurs. It may then be possible to maintain improvement by applying once a day or even less often. Betnovate-C Cream is often appropriate for moist or weeping surfaces, and Betnovate-C Ointment for dry, lichenified or scaly lesions, but this is not invariably so.

In the more resistant lesions, such as the thickened plaques of psoriasis on elbows and knees, the effect of Betnovate-C can be enhanced, if necessary, by occluding the treatment area with polythene film. Overnight occlusion only is usually adequate to bring about a satisfactory response in such cases, thereafter improvement can usually be maintained by regular application without occlusion.

Contra-indications, warnings, etc

Contra-indications: Rosacea, acne and peri-oral dermatitis.

Skin lesions caused by infection with viruses (e.g., herpes simplex, chickenpox), fungi (e.g., candidiasis; tinea) or bacteria (e.g., impetigo).

Hypersensitivity to the preparation.

Precautions: Long-term continuous topical therapy should be avoided where possible, particularly in infants and children, as adrenal suppression can occur even without occlusion.

The face, more than other areas of the body, may exhibit atrophic changes after prolonged treatment with potent topical corticosteroids. This must be borne in mind when treating such conditions as psoriasis, discoid lupus erythematosus and severe eczema with Betnovate. If applied to the eyelids, care is needed to ensure that the preparation does not enter the eye, as glaucoma might result.

If infection persists, systemic chemotherapy is required. Any spread of infection requires withdrawal of topical corticosteroid therapy. Bacterial infection is encouraged by the warm, moist conditions induced by occlusive dressings, and the skin should be cleansed before a fresh dressing is applied.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e., in large amounts

or for prolonged periods. Betnovate-C may stain hair, skin or fabric, and the application should be covered with a dressing to protect clothing.

Side-effects: Prolonged and intensive treatment with highly active corticosteroid preparations may cause local atrophic changes in the skin such as striae, thinning, and dilatation of the superficial blood vessels, particularly when occlusive dressings are used or when skin folds are involved.

As with other topical corticosteroids, prolonged use of large amounts, or treatment of extensive areas, can result in sufficient systemic absorption to produce the features of hypercorticism. This effect is more likely to occur in infants and children, and if occlusive dressings are used. In infants, the napkin may act as an occlusive dressing.

In rare instances, treatment of psoriasis with corticosteroids (or its withdrawal) is thought to have provoked the pustular form of the disease.

The Betnovate preparations are usually well tolerated, but if signs of hypersensitivity appear, application should stop immediately.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Betnovate-C Cream and Ointment are supplied in 15 and 30 g tubes.

Further information The least potent corticosteroid which will control the disease should be selected. These preparations do not contain lanolin or parabens.

Product licence numbers

Betnovate-C Cream 0004/5122

Betnovate-C Ointment 0004/5126

BETNOVATE*-N SKIN PREPARATIONS

Presentation The Betnovate-N skin preparations contain 0.1% betamethasone as the valerate ester and 0.5% neomycin sulphate (3,500 units per gram or per millilitre).

Betnovate-N Cream is a smooth, white, water-miscible cream.

Betnovate-N Ointment is a white, paraffin-based ointment.

Betnovate-N Lotion is a white, aqueous translucent fluid.

Uses Betamethasone valerate is an active topical corticosteroid which produces a rapid response in those inflammatory dermatoses that are normally responsive to topical corticosteroid therapy, and is often effective in the less responsive conditions such as psoriasis.

Neomycin sulphate is a broad-spectrum, bactericidal antibiotic effective against the majority of bacteria commonly associated with skin infections.

Betnovate-N preparations are indicated for the treatment of the following conditions where secondary bacterial infection is present, suspected, or likely to occur: Eczema, including atopic, infantile, discoid and stasis eczemas; prurigo; psoriasis; neurodermatoses, including lichen simplex; lichen planus; seborrhoeic dermatitis; intertrigo; contact sensitivity reactions; discoid lupus erythematosus; generalised erythroderma.

Betnovate-N preparations can also be used in the management of insect bites, sunburn, prickly heat, anal and vulval pruritus, and otitis externa (see 'Contra-indications').

Dosage and administration A small quantity should be applied to the affected area two or three times daily until improvement occurs. It may then be possible to maintain improvement by applying once a day or even less often. Betnovate-N Cream is especially appropriate for moist or weeping surfaces, and Betnovate-N Ointment for dry, lichenified or scaly lesions, but this is not invariably so. Betnovate-N Lotion is particularly suitable when a minimal application to a large area is required.

In the more resistant lesions, such as the thickened plaques of psoriasis on elbows and knees, the effect of Betnovate-N can be enhanced, if necessary, by occluding the treatment area with polythene film. Overnight occlusion only is usually adequate to bring about a satisfactory response in such cases, thereafter improvement can usually be maintained by regular application without occlusion.

Contra-indications, warnings, etc

Contra-indications: Rosacea, acne and peri-oral dermatitis.

Skin lesions caused by infection with viruses (e.g., herpes simplex, chickenpox), fungi (e.g., candidiasis; tinea) or bacteria (e.g., impetigo).

Preparations containing neomycin should not be used or the treatment of otitis externa when the ear drum is perforated, because of the risk of ototoxicity.

Hypersensitivity to the preparations.

Precautions: Long-term continuous topical therapy should be avoided where possible, particularly in infants and children, as adrenal suppression can occur even without occlusion.

The face, more than other areas of the body, may exhibit atrophic changes after prolonged treatment with potent topical corticosteroids. This must be borne in mind when treating such conditions as psoriasis, discoid lupus erythematosus and severe eczema with Betnovate. If applied to the eyelids, care is needed to ensure that the preparation does not enter the eye, as glaucoma might result.

If bacterial infection persists, systemic chemotherapy is required. Any spread of infection requires withdrawal of topical corticosteroid therapy. Bacterial infection is encouraged by the warm, moist conditions induced by occlusive dressings, and the skin should be cleansed before a fresh dressing is applied.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Side-effects: Prolonged and intensive treatment with highly active corticosteroid preparations may cause local atrophic changes in the skin such as striae, thinning and dilatation of the superficial blood vessels, particularly when occlusive dressings are used or when skin folds are involved.

As with other topical corticosteroids, prolonged use of large amounts, or treatment of extensive areas, can result in sufficient systemic absorption to produce the features of hypercorticism. This effect is more likely to occur in infants and children, and if occlusive dressings are used. In infants, the nappin may act as an occlusive dressing.

The Betnovate preparations are usually well tolerated, but if signs of hypersensitivity appear, application should stop immediately.

In rare instances, treatment of psoriasis with cortico-

steroids (or its withdrawal) is thought to have provoked the pustular form of the disease.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Betnovate-N Cream and Ointment are supplied in 15, 30 and 100 g tubes.

Betnovate-N Lotion is supplied in 20 ml bottles.

Further information The least potent corticosteroid which will control the disease should be selected. These preparations do not contain lanolin. Betnovate-N Cream and Betnovate-N Ointment do not contain parabens.

Product licence numbers

Betnovate-N Cream 0004/5123

Betnovate-N Ointment 0004/5127

Betnovate-N Lotion 0004/5131

BEXTASOL* INHALER

Presentation Bextasol Inhaler is a pressurised aerosol containing a suspension of betamethasone valerate in propellants. One canister delivers 200 metered puffs, each providing 100 mcg of betamethasone valerate. Bextasol Inhaler complies with the specification for Betamethasone Aerosol Inhaler, BNF.

Uses *Rationale:* Betamethasone valerate is a corticosteroid which possesses high topical activity relative to its systemic activity. Inhalation of this steroid in a low dose that is delivered direct to the respiratory tract can thus provide a considerable local therapeutic effect without causing depression of hypothalamic-pituitary-adrenal function when used in the recommended dosage. There is also evidence that the growth of asthmatic children is not retarded by Bextasol therapy.

Bextasol is a prophylactic treatment for asthma and it is important that patients understand that regular daily administration is necessary – a dose cannot give immediate relief. The full effect of Bextasol usually develops within three days, but occasionally a longer period is needed.

Bextasol is indicated for the treatment of extrinsic and intrinsic asthma in children and adults.

Unlike bronchodilators and sodium cromoglycate, Bextasol has a marked anti-inflammatory effect on the respiratory tract, so that it can often control asthma which is not fully controlled by bronchodilators or sodium cromoglycate as a result of local inflammation of the respiratory tract. Additionally, Bextasol can usually replace previous systemic corticosteroid therapy either entirely or in part.

Dosage and administration The recommended initial dosage of Bextasol Inhaler for treatment of asthma in both adults and children is 800 mcg daily, usually taken as 2 puffs four times each day, in addition to any other therapy that the patient is receiving. The container should be shaken before each puff. Where asthma is complicated by hypersecretion of mucus, Bextasol may not reach the mucosa in effective amounts. A short intensive course of systemic corticosteroid therapy will usually clear the bronchi and enable Bextasol to be fully effective.

Provided the asthma is fully controlled, the dosage of ancillary drugs such as bronchodilators and sodium cromoglycate can often be reduced slowly over a period of a few weeks. It is recommended that the daily dosage of Bextasol should then be reduced to the minimum necessary to control the asthma.

Where severe asthma has required maintenance treatment with systemic corticosteroids or ACTH, it is generally possible to reduce the dosage of these compounds, and often they can be withdrawn eventually, but great care is necessary in case of pituitary or adrenal hypofunction. The systemic steroid should be withdrawn slowly, e.g. by reducing the daily dosage by the equivalent of 1 mg prednisolone at weekly or monthly intervals. Corticosteroid withdrawal symptoms, including anorexia, nausea, vomiting and muscle and joint pains, may occur. Furthermore, atopic conditions such as rhinitis and eczema, which were suppressed by systemic corticosteroid, may be unmasked and require therapy.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to betamethasone valerate.

Precautions: Caution should be exercised in the presence of bacterial, mycobacterial, viral or fungal infections of the respiratory tract.

Hypothalamic-pituitary-adrenal function recovers only gradually after systemic corticosteroid therapy has been terminated, depending upon the dosage used and the duration of systemic therapy. The possibility that stress may precipitate acute adrenal insufficiency can remain for a year or longer.

Should stress arise, systemic steroid therapy should be reinstated or the existing dosage increased if there is doubt about the ability of the hypothalamic-pituitary-adrenal system to respond adequately. It may also be advisable to increase the dosage of Bextasol temporarily, where this has been reduced.

It is advisable for the patient to have a reserve supply of corticosteroid tablets, so that if the asthma deteriorates, or infection occurs, doses can be taken pending instructions from his physician.

In pregnant animals, administration of corticosteroids can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established.

Side-effects: Some patients have reported hoarseness. Occasionally localised colonisation by *Candida albicans* occurs in the mouth and throat, and this usually requires topical antifungal therapy. If the response is unsatisfactory, a temporary reduction in the dosage of Bextasol will often speed resolution.

Overdosage: Treatment is unlikely to be needed in cases of acute overdosage.

Pharmaceutical precautions Store below 25°C away from sunlight. Do not puncture or burn the can.

Legal category POM.

Package quantities Single canisters.

Further information Each pack contains an illustrated leaflet describing how the asthmatic patient should use Bextasol.

Product licence number 0004/0142.

CEPOREX®

Presentation Ceporex Tablets are pink, film-coated tablets, each containing 250 mg or 500 mg cephalixin. They are engraved 'Ceporex 250' or 'Ceporex 500' respectively on one side and 'Glaxo' on the reverse. They comply with the BP, BNF specification for Cephalixin Tablets.

Ceporex Capsules are caramel and grey, hard gelatine capsules, each containing 250 mg or 500 mg cephalixin. They are marked 'Ceporex 250' or 'Ceporex 500' respectively, and 'Glaxo'. They comply with the BP, BNF specification for Cephalixin Capsules.

Ceporex Syrups are prepared by adding water to the granules to give orange-flavoured and coloured suspensions containing 125 mg, 250 mg or 500 mg cephalixin in each 5 ml. All strengths comply with the BPC 1973 specification for Cephalixin Mixture; the 250 mg/5 ml strength complies with the BNF requirements.

Ceporex Paediatric Drops are prepared by adding water to give 10 ml of orange-flavoured and coloured suspension containing 125 mg cephalixin in each 1.25 ml. The dropper is calibrated at 125 mg and 62.5 mg. This product complies with the BPC 1973 specification for Cephalixin Mixture.

Ceporex Suspension is a ready-prepared, yellow banana-flavoured suspension of cephalixin in vegetable oil. Each 5 ml contains 125 mg or 250 mg cephalixin.

Uses Ceporex is a bactericidal antibiotic of the cephalosporin group which is active against a wide range of Gram-positive and Gram-negative organisms. It is indicated for treatment of the following conditions when caused by susceptible bacteria.

Respiratory tract infections: acute and chronic bronchitis and infected bronchiectasis.

Ear, nose and throat infections: otitis media; mastoiditis; sinusitis; follicular tonsillitis and pharyngitis.

Urinary tract infections: acute and chronic pyelonephritis, cystitis and prostatitis. Prophylaxis of recurrent urinary tract infection.

Gynaecological and obstetrical infections.

Skin, soft-tissue and bone infections.

Gonorrhoea and syphilis (when Penicillin is unsuitable).

Dental procedures: temporary replacement of penicillin prophylaxis in patients with heart disease who are undergoing dental treatment.

Dosage and administration Many infections in adults will respond to oral dosage of 1 gram to 2 grams per day in divided doses; however, for most infections the following simple dosage scheme will be found satisfactory:

Adults and children over 12 years	500 mg t.d.s.
Children 5 to 12 years	250 mg t.d.s.
Children 1 to 5 years	125 mg t.d.s.
Children under 1 year	125 mg b.d.s.

To aid compliance, especially in ambulatory patients, the daily dosage may be given in two equal doses, e.g., 1 twice daily in adults with urinary tract infections.

The following additional information should also be considered:

Adults: For severe or deep-seated infections, special when less sensitive organisms are involved, the dosage should be increased to 1 g t.d.s. or 1.5 g q.d.s.

For prophylaxis of recurrent urinary tract infections in adults, a dose of 125 mg each night is recommended.

and may be continued for several months. (The 125 mg/5 ml Suspension is suitable for this purpose.)

Children: Ideally, dosage should be calculated on a body-weight basis, particularly in infants. The following dosage recommendations for children are derived from a normal dosage of 25 to 60 mg/kg/day. For chronic, severe or deep-seated infections, this should be increased to 100 mg/kg/day (maximum 4 g/day).

0–3 months: 62.5–125 mg twice daily.

4 months to 2 years: 62.5–125 mg four times daily or 25–250 mg twice daily.

3 to 6 years: 125–250 mg four times daily or 250–500 mg twice daily.

7 to 12 years: 250–500 mg four times daily or 500 mg twice daily.

Notes: For most acute infections, treatment should continue for at least two days after signs have returned to normal and symptoms have subsided, but in chronic, recurrent or complicated urinary tract infections and syphilis, treatment for two weeks (giving 500 mg four times daily) is recommended. For gonorrhoea, a single dose of 3 g with 1 g probenecid for males or 2 g with 1.5 g probenecid for females is usually effective. Concurrent administration of probenecid delays excretion of cephalixin and raises the serum levels by 50–100%.

Ceporex has not been shown to have a toxic effect on the kidney, but as with other antibiotics which are excreted mainly by the kidneys, unnecessary accumulation may occur in the body when renal function is below about half of normal. Therefore the maximum recommended dosages (i.e., adults, 6 g/day, children 4 g/day) should be reduced proportionately in these patients.

Adult patients receiving intermittent dialysis should be given an additional 500 mg Ceporex after each dialysis, i.e., a total dosage of up to 1 g on that day. Children should receive an additional 8 mg per kg.

Contra-indications, warnings, etc. *Contra-indications:* Hypersensitivity to cephalosporins.

Precautions: Ceporex is usually well tolerated by patients allergic to penicillin, but cross-reaction has been encountered rarely. As with other antibiotics that are excreted mainly by the kidneys, when renal function is poor, dosage of Ceporex should be suitably reduced (see 'Dosage and administration'). Laboratory experiments and clinical experience show no evidence of teratogenicity, but it would be wise to proceed with caution during the early months of pregnancy, as with all drugs.

In patients receiving Ceporex, a false-positive reaction for glucose in the urine may be given, with Benedict's or Fehling's solution, or with 'Clinitest' tablets, but not with enzyme-based tests.

Ceporex can interfere with the alkaline picrate assay for creatinine, giving a falsely high reading, but the degree of elevation is unlikely to be of clinical importance.

Side-effects: A small proportion of patients receiving ceporex experience gastro-intestinal disturbances such as nausea, vomiting and diarrhoea. As with other antibiotics, prolonged use may result in the overgrowth of non-susceptible organisms, e.g., *Candida*. This may present as vulvo-vaginitis.

Reversible neutropenia has occurred in a few patients, but it is very rare. Drug rashes – both urticarial and aculopapular – are uncommon.

Overdosage: Serum levels of cephalixin can be reduced greatly by peritoneal dialysis or haemodialysis.

Pharmaceutical precautions Ceporex Tablets and Capsules should be protected from light. Ceporex Suspension should not be refrigerated.

The reconstituted syrups retain their potency for 10 days when kept in a cool place, preferably a refrigerator. The reconstituted syrups may be diluted with water (not Syrup BP), after which they should be used within seven days. Ceporex Suspension must not be diluted with water or syrup.

Legal category POM.

Package quantities *Tablets 250 mg and 500 mg:* Bottles of 20, 100 and 500.

Capsules 250 mg and 500 mg: Bottles of 20, 100 and 500.

Syrup 125 mg/5 ml, 250 mg/5 ml and 500 mg/5 ml: Bottles of 100 ml.

Paediatric Drops 125 mg/1.25 ml: Bottles of 10 ml.

Suspension 125 mg/5 ml and 250 mg/5 ml: Bottles of 100 ml.

Further information Ceporex is resistant to the action of staphylococcal penicillinase, and is therefore active against strains of *Staph. aureus* that are insensitive to penicillin (or ampicillin) through production of that enzyme. Ceporex is also active against the majority of ampicillin-resistant *E. coli*.

Absorption of Ceporex is almost complete, even in the presence of food, and is not adversely affected by coeliac disease, partial gastrectomy, achlorhydria, jaundice or diverticulosis (duodenal or jejunal). Ceporex is excreted in the urine in high concentration.

The serum half-life is normally about one hour, but is longer in the newborn (see 'Dosage and administration'). Ceporex has a wide margin of safety.

Product licence numbers

Ceporex Tablets 250 mg	0004/5046
Ceporex Tablets 500 mg	0004/5047
Ceporex Capsules 250 mg	0004/5041
Ceporex Capsules 500 mg	0004/5042
Ceporex Syrup 125 mg	0004/5043
Ceporex Syrup 250 mg	0004/5044
Ceporex Syrup 500 mg	0004/5045
Ceporex Paediatric Drops	
Ceporex Suspension 125 mg	0004/0268
Ceporex Suspension 250 mg	0004/0269

CEPORIN*

Approved name: Cephaloridine

Presentation Vials containing 250 mg, 500 mg or 1 g of Cephaloridine BP (δ form) as a white or almost white water-soluble crystalline powder. When dissolved in Water for Injections, it forms Cephaloridine Injection BP, BNF.

Uses Ceporin is a bactericidal cephalosporin antibiotic which is active against many Gram-positive and Gram-negative organisms. It is indicated for treatment and prophylaxis of infections caused by sensitive bacteria.

Treatment

Respiratory tract infections: Acute and chronic bronchitis, infected bronchiectasis, bacterial pneumonia, post-operative chest infections and empyema.

Ear, nose and throat infections: Otitis media, mastoiditis, sinusitis, pharyngitis and follicular tonsillitis.

Urinary tract infections: Pyelonephritis, cystitis and bacterial prostatitis.

Soft-tissue infections: Cellulitis, erysipelas, infected gangrene and peritonitis.

Obstetrical and gynaecological infections: Septic abortion, uterine infections, amnionitis, pelvic and breast abscesses.

Venereal diseases: Gonorrhoea and syphilis when penicillin is unsuitable due to allergy.

Bone and joint infections: Osteomyelitis and septic arthritis.

Other infections: Neo-natal infections, septicaemia (Gram-positive or Gram-negative), bacterial endocarditis (acute or subacute) and meningitis, more particularly if pneumococcal.

Prophylaxis

Surgery: Abdominal and orthopaedic (where there is an increased risk of infection), cardiac, vascular, genitourinary, caesarean section, and amputation undertaken because of inadequate blood supply to limbs.

Obstetrics: Prolonged labour.

Paediatrics: Babies at risk after complicated delivery.

Dialysis: Renal and peritoneal.

Dental: Temporary replacement of penicillin prophylaxis in patients with rheumatic heart disease who are undergoing dental treatment.

Bacteriology

Ceporin is highly active against *Staphylococcus aureus*, including strains which are resistant to penicillin (but not the rare methicillin-resistant strains). *Streptococcus pyogenes*, *Str. viridans*, *Str. pneumoniae*, *Corynebacterium diphtheriae*, *Bacillus anthracis*. Clostridia spp. and some strains of *Str. faecalis*. Ceporin is also bactericidal against most strains of *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis* and many strains of *Haemophilus influenzae*. *Neisseria meningitidis* and nearly all strains of *N. gonorrhoeae* are highly sensitive. Shigellae and salmonellae are also sensitive, but bowel infections may not respond.

Distribution and excretion:

Serum levels: Peak levels attained after intramuscular injection are usually 5–10 mcg/ml after a 250 mg dose, 15–20 mcg/ml after 500 mg, 30–35 mcg/ml after 1 g, and 45–60 mcg/ml after 2 g.

Ceporin is not appreciably bound to serum proteins.

Excretion: About 85% of Ceporin is excreted in unchanged active form in the urine by glomerular filtration. Concurrent administration of probenecid does not markedly affect the rate of excretion.

The concentration of Ceporin in the bile is about one-third to one-half of that in the serum.

Placenta and breast milk: Ceporin crosses the placenta, and concentrations of 1–8 mcg per ml are usually found in the amniotic fluid and in the infant's serum and cord when 1–2 g of Ceporin are given 12-hourly to the mother. The peak concentration in breast milk after a 1 g dose by intramuscular injection is approximately 2.5 mcg/ml occurring after one hour, with a half-life of about four hours.

Cerebrospinal fluid: Ceporin does not enter cerebrospinal fluid in significant amounts through non-inflamed meninges, but when the meninges are inflamed, cerebro-

spinal fluid concentrations reach 25–50% or more of the serum concentrations.

Eye: Ceporin readily enters the primary aqueous humour in the presence of anterior segment inflammation, and therapeutic levels have been reported after an intramuscular injection of 30 mg Ceporin per kg body weight. Lower antibiotic levels occur in the absence of inflammation.

Joints and bone: Systemically administered Ceporin enters synovial fluid in therapeutic amounts. In osteomyelitis, inflammation can be markedly reduced after only a few days when an appropriate dosage of Ceporin is used.

Dosage and administration Ceporin is not absorbed from the gastro-intestinal tract and must be given parenterally. Administration of the solution by intravenous, intramuscular or deep subcutaneous injection is virtually painless and well tolerated.

General dosage for adults and children: Maximum daily dosage: children, 4 g; adults with normal kidney function under 50 years of age, 6 g. Maximum daily dose for patients over 50 years of age or who have undergone surgery within the previous 48 hours is 4 g. See 'Precautions' if administering aminoglycoside antibiotic or potent diuretics concurrently.

Usual dosage in infections of mild to moderate degree due to Gram-positive organisms and urinary tract infections: 15–30 mg/kg/day (1–2 g/day in adults) in 1 or 3 divided doses. In simple soft-tissue infections: 15 mg/kg/day may be given as a single dose, or as 2 divided doses.

Infections due to Gram-negative organisms and severe infections due to Gram-positive organisms: 40–60 mg/kg/day (3–4.5 g/day in adults) in 2–4 divided doses.

Infections of exceptional severity, e.g. bacterial endocarditis and septicaemia: 60–100 mg/kg/day (4.5–6 g/day in adults) in 2–4 divided doses.

Neonates: 30 mg/kg/day in 2 divided doses for the treatment of infections, but for prophylaxis the dose may be given as one injection each day. This dosage is adequate for a wide range of infections in neonates because of their slower renal excretion.

Other dosage recommendations: **Venereal diseases:** Gonorrhoea – 1 single injection of 2 g (30 mg/kg), possible repeated once 24 hours later. Syphilis – 1–2 (15–30 mg/kg) once daily for 10–14 days.

Meningitis: 70–100 mg/kg/day systemically in 4 divided doses, which may be supplemented with a suitable dose by the intrathecal route once a day or on alternate days for the first five to seven days (see 'Administration by other routes' below).

Prophylaxis of infection in abdominal and orthopaedic surgery: Three 1 g systemic doses given at intervals of six hours, commencing at the time of induction of anaesthesia, have reduced significantly the incidence of wound infection. Alternatively, for abdominal operation instillation of a solution containing 1 g Ceporin dissolved in 2 ml Water for Injections into the wound on closure has been shown to be similarly effective.

Impaired renal function: When kidney function is poor the degree of impairment should be checked regularly and the dosage of Ceporin reduced after giving a standard dose (i.e., that applicable to a patient with normal renal function) as indicated in the table overleaf:

Serum creatinine (mg/100 ml)	Creatinine clearance (ml/min)	Ceporin serum half-life (hours)	Maximum dosage	
			Adults (g per day)	Children (mg/kg/ day)
1-3	75-40	2-5	2-3	50
1-6	40-20	4-6	1-2	25
1-9	20-10	5-10	1	16
>9	<10	8-20	0.5	8

Ceporin can interfere with the alkaline picrate assay for creatinine by giving a falsely high reading, but the degree of elevation is unlikely to be of clinical importance.

Serum levels of Ceporin should be monitored if possible and dosage further reduced if the level exceeds 100 mcg/ml or if progressively increasing levels are found.

In renal impairment, it is often preferable to increase the interval between doses instead of reducing the size of each dose. If the blood urea or BUN is known, a guide to the desired interval between standard doses (i.e., doses appropriate to a patient without renal impairment) can be estimated as follows:

$\left. \begin{aligned} \text{blood urea (mg/100 ml)} \div 6 \\ \text{blood urea (mmol/litre)} \div 1 \\ \text{BUN (mg/100 ml)} \div 3 \end{aligned} \right\} \begin{aligned} &\text{Interval between} \\ &\text{Ceporin injections} \\ &\text{in hours} \end{aligned}$

Thus, if the blood urea is 72 mg per 100 ml, the indicated interval between doses is 12 hours.

Administration by other routes:

In most cases systemic dosage is given in addition.

Intrathecal: The maximum daily dose for adults is 50 mg; for children, 25 mg; for infants, 12.5 mg. As with other cephalosporins and the penicillins, overdosage is dangerous.

Intrapleural: In the treatment of empyema, 250 mg Ceporin may be instilled into the pleural cavity daily.

Intracavitary: 50 mg dissolved in 0.5 ml of Water for injections is suitable.

Preparation of solutions:

Intramuscular or deep subcutaneous injection: Dissolve Ceporin in Water for Injections which has been warmed to body temperature using 4 ml for 2 g, 3 ml for 1 g, 2 ml for 500 mg and 1 ml for 250 mg. Shake until dissolved. Solutions should be used without delay, as crystallisation may occur. It is recommended that a fresh solution should be prepared for each injection.

Intravenous administration: 0.5-1 g Ceporin may be dissolved in 3 ml of Sodium Chloride or 5% Dextrose solution which has been warmed to body temperature. The clear solution should be diluted to 10 to 20 ml before injection into the vein or, when the patient is receiving parenteral fluids, into the tubing of the giving set, taking three to five minutes. Ceporin may also be given as a short intravenous infusion administered over a period of 30-60 minutes, or as a continuous infusion. In the latter case, a fresh solution should be prepared at least every six hours. Ceporin is compatible with the solutions commonly infused, including dextran solutions, Arrow's and Ringer's and Hartmann's solutions and 5% sodium bicarbonate.

Intrathecal injection: A small dose (see above) of the antibiotic is dissolved in 2-10 ml Sodium Chloride solution or the patient's own CSF. Use of a disposable

membrane filter unit of 0.45 micron pore size is convenient for ensuring clarity of the solution.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to cephalosporin antibiotics.

Precautions: The daily dosage for patients over the age of 50 years, and those who have undergone surgery within 48 hours previously, should not exceed 4 g. When renal function is poor, the dosage of Ceporin must be suitably reduced and other steps taken (see 'Dosage and administration' section). Patients given high dosage of Ceporin should have their renal function checked regularly during treatment.

Concurrent administration of potent diuretics such as frusemide, or potentially nephrotoxic antibiotics such as gentamicin, increases the risk of renal toxicity associated with high dosage of Ceporin. In these circumstances, the maximum recommended dosage of Ceporin should be reduced by about one-third.

Hypersensitivity: Ceporin is usually well tolerated by patients who are hypersensitive to the penicillins, but cross-reaction has been encountered rarely. Especial care is indicated in patients who have experienced an anaphylactic reaction to penicillin.

Pregnancy: There is no experimental or clinical evidence of embryopathic or teratogenic effects attributable to Ceporin, but it would be wise to proceed with caution during the early months of pregnancy.

Urine tests: A false-positive reaction for glucose in the urine may occur with Benedict's or Fehling's solutions or with 'Clinitest', but not with enzyme-based tests.

Side-effects: Very high blood levels of Ceporin may cause renal damage. This effect is more likely to occur in patients with existing impairment of renal function.

Hypersensitivity reactions, mostly skin rashes occasionally occur. When these happen, the drug should be withdrawn and not used again in that patient. Very rarely, an anaphylactic reaction has developed. Reversible neutropenia has occurred in a few patients but is very rare. Occasionally, a temporary slight rise in serum glutamic-oxalacetic transaminase occurs. Increased prothrombin time has been reported.

Positive Coombs' tests have been found in some patients receiving Ceporin, but these are more likely to occur with high dosage, in the presence of renal impairment or in the elderly. This phenomenon can interfere with cross-matching of blood.

Prolonged use may result in the overgrowth of non-susceptible organisms, e.g., *Candida*.

Overdosage: Serum levels of cephaloridine may be reduced by 25-50% by peritoneal dialysis or haemodialysis.

Pharmaceutical precautions: Ceporin (δ form) is best stored at room temperature.

Solutions of Ceporin should be injected as soon as possible after preparation. If they are allowed to stand, crystallisation may occur.

Solutions retain satisfactory potency for 24 hours if stored below 25°C, and for four days when kept in a refrigerator. Even if clear, stored solutions may be supersaturated and should be warmed, preferably by holding the vial in warm water for about 30 seconds. Shake thoroughly before use, to avoid possible crystallisation in the syringe.

Legal category POM.

Package quantities Vials containing 250 mg, 500 mg or 1 g in boxes of 5.

Further information There is evidence that Ceporin can act synergistically with streptomycin and kanamycin against strong penicillinase-producing staphylococci.

Ceporin contains no inorganic ion, and therefore has no influence on electrolyte balance. The displacement value in solution is 0.7 ml per gram.

Product licence number 0004/5142.

CORLAN* PELLETS

Presentation Small white pellets engraved 'Corlan Glaxo' on one side. Each pellet contains 2.5 mg hydrocortisone in the form of the water-soluble ester hydrocortisone sodium succinate. The pellets comply with the specification for Hydrocortisone Lozenges BPC, BNF.

Uses Local use in aphthous ulceration of the mouth, whether simple or occurring as a complication in diseases such as sprue, idiopathic steatorrhoea and ulcerative colitis.

Dosage and administration *Adults and children:* Corlan Pellets should not be sucked, but be kept in the mouth and allowed to dissolve slowly in close proximity to the ulcers. One pellet should be used in this way four times a day. When ulcers recur quickly after withdrawal of treatment, maintenance therapy with reduced dosage is desirable for a period.

Contra-indications, warnings, etc

Contra-indications: Corlan Pellets should not be used in the presence of oral infection unless effective chemotherapy is also employed. Hypersensitivity to any component of the product.

Precautions: In pregnant animals, systemic administration of corticosteroids can cause abnormalities of fetal development. The relevance of this finding to humans has not been established.

Side-effects: Corticosteroids may worsen diabetes.

Overdosage: Treatment is unlikely to be needed in cases of acute overdosage.

Pharmaceutical precautions Replace cap firmly after use.

Legal category POM.

Package quantities Vial of 20 pellets.

Further information Nil.

Product licence number 0004/5077.

CORTELAN* TABLETS

Presentation White tablets engraved 'Cortelan Glaxo' on one side and scored on the reverse. Each tablet contains 25 mg cortisone acetate, and complies with the specification for Cortisone Tablets BP, BNF.

Uses Replacement therapy in Addison's disease and following adrenalectomy.

Dosage and administration In adults with Addison's disease, 25–40 mg daily are usually needed, divided into 2 doses. In replacement therapy after adrenalectomy, the dosage required may be slightly higher.

During intercurrent infection, dosage requirements may be increased to between 75 and 100 mg a day.

Children may require lower dosage.

Contra-indications, warnings, etc

Contra-indications: Systemic infections, unless specific anti-infective therapy is employed. Hypersensitivity to any component of the tablet.

Precautions: In infections (including latent tuberculosis), effective chemotherapy should be given. In pregnant animals, systemic administration of corticosteroids can cause abnormalities of fetal development. The relevance of this finding to humans has not been established.

Side-effects: Long term treatment in high dosage may cause any of the features associated with hypercorticism.

Overdosage: Treatment is unlikely to be needed in cases of acute overdosage.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Bottles of 100 tablets.

Further information Nil.

Product licence number 0004/5078.

CRYSTAPEN* INJECTION

Presentation Vials containing sodium benzylpenicillin (penicillin G) as a white, crystalline, water-soluble powder. Also vials containing sodium benzylpenicillin with 4.5% sodium citrate as a buffer (5 and 10 mega units vials only). For preparation of Benzylpenicillin Injection BP, BNF.

Ampoules of Crystapen Intrathecal containing freeze-dried sodium benzylpenicillin.

Uses Crystapen has bactericidal activity in infection due to penicillin-sensitive organisms, particularly streptococci, pneumococci (*Streptococcus pneumoniae*), meningococci, gonococci and staphylococci (excluding penicillinase-producing strains). Crystapen is indicated for most wound infections, pyogenic infections of the skin, soft tissue infections and infections of the nose, throat, nasal sinuses, respiratory tract and middle ear, etc.

Generalised infections, septicaemia and pyaemia from susceptible bacteria. Acute and chronic osteomyelitis, subacute bacterial endocarditis, and meningitis caused by susceptible organisms. Gonorrhoea.

Dosage and administration The following dosage applies to both intramuscular and intravenous injection.

Adults: Usually 600–1,200 mg (1–2 mega units) daily divided into 2 to 4 doses. In bacterial endocarditis, mega units or more may be given daily in divided doses by the intravenous route, often by infusion. Intravenous doses in excess of 1.2 g (2 mega units) should be given slowly, taking at least one minute for each 300 mg (0.3 mega unit) to avoid high levels causing irritation of the central nervous system. High dosage of sodium benzylpenicillin may result in hypernatraemia and hypokalaemia unless the sodium content is taken into account.

Children aged 1 month to 12 years: 10–20 mg (17,000–34,000 units) per kilogram body weight in 24 hours usually divided into 4 doses. In meningitis the dosage may be doubled.

Newborn infants: 30 mg/kg/day (50,000 units) in divided doses, usually twice daily in the first few days of life, then three or four times a day. In meningitis the systemic dosage may be increased to 60–90 mg/kg/day (100,000–150,000 units) divided into 3 or 4 doses.

PREPARATION OF SOLUTIONS

Intramuscular injection: A 600 mg (1 mega unit) dose is usually dissolved in 1.6 to 2.0 ml of Water for Injections.

Intravenous injection: A suitable concentration is 100 mg (1 mega unit) dissolved in 4 to 10 ml of Water for Injections.

Intravenous infusion: It is recommended that 600 mg (1 mega unit) should be dissolved in at least 10 ml of Sodium Chloride Injection or other transfusion solution.

OTHER ROUTES OF ADMINISTRATION

These usually supplement systemic dosage.

Subconjunctival injection: 300 or 600 mg dissolved in 0.5–1 ml of Water for Injections.

Intrathecal injection: For adults, 6 mg (10,000 units) dissolved in 10 ml of Sodium Chloride Injection BP, or 10 ml of the patient's own cerebrospinal fluid. Maximum dose, 12 mg (20,000 units). For infants and children, 0.1 mg/kg (170 units/kg) is suitable. The concentration of penicillin in the injection should not exceed 0.6 mg/ml (1,000 units/ml). **Overdosage is dangerous.**

Use of a disposable membrane filter of 0.45 micron pore size is convenient for ensuring clarity of the solution; the special freeze-dried Crystapen is not available.

Contra-indications, warnings, etc

Contra-indications: Allergy to penicillins.

Precautions: Massive doses of sodium penicillin can cause hypokalaemia and sometimes hypernatraemia. Use of a potassium-sparing diuretic may be helpful. If renal function is very poor, large doses of penicillin (e.g. 2 mega units or more) can cause cerebral irritation and ts.

Skin sensitisation may occur in persons handling the antibiotic, and care should be taken to avoid contact with the substance.

It should be recognised that any patient with a history of allergy, especially to drugs, is more likely to develop hypersensitivity reaction to penicillin.

Side-effects: Occasionally hypersensitivity to penicillin, in the form of urticarial rash, may occur; it may be treated with antihistamine drugs. More rarely, anaphylactic reactions have been reported. Haemolytic anaemia (sometimes with leucopenia) can be induced by high dosage of penicillin.

Overdosage: Excessive blood levels of penicillin G can be corrected by haemodialysis.

Pharmaceutical precautions Solutions of penicillin should be used promptly although unbuffered solutions will retain satisfactory potency for up to seven days if refrigerated. Buffered solutions retain satisfactory potency for up to three days at temperatures not exceeding 25°C (77°F), and for up to 14 days if refrigerated at 2–10°C.

Legal category POM.

Package quantities *Ampoules:* 12 mg (20,000 units) unbuffered for intrathecal injection, box of 3.

ials: 300 mg (500,000 units) unbuffered, box of 10, 6 g (1,000,000 units) unbuffered, box of 10.

Bottles: 3 g (5 mega units) buffered and 6 g (10 mega units) buffered.

Further information 600 mg Crystapen in solution displaces 0.4 ml. Each mega unit of unbuffered Crystapen represents 1.68 mEq of sodium; the figure for buffered Crystapen is 2.08 mEq.

Product licence numbers

Crystapen 12 mg	0004/5074
Crystapen 300 mg	0004/5069
Crystapen 0.6 g	0004/5070
Crystapen 3.0 g	0004/5072
Crystapen 6.0 g	0004/5073

CRYSTAPEN* G TABLETS AND SYRUPS

Presentation Crystapen G Tablets are yellow, film-coated tablets each containing 250 mg potassium penicillin G and engraved 'Crystapen G 250' on one side and 'Glaxo' on the reverse. They comply with the specification for Benzylpenicillin Tablets BP.

Crystapen G Syrups are prepared by adding water to the granules to produce a creamy-yellow, pleasant-flavoured, clear syrup containing 125 mg or 250 mg potassium penicillin G in each 5 ml.

Uses Infections due to penicillin-susceptible organisms, e.g., those due to beta-haemolytic streptococci, pneumococci and some staphylococci. Prophylaxis before and after surgery and dental extractions to prevent subacute bacterial endocarditis in patients with congenital or rheumatic heart disease.

Dosage and administration *Infants:* 62.5–125 mg.

Children: 125–250 mg.

Adults: 250–500 mg.

All given four times a day, preferably before meals. These doses are usually effective, but higher or more frequent dosage may sometimes be indicated.

N.B. In serious and overwhelming infections when rapid control is essential, injections of sodium penicillin G are necessary initially.

In patients with beta-haemolytic streptococcal infection it is advisable to continue treatment for 10 days to prevent bacteriological relapse and complications such as rheumatic fever or acute nephritis.

Contra-indications, warnings, etc

Contra-indications: Allergy to penicillins.

Precautions: It should be recognised that any patient with a history of allergy, especially to drugs, is more likely to develop a hypersensitivity reaction.

Side-effects: Occasionally patients experience diarrhoea.

Sensitivity reactions such as urticarial rash are uncommon, and anaphylaxis is very rare.

Overdosage: Toxic blood levels are unlikely to occur following oral administration. However, if they do, treatment should be symptomatic in the first instance, with haemodialysis for those patients who do not respond quickly.

Pharmaceutical precautions Replace cap firmly after using the tablets.

Crystapen G Syrups, when reconstituted, should be used within five days if kept below 20°C, or within 14 days if kept in a refrigerator. Keep bottle well closed.

Crystapen G Syrups can be diluted with Syrup BP if required.

Legal category POM.

Package quantities *Crystapen G Tablets*: Bottles of 100 and 500.

Crystapen G Syrups: Granules to produce 100 ml of syrup in each bottle when reconstituted with 60 ml water.

Further information Nil.

Product licence numbers

Crystapen G Tablets	0004/5055
Crystapen G Syrup 125 mg	0004/5053
Crystapen G Syrup 250mg	0004/5054

CRYSTAPEN* V PREPARATIONS

Presentation Crystapen V Tablets are orange, film-coated tablets each containing 250 mg penicillin V as the potassium salt and engraved 'Crystapen V' on one side and 'Glaxo' on the reverse. The product complies with the specification for Penicillin V-K Tablets BP, BNF.

Crystapen V Syrups are prepared by adding water to the granules to produce a red, pleasant-flavoured, clear syrup. Each 5 ml syrup contains 125 mg or 250 mg penicillin V as the potassium salt. The products comply with the specification for Penicillin V Elixir BPC, BNF.

Crystapen V Suspension is a white, opaque, caramel-flavoured suspension of calcium penicillin V in a vegetable-oil vehicle. Each 5 ml contains 125 mg penicillin V as the calcium salt. The product complies with the specification for Penicillin V Mixture BPC, BNF.

Uses Crystapen V has bactericidal activity in infections due to penicillin-susceptible organisms, e.g., those due to beta-haemolytic streptococci, pneumococci and some staphylococci. Prophylaxis before and after surgery and dental extractions to prevent subacute bacterial endocarditis in patients with congenital or rheumatic heart disease.

Dosage and administration *Infants*: 62.5–125 mg.

Children: 125–250 mg.

Adults: 250–500 mg.

All given four times a day, preferably before meals. Higher or more frequent dosage may sometimes be indicated.

N.B. In serious and overwhelming infections when rapid control is essential, injections of sodium penicillin G are necessary initially.

In patients with beta-haemolytic streptococcal infection it is advisable to continue treatment for 10 days to prevent bacteriological relapse and complications such as rheumatic fever or acute nephritis.

Contra-indications, warnings, etc

Contra-indications: Allergy to penicillins.

Precautions: It should be recognised that any patient with a history of allergy, especially to drugs, is more likely to develop a hypersensitivity reaction to penicillin V.

Side-effects: Occasionally patients experience diarrhoea. Sensitivity reactions such as urticarial rash are uncommon, and anaphylaxis is very rare.

Overdosage: Toxic blood levels are unlikely to occur following oral administration. However, if they do, treatment should be symptomatic.

Pharmaceutical precautions Crystapen V Suspension should not be refrigerated.

Crystapen V Syrups, when reconstituted, should be used within seven days if kept below 20°C, or within 14 days if kept in a refrigerator.

Crystapen V Syrups can be diluted with Syrup BP if required.

Crystapen V Suspension can be diluted with fractionated coconut oil.

Legal category POM.

Package quantities *Crystapen V Tablets*: Bottles of 500 and 1,000.

Crystapen V Syrups: Granules to produce 100 ml of syrup in each bottle when reconstituted with 51 ml water for 250 mg Syrup, or 60 ml water for 125 mg Syrup.

Crystapen V Suspension: Bottle of 100 ml.

Further information Nil.

Product licence numbers

Crystapen V Tablets	0004/5059
Crystapen V Syrup 125 mg	0004/5057
Crystapen V Syrup 250 mg	0004/5058
Crystapen V Suspension	0004/5056

CYTAcon* LIQUID AND TABLETS

Presentation Cytacon Tablets are white, film-coated and engraved 'Cytacon' on one side and 'Glaxo' on the reverse. Each contains 50 mcg cyanocobalamin.

Cytacon Liquid is red coloured and contains 35 mcg cyanocobalamin in each 5 ml.

Uses *Post-gastrectomy deficiency*. As many as 50% of patients who have had a partial gastrectomy are likely to develop abnormally low serum-vitamin B₁₂ levels within five years of the operation unless supplementary vitamin B₁₂ is given. Megaloblastic anaemia is not uncommon and subacute degeneration of the cord has been reported. After total gastrectomy, it is better to administer vitamin B₁₂ by injection (as Neo-Cytamen or Cytacon rather than orally).

Diseases of the alimentary tract, such as 'blind-loop' syndrome and small-bowel diverticula, may also be associated with vitamin B₁₂ deficiency.

Nutritional deficiency. Low serum-vitamin B₁₂ level may occur in strict vegetarians, and in old people subsisting on limited diets. The diagnosis of pernicious anaemia should be excluded before administering or vitamin B₁₂.

Tropical sprue: Both folic acid and vitamin B₁₂ may be needed; in some cases oral vitamin B₁₂ may be sufficiently well absorbed to avoid the need for injection.

Pernicious anaemia: If injections of vitamin B₁₂ (Neo-Cytamen or Cytacon) cannot be used, large daily or doses may be substituted, but the blood must be examined at least every three months.

Dosage and administration Doses should be adjusted according to particular needs, and taken between meals if possible.

Adults: 1–3 tablets or more daily. Alternatively, 5–10 ml of Cytacon Liquid can be given two or three times daily. In pernicious anaemia at least 300 mcg should be given daily.

Children: 5 ml Cytacon Liquid two or three times daily.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to oral cyanocobalamin.

Precautions: In pernicious anaemia, an adequate dose must be used and the blood picture must be examined regularly at least every three months.

Side-effects: Cytacon appears to be virtually free from diverse effects. Hypersensitivity reactions are very rare, and persons who have become sensitised to cyanocobalamin by injection are often able to take it by the oral route without trouble.

Overdosage: Treatment is unlikely to be needed in cases of overdosage.

Pharmaceutical precautions None.

Legal category P.

Package quantities *Cytacon Tablets:* Bottles of 25 and 250.

Cytacon Liquid: Bottles of 200 ml and 2 L.

Further information Nil.

Product licence numbers

Cytacon Tablets 0004/5015

Cytacon Liquid 0004/5014

CYTAMEN*

Presentation Cytacon '250' is a clear, red solution containing 250 mcg cyanocobalamin per millilitre.

Cytacon '1000' is a clear, red solution containing 1,000 mcg cyanocobalamin per millilitre.

Cytacon complies with the specification for Cyanocobalamin Injection, BP.

Uses Addisonian pernicious anaemia. Prophylaxis and treatment of other macrocytic anaemias associated with vitamin B₁₂ deficiency. Schilling test.

Not indicated for treatment of toxic amblyopias – use Neo-Cytamen.

Dosage and administration *Addisonian pernicious anaemia and other macrocytic anaemias without neurological involvement:* Initially: 250–1,000 mcg intramuscularly on alternate days for one to two weeks, then 250 mcg weekly until the blood count is normal.

Maintenance: 1,000 mcg monthly.

Addisonian pernicious anaemia and other macrocytic anaemias with neurological complications: Initially: 1,000 mcg intramuscularly on alternate days as long as improvement is occurring.

Maintenance: 1,000 mcg monthly.

Prophylaxis of macrocytic anaemia associated with vitamin B₁₂ deficiency resulting from gastrectomy, some malabsorption syndromes and strict vegetarianism: 250–1,000 mcg monthly.

Schilling test: An intramuscular injection of 1,000 mcg cyanocobalamin is an essential part of this test.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to cyanocobalamin.

Precautions: Doses in excess of 10 mcg daily may produce a haematological response in patients with platelet deficiency. Indiscriminate administration may mask the true diagnosis.

Side-effects: Sensitisation to vitamin B₁₂ is rare, but it may present as an itching exanthema, and, exceptionally, as anaphylactic shock.

Overdosage: Treatment is unlikely to be needed in cases of overdosage.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Ampoules of 1 ml in boxes of 5.

Further information Nil.

Product licence numbers

Cytacon 250 0004/5016

Cytacon 1000 0004/5017

DERMOVATE* CREAM AND OINTMENT

Presentation Dermovate Cream and Ointment each contain 0.05% w/w clobetasol propionate. The water-miscible cream and the paraffin-based ointment are both white in appearance.

Uses Clobetasol propionate is a very active topical corticosteroid which is of particular value when used in short courses for the treatment of more resistant dermatoses such as psoriasis, recalcitrant eczemas, lichen planus, discoid lupus erythematosus, and other conditions which do not respond satisfactorily to less-active steroids.

Dosage and administration Apply sparingly to the affected area once or twice daily until improvement occurs. As with other highly-active topical steroid preparations, therapy should be discontinued when control is achieved. In the more responsive conditions this may be within a few days. If a longer course is necessary, it is recommended that treatment should not be continued for more than four weeks without the patient's condition being reviewed. Repeated short courses of Dermovate may be used to control exacerbations. If continuous steroid treatment is necessary, a less potent preparation should be used.

In very resistant lesions, especially where there is hyperkeratosis, the anti-inflammatory effect of Dermovate can be enhanced, if necessary, by occluding the treatment area with polythene film. Overnight occlusion only is usually adequate to bring about a satisfactory response. Thereafter improvement can usually be maintained by application without occlusion.

Contra-indications, warnings, etc

Contra-indications: Rosacea, acne and peri-oral dermatitis.

Skin lesions caused by infection with viruses (e.g., herpes simplex, chickenpox), fungi (e.g., candidiasis, tinea) or bacteria (e.g., impetigo).

Hypersensitivity to the preparation.

Precautions: Long-term continuous therapy with Dermovate should be avoided, particularly in infants and children, in whom adrenal suppression occurs readily. If Dermovate is required for use in children, it is recommended that the treatment should be reviewed weekly. It should be noted that the infant's napkin may act as an occlusive dressing.

The face, more than other areas of the body, may exhibit atrophic changes after prolonged treatment with potent topical corticosteroids. This must be borne in

mind when treating facial conditions which warrant use of Dermovate, and frequent observation of the patient is important. If applied to the eyelids, care is needed to ensure that the preparation does not enter the eye, as glaucoma might result.

Appropriate antimicrobial therapy should be used whenever treating inflammatory lesions which have become infected. Any spread of infection requires withdrawal of topical corticosteroid therapy and institution of suitable systemic chemotherapy.

Bacterial infection is encouraged by the warm, moist conditions induced by occlusive dressings, and the skin should be cleansed before a fresh dressing is applied.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e., in large amounts or for prolonged periods.

Side-effects: Provided the weekly dosage is less than 50 g in adults, any pituitary-adrenal suppression is likely to be transient with a rapid return to normal values once the short course of steroid therapy has ceased. The same applies to children given proportionate dosage. Use of occlusive dressings increases the absorption of topical corticosteroids.

Prolonged and intense treatment with highly-active corticosteroid preparations may cause atrophic changes, such as striae, thinning of the skin, and dilatation of the superficial blood vessels, particularly when occlusive dressings are used, or where skin folds are involved.

In rare instances, treatment of psoriasis with corticosteroids (or its withdrawal) is thought to have provoked the pustular form of the disease.

Dermovate is usually well tolerated, but if signs of hypersensitivity appear, application should be stopped immediately.

Pharmaceutical precautions None.

Legal category POM.

Package quantities Tubes of 25 and 100 g.

Further information The least potent corticosteroid which will control the disease should be selected. Dermovate preparations do not contain lanolin or parabens.

Product licence numbers

Dermovate Ointment 0004/0220

Dermovate Cream 0004/0219

DERMOVATE* SCALP APPLICATION

Presentation Dermovate Scalp Application is a transparent, slightly gelled solution containing 0.05% w/w clobetasol propionate. The vehicle contains 50% isopropyl alcohol, which has antibacterial activity.

Uses Psoriasis and recalcitrant eczemas of the scalp. Clobetasol propionate is a highly-active topical corticosteroid which is indicated for use in short courses for conditions which do not respond satisfactorily to less active steroids.

Dosage and administration Apply sparingly to the scalp night and morning until improvement occurs. As with other highly-active topical steroid preparations, therapy should be discontinued when control is

achieved. Repeated short courses of Dermovate Scalp Application may be used to control exacerbations. If continuous steroid treatment is necessary, a less potent preparation should be used.

Contra-indications, warnings, etc

Contra-indications: Infections of the scalp.

Hypersensitivity to the preparation.

Precautions: Care must be taken to keep the preparation away from the eyes. Do not use near a naked flame.

Long-term continuous therapy with Dermovate Scalp Application should be avoided, particularly in infants and children, in whom adrenal suppression occurs readily.

Development of secondary infection requires withdrawal of topical corticosteroid therapy and commencement of appropriate systemic antimicrobial therapy.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e., in large amounts or for prolonged periods.

Side-effects: Dermovate preparations are usually well tolerated, but if signs of hypersensitivity appear, application should be stopped immediately.

As with other topical corticosteroids, local atrophy may result from prolonged treatment, particularly if occlusive dressings are used.

When extensive areas are treated, sufficient systemic absorption may occur to produce the features of hypercorticism, especially in infants and children. This effect is more likely to occur after prolonged treatment particularly if occlusive dressings are used.

In rare instances, treatment of psoriasis with corticosteroids (or its withdrawal) is thought to have provoked the pustular form of the disease.

Pharmaceutical precautions None.

Legal category POM.

Package quantities Plastic squeeze bottle with elongated nozzle containing 25 or 100 ml.

Further information The least potent corticosteroid which will control the disease should be selected. The viscosity of the scalp application has been adjusted so that the preparation spreads easily without being too fluid. The specially-designed bottle and nozzle allow easy application direct to the scalp through the hair.

Product licence number 0004/0242.

DERMOVATE*-NN SKIN PREPARATIONS

Presentation Dermovate-NN skin preparations contain clobetasol propionate 0.05% w/w, neomycin sulphate 0.5% and nystatin 100,000 units per gram.

Dermovate-NN Ointment is a buff paraffin-based ointment.

Dermovate-NN Cream is buff in colour.

Uses Clobetasol propionate is a highly active topical corticosteroid which is of particular value when used in short courses for the treatment of recalcitrant eczemas, neurodermatoses, and other conditions which do not respond satisfactorily to less active steroids.

Dermovate-NN is indicated in those dermatoses where secondary bacterial or candidal infection is present, suspected, or likely to occur, as when using occlusive dressings in conditions such as psoriasis.

usage and administration Apply sparingly to the affected area once or twice daily until improvement occurs. As with other highly-active topical steroid preparations therapy should be discontinued when control is achieved. In the more responsive conditions this may be within a few days. If a longer course is necessary, it is recommended that treatment should not be continued for more than four weeks without the patient's condition being reviewed. Repeated short courses of Dermovate-NN may be used to control exacerbations. If continuous steroid treatment is necessary, a less potent preparation should be used.

In very resistant lesions, especially where there is hyperkeratosis, the anti-inflammatory effect of Dermovate-NN can be enhanced, if necessary, by occluding the treatment area with polythene. Overnight occlusion is usually adequate to bring about a satisfactory response, thereafter improvement can usually be maintained by application without occlusion.

contra-indications, warnings, etc

contra-indications: Rosacea, acne and peri-oral dermatitis.

Skin lesions caused by infection with viruses (e.g., herpes simplex, chickenpox), fungi (e.g., candidiasis, tinea) or bacteria (e.g., impetigo).

Preparations containing neomycin should not be used for the treatment of otitis externa when the ear drum is perforated, because of the risk of ototoxicity.

Hypersensitivity to the preparations.

precautions: Long-term continuous therapy with Dermovate-NN should be avoided, particularly in infants and children, in whom adrenal suppression occurs readily. If Dermovate-NN is required for use in children, it is recommended that the treatment should be reviewed weekly. It should be noted that the infant's napkin may act as an occlusive dressing.

The face, more than other areas of the body, may exhibit atrophic changes after prolonged treatment with potent topical corticosteroids. This must be borne in mind when treating facial conditions which warrant use.

Dermovate-NN, and frequent observation of the patient is important. If applied to the eyelids, care is needed to ensure that the preparation does not enter the eye, as glaucoma might result.

If infection persists, systemic chemotherapy is required. Any spread of infection requires withdrawal of topical corticosteroid therapy. Bacterial infection is encouraged by the warm, moist conditions induced by occlusive dressings, and the skin should be cleansed before a fresh dressing is applied.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e., in large amounts for prolonged periods.

side-effects: Provided the weekly dosage is less than 10 g in adults, any pituitary adrenal suppression is likely to be transient with a rapid return to normal values once a short course of steroid therapy has ceased. The same applies to children given proportionate dosage. Use of occlusive dressings increases the absorption of topical corticosteroids.

Prolonged and intensive treatment with highly-active corticosteroid preparations may cause atrophic changes such as striae, thinning of the skin, and dilatation of the superficial blood vessels, particularly when occlusive dressings are used, or where skin folds are involved.

Dermovate-NN is usually well tolerated, but if signs of hypersensitivity appear, application should be stopped immediately.

In rare instances, treatment of psoriasis with corticosteroids (or its withdrawal) is thought to have provoked the pustular form of the disease.

Pharmaceutical precautions None.

Legal category POM.

Package quantities Tubes of 25 g.

Further information The least potent corticosteroid which will control the disease should be selected. Dermovate-NN preparations contain neither lanolin nor parabens.

Product licence numbers

Dermovate-NN Ointment 0004/0237

Dermovate-NN Cream 0004/0255

DIONOSIL* SUSPENSIONS

Presentation Dionosil Aqueous Suspension contains 50% w/v propylidone. It complies with the BP specification for Propylidone Suspension.

Dionosil Oily Suspension contains 60% w/v propylidone in arachis oil. It complies with the BP specification for Propylidone Oily Suspension.

Uses Radiographic visualisation of the bronchial tree. Propylidone is distributed on the mucosal surfaces of the bronchi without filling the lumen. Thus, if coughing occurs, alveolar filling is unlikely. Shadows remain well defined for at least 30 minutes; any contrast agent remaining in the lungs usually disappears within three days, but may persist longer in bronchoectatic cavities. It is excreted by the kidneys.

Dosage and administration The volume of Dionosil required is normally 0.75 to 1 ml for each year of age up to a maximum of 18 ml for an adult. The contrast medium is best administered into the trachea, but can be given by the cricothyroid route. The 'over the tongue' route is best avoided with Dionosil Aqueous.

Before use, it is essential to shake the vial vigorously until the propylidone is completely suspended. This normally takes about half a minute.

The temperature of the suspension should be not lower than room temperature, nor higher than body temperature at the time of instillation. If Dionosil Aqueous is used in an all-glass syringe, it is advisable to lubricate the piston to avoid the slight risk of jamming. Arachis oil is a suitable lubricant.

Contra-indications, warnings, etc

Contra-indications: No absolute contra-indication is known.

Warning: Patients sensitive to iodine may also be sensitive to propylidone, and the risk involved must be balanced against the importance of the information required. Caution should be exercised in all patients with a history of allergy or hypersensitivity to drugs.

Precautions: As with all bronchographic contrast media, if Dionosil is introduced too rapidly, or the volume is excessive, occlusion of the smaller bronchi can cause lung collapse. Where respiratory function is reduced, as in asthmatics, special care should be taken; if bilateral bronchography is necessary in such patients, it is wise to allow an interval of several days between the investiga-

tion of each side. Where respiratory function is normal, it is advisable to allow at least 15 minutes between right-sided and left-sided bronchography in case an immediate hypersensitivity reaction occurs.

Adequate anaesthesia, local and/or general, must be employed in order to suppress the cough reflex. In children under general anaesthesia, Dionosil should be removed from one lung before the other is examined. If inadvertently injected into the tissues, Dionosil is non-irritant, but may be rather persistent.

Administration of iodine-containing media may invalidate PBI determination for 3 to 12 months.

Side-effects: Hypersensitivity reactions are uncommon, but may cause respiratory dysfunction and skin eruptions. Following bronchography with Dionosil there may occur a transient pyrexia sometimes associated with malaise and aching of the joints. The cause is unknown. It has been noted following the use of all bronchographic media but is more common with aqueous than with oily preparations. The symptoms usually subside spontaneously within 48 hours and require no specific treatment. Alveolarisation and atelectasis have been reported.

Overdosage: Remove the Dionosil by postural drainage and/or a bronchoscope. Systemic use of corticosteroids and potent diuretics may be needed if there is excessive effusion of fluid.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities 20 ml vial.

Further information Nil.

Product licence numbers

Dionosil Aqueous Suspension 0004/5097

Dionosil Oily Suspension 0004/5098

EFCORTELAN* SKIN PREPARATIONS

Presentation Efcortelan Cream contains 0.5%, 1% or 2.5% hydrocortisone in a smooth, white, water-miscible cream base.

Efcortelan Ointment contains 0.5%, 1% or 2.5% hydrocortisone in an off-white paraffin-based ointment.

Efcortelan Lotion contains 1% hydrocortisone in a white, aqueous, translucent fluid.

Efcortelan Cream 1% complies with the specification for Hydrocortisone Cream BPC, BNF.

Efcortelan Ointments comply with the specification for Hydrocortisone Ointment BP, BNF.

Efcortelan Lotion complies with the specification for Hydrocortisone Lotion BPC, BNF.

Uses Hydrocortisone has topical anti-inflammatory activity of value in the treatment of a wide variety of dermatological conditions, including the following: eczema, including atopic, infantile, discoid and stasis eczemas; prurigo, neurodermatoses, including lichen simplex, seborrhoeic dermatitis, intertrigo, contact sensitivity reactions; discoid lupus erythematosus, generalised erythroderma.

Efcortelan preparations can also be used in the management of insect bites, sunburn, prickly heat, and otitis externa.

Dosage and administration A small quantity should be applied to the affected area two or three times daily.

Efcortelan Cream is often appropriate for moist or

weeping surfaces, and Efcortelan Ointment for dry lichenified or scaly lesions, but this is not invariably so. Efcortelan Lotion is particularly suitable when a minima application to a large area is required.

Contra-indications, warnings, etc

Contra-indications: Skin lesions caused by infection with viruses (e.g., herpes simplex, chickenpox), fung (e.g., candidiasis, tinea) or bacteria (e.g., impetigo).

Hypersensitivity to the preparations.

Precautions: In infants and children, long-term continuous topical therapy should be avoided where possible as adrenal suppression can occur even without occlusion. In infants, the napkin may act as an occlusive dressing, and increase absorption.

Appropriate antimicrobial therapy should be used whenever treating inflammatory lesions which have become infected. Any spread of infection requires withdrawal of topical corticosteroid therapy, and systemic administration of antimicrobial agents.

As with all corticosteroids, prolonged application to the face is undesirable.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e., in large amount or for prolonged periods.

Side-effects: Efcortelan preparations are usually well tolerated, but if signs of hypersensitivity appear, application should stop immediately.

Local atrophic changes may occur where skin folds are involved, or in areas such as the nappy area in small children, where constant moist conditions favour the absorption of hydrocortisone. Sufficient systemic absorption may also occur in such sites to produce the features of hypercorticism after prolonged treatment. This effect is more likely to occur in infants and children and if occlusive dressings are used.

Pharmaceutical precautions None.

Legal category POM.

Package quantities Efcortelan Cream and Ointment 1% are supplied in 15 and 50 g tubes.

Efcortelan Cream and Ointment 0.5% and 2.5% are supplied in 15 g tubes.

Efcortelan Lotion is supplied in 20 ml bottles.

Further information The least potent corticosteroid which will control the disease should be selected. None of these preparations contain lanolin. Efcortelan Cream and Efcortelan Ointment are free from parabens.

Product licence numbers

Efcortelan Cream 5% 0004/5080

Efcortelan Cream 1% 0004/5081

Efcortelan Cream 2.5% 0004/5082

Efcortelan Ointment 0.5% 0004/5085

Efcortelan Ointment 1% 0004/5086

Efcortelan Ointment 2.5% 0004/5087

Efcortelan Lotion 1% 0004/5084

EFCORTELAN* SOLUBLE

Presentation Vials of Efcortelan Soluble contain freeze-dried hydrocortisone sodium succinate as a white plug. Each vial contains 100 mg hydrocortisone as the

sodium succinate ester; this readily dissolves in the 2 ml ampoule of Water for Injections supplied with the vial. When prepared as directed, this preparation complies with the specification for Hydrocortisone Sodium Succinate Injection BP, BNF.

Uses Status asthmaticus and acute allergic reactions, in anaphylactic reaction to drugs. Efcortelan Soluble supplements the action of adrenaline.

Severe shock arising from surgical or accidental trauma or overwhelming infection.

Adrenal crisis precipitated by abnormal stress in Addison's disease, Simmond's disease, following adrenalectomy, and when adrenocortical function has been suppressed by prolonged corticosteroid therapy.

Intrathecal injection and adjunctive treatment in tuberculous meningitis and other meningitides.

Note: Efcortelan Soluble does not replace other forms of therapy for the treatment of shock and status asthmaticus.

Dosage and administration For intravenous injection, 100 mg Efcortelan Soluble may be dissolved in 2 ml Water for Injections immediately before administration. Efcortelan Soluble may also be given as an intravenous infusion.

A clinical effect is seen in two to four hours, and it persists for up to eight hours after intravenous injection.

Efcortelan Soluble can be given by intramuscular injection, but the response is likely to be less rapid, especially in shock.

Systemic therapy in adults: 100–500 mg administered by slow intravenous injection taking half to one minute. This dose can be repeated three or four times in 24 hours, or as required, depending upon the condition being treated and the patient's response.

Systemic therapy in children: Infants up to 1 year may be given 25 mg hydrocortisone intravenously; children 1–5 years, 50 mg; 6–12 years, 100 mg.

Other uses: Intrathecal injection. For children, intrathecal doses between 10 and 20 mg, according to age, have been used. A 20 mg dose is suitable for adults. Intrathecal injections may be given daily for a few days if required; then the interval between injections is usually increased. Use of a disposable membrane filter of 0.45 micron pore size is convenient for ensuring clarity of the solution.

Local treatment of soft tissue lesions – up to 200 mg of Efcortelan Soluble can be used.

Contra-indications, warnings, etc

Contra-indications: Systemic infections, unless specific anti-infective therapy is employed.

Efcortelan Soluble should not be injected directly into tendons.

Precautions: Administration of corticosteroids may impair the ability to resist and counteract infection; in addition, clinical signs and symptoms of infection are suppressed.

In pregnant animals, systemic administration of corticosteroids can cause abnormalities of fetal development. The relevance of this finding to humans has not been established.

Side-effects: In the short term, high levels of hydrocortisone involve little risk of adverse reactions, except that peptic ulceration may occur, or be aggravated. With continued use, signs of hypercorticism may become apparent.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Vials of 100 mg hydrocortisone with a 2 ml ampoule of Water for Injections.

Further information Each vial provides 8.5 mg (0.37 mEq) of sodium and 0.15 mEq of phosphate (PO_4).

Product licence number 0004/5088.

EFORTESOL* INJECTION

Presentation Ampoules of Efcortelan Injection contain an aqueous, ready-prepared buffered solution of hydrocortisone sodium phosphate. Each millilitre contains 100 mg hydrocortisone as the sodium phosphate ester. The solution is clear and colourless or pale yellow. Efcortelan Injection complies with the specification for Hydrocortisone Sodium Phosphate Injection BP.

Uses This presentation permits rapid use in emergency situations involving the following conditions.

Status asthmaticus and acute allergic reactions, in anaphylactic reaction to drugs. Efcortelan supplements the action of adrenaline.

Severe shock arising from surgical or accidental trauma or overwhelming infection.

Adrenal crisis precipitated by abnormal stress in Addison's disease, Simmond's disease, following adrenalectomy, and when adrenocortical function has been suppressed by prolonged corticosteroid therapy.

Soft tissue lesions.

Note: Efcortelan does not replace other forms of therapy for the treatment of shock and status asthmaticus.

Dosage and administration *Systemic therapy in adults:* 100–500 mg hydrocortisone (1–5 ml) administered by slow intravenous injection, taking at least half to one minute. This dose can be repeated three or four times in 24 hours, or as required, depending upon the condition being treated and the patient's response. Alternatively, Efcortelan injection may be given as an intravenous infusion. A clinical effect is seen in two to four hours, and it persists for up to eight hours after intravenous injection. The same dose can be given by intramuscular injection, but the response is likely to be less rapid, especially in shock.

Systemic therapy in children: As a guide, infants up to 1 year may be given 25 mg hydrocortisone intravenously; children 1–5 years, 50 mg; 6–12 years, 100 mg (1 ml).

Other uses: Local treatment of soft tissue lesions – 100–200 mg.

Efcortelan Injection is not recommended for intrathecal use.

Contra-indications, warnings, etc

Contra-indications: Systemic infections, unless specific anti-infective therapy is employed. Hypersensitivity to any component.

Efcortelan Injection should not be injected directly into tendons.

Precautions: Administration of corticosteroids may impair the ability to resist and counteract infection; in addition clinical signs and symptoms of infection are suppressed. In pregnant animals, systemic administration of corticosteroids can cause abnormalities of fetal development. The relevance of this finding to humans has not been established.

Side-effects: On receiving a bolus dose by intravenous injection, some patients have experienced paraesthesia, often localised in the genital area. The unpleasant sensation usually passes off within a few minutes, and no sequelae have been reported. This effect has not been reported after use of Betnesol Injection or Efcortelan Soluble Injection.

In the short term, high dosage of hydrocortisone involves little risk of adverse reactions, except that peptic ulceration may occur, or be aggravated. With continued use, signs of hypercorticism may become apparent.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Ampoules 1 ml (100 mg) in box of 5.

Ampoules 5 ml (500 mg) in box of 10.

Further information It should be noted that 10 ml Efcortelan Injection contains 152 mg (6.6 mEq) sodium and 298 mg (9.4 mEq) phosphate (PO₄).

Product licence number 0004/5089.

ELTROXIN* TABLETS

Presentation Small white tablets engraved 'Eltroxin 50 Glaxo' or 'Eltroxin 100 Glaxo' containing 50 mcg (0.05 mg) or 100 mcg (0.1 mg) anhydrous thyroxine sodium respectively. The lower-strength tablets are scored. Eltroxin Tablets comply with the specification for Thyroxine Tablets BP, BNF.

Uses Hypothyroidism.

Dosage and administration *Adults:* Initially 50–100 mcg daily, preferably taken before breakfast, and adjusted at three to four week intervals by 50 mcg until normal metabolism is steadily maintained; this may require doses of 150 to 300 mcg daily. With patients aged over 50 years, it is not advisable to exceed 50 mcg a day initially, and where there is cardiac disease, 25 mcg daily, or 50 mcg on alternate days, is more suitable. In this condition the daily dosage may be increased by 25 mcg at intervals of perhaps four weeks.

In younger patients, and in the absence of heart disease, a serum thyroxine (T₄) level of about 70 to 160 nanomols per litre, or a serum thyrotrophin level of less than 5 milli-units per litre, should be aimed at. In those aged over 50, and/or in the presence of heart disease, clinical response is probably a more acceptable criterion of dosage than serum levels.

A pre-therapy ECG is valuable, as changes induced by hypothyroidism may be confused with ECG evidence of ischaemia. If too rapid an increase of metabolism is produced (causing diarrhoea, nervousness, rapid pulse, insomnia, tremors and sometimes anginal pain where there is latent myocardial ischaemia) dosage must be reduced or withheld for a day or two, then begun again at a lower level.

Cretenism and juvenile myxoedema: The largest dose consistent with freedom from toxic effects should be given. Clinically, normal pulse rate and absence of diarrhoea or constipation are the most useful indications. For cretinous infants, a suitable starting dose is 25 mcg Eltroxin daily, with increments of 25 mcg every two to four weeks until mild toxic symptoms appear. Dosage is then slightly reduced. The same applies to juvenile myxoedema, except that the starting dose for children older than one year may be 2.5 to 5 mcg/kg/day.

Contra-indications, warnings, etc

Contra-indications: Thyrotoxicosis. Hypersensitivity to any component.

Precautions: Patients with panhypopituitarism or other causes predisposing to adrenal insufficiency may react unfavourably to thyroxine treatment, and it is advisable to initiate corticosteroid therapy before giving thyroxine in these cases.

Especial care is needed when there are symptoms of myocardial insufficiency or ECG evidence of myocardial infarction.

Side-effects: The following effects are indicative of excessive dosage, and usually disappear on reduction of dosage or withdrawal of treatment for a few days. Anginal pain, cardiac arrhythmias, palpitation, and cramps in skeletal muscle; also tachycardia, diarrhoea, restlessness, excitability, headache, flushing, sweating, excessive loss of weight and muscular weakness.

Overdosage: Gastric lavage or emesis is required if the patient is seen within several hours of taking the dose. The appearance of clinical hyperthyroidism may be delayed for up to five days. Treatment is symptomatic, and tachycardia has been controlled in an adult by 40 mg doses of propranolol given every six hours.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Bottles of 100 and 1,000 tablets.

Further information 100 mcg thyroxine is equivalent in activity to 20–30 mcg liothyronine or 60 mg Thyroid BP.

Product licence numbers

Tablets 50 mcg 0004/5018

Tablets 100 mcg 0004/5019

EUMOVATE* CREAM AND OINTMENT

Presentation Eumovate Cream and Ointment contain 0.05% clobetasone butyrate, and are white in appearance. The emollient cream is water-miscible, whilst the ointment has a paraffin base.

Uses Clobetasone butyrate is a topically active corticosteroid which provides an exceptional combination of activity and safety. When formulated as Eumovate it is more effective in the treatment of eczemas than 1% hydrocortisone, or the less-active synthetic steroid preparations that are in common use, yet has little effect on hypothalamic-pituitary-adrenal function. This has been so even when Eumovate was applied to adults in large amounts under whole-body occlusion. All topical corticosteroids can cause cutaneous atrophy if grossly misused. However, studies in animal and human models indicate that Eumovate and hydrocortisone cause less thinning of the epidermis than the other topical steroids tested.

Eumovate is suitable for treating the milder forms of eczema, seborrhoeic dermatitis, and other steroid responsive skin conditions, e.g., sunburn, which do not require the use of a more active topical corticosteroid. In the more resistant dermatoses, Eumovate may be used as maintenance therapy between courses of one of the more active topical steroids.

Use of Eumovate is particularly appropriate when treating infants and young children, who are more liable to experience undesirable effects after prolonged appli-

ation of steroid preparations than are older patients. Eumovate may be used as the standard corticosteroid treatment for napkin rash, seborrhoeic dermatitis and itopic eczema, reserving the more potent preparations or use in short courses on resistant areas.

Dosage and administration Eumovate should be applied to the affected area up to four times a day until improvement occurs, when the frequency of application may be reduced.

Contra-indications, warnings, etc

Contra-indications: Skin lesions caused by infection with viruses (e.g., herpes simplex, chickenpox), fungi (e.g., candidiasis, tinea) or bacteria (e.g., impetigo).

Hypersensitivity to the preparations.

Precautions: In infants and children, long-term continuous topical corticosteroid therapy should be avoided where possible, as adrenal suppression can occur even without occlusion. In infants, the napkin may act as an occlusive dressing, and increase absorption.

Appropriate antimicrobial therapy should be used whenever treating inflammatory lesions which have become infected. Any spread of infection requires withdrawal of topical corticosteroid therapy, and systemic administration of antimicrobial agents.

As with all corticosteroids, prolonged application to the face is undesirable.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e., in large amounts or for prolonged periods.

Side-effects: In the unlikely event of signs of hypersensitivity appearing, application should stop immediately. When large areas of the body are being treated with Eumovate it is possible that some patients will absorb sufficient steroid to cause transient adrenal depression despite the low degree of systemic activity associated with clobetasone butyrate.

Local atrophic changes could possibly occur in situations where moisture increases absorption of clobetasone butyrate, but only after prolonged use.

Pharmaceutical precautions None.

Legal category POM.

Package quantities Tubes of 25 and 100 g.

Further information The least potent corticosteroid which will control the disease should be selected. Neither of these preparations contain lanolin or parabens.

Product licence numbers

Eumovate Cream 0004/0233

Eumovate Ointment 0004/0254

UMOVATE* EYE DROPS ▼

Presentation Eumovate Drops contain clobetasone 7-butyrate 0.1% w/v, with benzalkonium chloride 0.01% w/v as a preservative, as an off-white suspension that is sterile until the bottle is opened.

Uses Eumovate Eye Drops are indicated for the treatment of non-infected inflammatory conditions of the eye including diseases of the external eye and of the anterior segments. In these conditions it has been shown

to have comparable anti-inflammatory activity to Beta-methasone Sodium Phosphate Eye Drops.

Eumovate Eye Drops have less adverse effect on intra-ocular pressure than hydrocortisone (1%), betamethasone sodium phosphate (0.1%), prednisolone sodium phosphate (0.5%), or dexamethasone (0.1%) eye drops.

Dosage and administration The usual dosage is one or two drops four times a day; for severe inflammatory conditions one or two drops should be instilled into the eye every one or two hours until signs of improvement are apparent, when the frequency may be reduced.

Contra-indications, warnings, etc

Contra-indications: Viral, fungal, tuberculous, or purulent conditions of the eye, hypersensitivity to any component of the preparation. Use is contra-indicated if glaucoma is present.

Eumovate Eye Drops contain benzalkonium chloride as a preservative and therefore should not be used to treat patients who wear soft contact lenses.

Precautions: Although Eumovate Eye Drops have been shown to have little adverse effect on intra-ocular pressure in most patients, those patients receiving long term treatment should have their intra-ocular pressure monitored frequently.

Cataract is reported to have occurred after unduly prolonged treatment with some topical corticosteroids and in those diseases which cause thinning of the cornea, perforation has been known to occur.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Side-effects: Rises in intra-ocular pressure have been reported in susceptible patients but these are generally much less than with other corticosteroid eye preparations, including hydrocortisone.

Pharmaceutical precautions The contents should not be used more than four weeks after first opening the bottle.

Legal category POM.

Package quantities Plastic dropper bottles containing 5 or 10 ml.

Further information Nil.

Product licence number 0004/0260.

EUMOVATE*-N EYE DROPS ▼

Presentation Eumovate-N Drops contain clobetasone 17-butyrate 0.1%, and neomycin sulphate 0.5% w/v, with benzalkonium chloride 0.01% w/v as a preservative, as an off-white suspension that is sterile until the bottle is opened.

Uses Eumovate-N Eye Drops are indicated for the treatment of inflammatory conditions of the eye where secondary bacterial infection is likely to occur. In these conditions it has been shown to have comparable anti-inflammatory activity to Betamethasone Sodium Phosphate with Neomycin Eye Drops.

Eumovate-N Eye Drops have less adverse effect on intra-ocular pressure than hydrocortisone (1%), betamethasone sodium phosphate (0.1%), prednisolone

sodium phosphate (0.5%), or dexamethasone (0.1%) eye drops.

Dosage and administration The usual dosage is one or two drops four times a day; for severe inflammatory conditions one or two drops should be instilled into the eye every one or two hours until signs of improvement are apparent, when the frequency may be reduced.

Contra-indications, warnings, etc

Contra-indications: Viral, fungal, tuberculous, or purulent conditions of the eye, hypersensitivity to any component of the preparation. Use is contra-indicated if glaucoma is present.

Eumovate-N Eye Drops contain benzalkonium chloride as a preservative and therefore should not be used to treat patients who wear soft contact lenses.

Precautions: Although Eumovate-N Eye Drops have been shown to have little adverse effect on intra-ocular pressure in most patients, those patients receiving long term treatment should have their intra-ocular pressure monitored frequently.

Cataract is reported to have occurred after unduly prolonged treatment with some topical corticosteroids and in those diseases which cause thinning of the cornea, perforation has been known to occur.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Side-effects: Rises in intra-ocular pressure have been reported in susceptible patients but these are generally much less than with other corticosteroid eye preparations, including hydrocortisone.

Pharmaceutical precautions The contents should not be used more than four weeks after first opening the bottle.

Legal category POM.

Package quantities Plastic dropper bottles containing 5 or 10 ml.

Further information Nil.

Product licence number 0004/0276.

FERSADAY* TABLETS

Presentation Ochre, film-coated tablets engraved 'Fersaday' on one side, and 'Glaxo' on the reverse. Each tablet contains Ferrous Fumarate BP equivalent to 100 mg ferrous iron. Fersaday Tablets comply with the specification for Ferrous Fumarate Tablets BP.

Uses Prophylaxis and treatment of iron-deficiency states.

Dosage and administration The usual adult dose is one tablet daily. (The foil enclosing each tablet is printed with a day of the week in sequence.) In severe or refractory iron deficiency, one Fersaday Tablet may be given twice daily.

This presentation of ferrous fumarate is not intended for the treatment of children.

Contra-indications, warnings, etc There are no known contra-indications.

Precautions: Some post-gastrectomy patients show poor absorption; careful surveillance of this group is advised.

As with all drugs, Fersaday should be kept out of the reach of children.

Care is required when treating patients with peptic ulceration. Concurrent administration of antacids may reduce absorption of iron preparations.

Side-effects: Diarrhoea or constipation are uncommon.

Overdosage: Ingestion of an overdose of iron orally requires emergency treatment along the following lines. Vomiting should be induced immediately, followed as soon as possible by parenteral injection of desferrioxamine mesylate, and then gastric lavage. In the meantime it is helpful to give milk and/or 5% sodium bicarbonate solution by mouth.

Dissolve 2 g desferrioxamine mesylate in 2 or 3 ml of Water for Injections and give intramuscularly. A solution of 5 g desferrioxamine in 50 to 100 ml of fluid may be left in the stomach. If desferrioxamine is not available leave 300 ml of 1% to 5% sodium bicarbonate solution in the stomach. Fluid replacement is essential.

Pharmaceutical precautions Protect from light.

Legal category P.

Package quantities Calendar wallet of 28 tablets.

Further information Nil.

Product licence number 0004/5020.

FERSAMAL* TABLETS AND SYRUP

Presentation *Fersamal Tablets:* Small light brown tablets engraved 'Fersamal Glaxo' on one side. Each Tablet contains 200 mg anhydrous ferrous fumarate providing approximately 65 mg ferrous iron. Fersamal Tablets comply with the specification for Ferrous Fumarate Tablets BP.

Fersamal Syrup: Brown, aqueous suspension containing 140 mg ferrous fumarate, equivalent to approximately 45 mg ferrous iron, per 5 ml. Fersamal Syrup complies with the specification for Ferrous Fumarate Mixture BPC.

Uses For prophylaxis and treatment of iron-deficiency states.

Dosage and administration *Adults:* 1 tablet three times a day, or 10 ml of syrup twice a day. Double dose may be given if desired. The tablets are easily swallowed but may also be crushed or chewed, being almost tasteless.

Full-term infants and young children: 2.5–5 ml Syrup twice a day.

Premature infants: The usual dosage is 0.6 ml/kg/day but some may require 2.4 ml/kg/day.

Contra-indications, warnings, etc There are no known contra-indications.

Precautions: Some post-gastrectomy patients show poor absorption, careful surveillance of this group is advised.

Fersamal should be kept out of reach of children.

Care is needed when treating patients with peptic ulceration.

Side-effects: Diarrhoea or constipation is uncommon.

Overdosage: Ingestion of an overdose of iron orally requires emergency treatment along the following lines. Vomiting should be induced immediately, followed as soon as possible by parenteral injection of desferrioxamine mesylate, and then gastric lavage. In the meantime, it is helpful to give milk and/or 5% sodium bicarbonate solution by mouth.

Dissolve 2 g desferrioxamine mesylate in 2 to 3 ml of Water for Injections and give intramuscularly. A solution of 5 g desferrioxamine in 50 to 100 ml of fluid may be left in the stomach. If desferrioxamine is not available, leave 300 ml of 1% or 5% sodium bicarbonate solution in the stomach. Fluid replacement is essential.

Pharmaceutical precautions Protect from light.

Legal category P.

Package quantities *Tablets:* Bottles of 100 and 1,000.

Syrup: Bottles of 200 ml.

Further information Fersamal Syrup may be diluted with Syrup BP at the time of dispensing if required.

Product licence numbers

Tablets 0004/5021

Syrup 0004/5022

GRISOVIN* TABLETS

Presentation Grisovin Tablets contain 125 mg or 500 mg of the antibiotic griseofulvin in fine particle form. Both are white, film-coated, bi-convex tablets engraved 'Grisovin 125' or 'Grisovin 500' on one side as appropriate and 'Glaxo' on the other. They comply with the specification for Griseofulvin Tablets BP, BNF.

Uses When griseofulvin is given orally for systemic treatment of ringworm infections, it enables newly formed keratin of the skin, hair and nails to resist attack by the fungi. As the new keratin extends, the old infected keratin is shed.

Grisovin is effective against the dermatophytes causing ringworm (tinea), including *Microsporum canis*, *Trichophyton rubrum* and *T. verrucosum*.

Grisovin is not effective in infections caused by *Candida albicans* (monilia), *Aspergilli*, *Malassezia furfur* (Pityriasis versicolor) and *Nocardia* species.

Dosage and administration Doses should be taken after meals, otherwise absorption is likely to be inadequate.

Adults: Normally 500–1,000 mg daily, but not less than 10 mg/kg body weight daily. A single dose daily is often satisfactory, but divided doses may be more effective in patients who respond poorly.

Children: Usually 10 mg per kg (5 mg/lb) body weight daily in divided doses.

Duration of treatment: This depends upon the thickness of keratin at the site of infection. For hair or skin at least four weeks' treatment is required, whereas toe or finger nails may need six to twelve months' treatment. Therapy should be continued for at least two weeks after all signs of infection have disappeared.

Contra-indications, warnings, etc

Contra-indications: Porphyrria or severe liver disease. Griseofulvin may cause liver disease to deteriorate, and liver function should be monitored in such conditions.

Precautions: Griseofulvin may decrease the effect of the coumarin anticoagulants.

Absorption of griseofulvin is inhibited when phenobarbitone is taken concurrently. The blood level, and hence efficacy, of griseofulvin may also be impaired as the result of concurrent administration of substances such as phenylbutazone and sedative and hypnotic drugs which induce metabolising enzymes.

Photosensitivity reactions can occur on exposure to intense natural or artificial sunlight.

In those rare cases where individuals are affected by drowsiness whilst taking griseofulvin, they should not drive vehicles or operate machinery. Patients should be warned that an enhancement of the effects of alcohol by griseofulvin has been reported.

In pregnant animals, administration of very high doses of griseofulvin can cause abnormalities of fetal development. The relevance of this finding to humans has not been established, but use during pregnancy is best avoided.

Side-effects: Headache and gastric discomfort sometimes occur, but usually disappear as treatment continues. On rare occasions urticarial reactions, erythematous rashes and aggravation or precipitation of systemic lupus erythematosus have been reported.

Overdosage: Treatment is unlikely to be required in cases of acute overdosage.

Pharmaceutical precautions None.

Legal category POM.

Package quantities *125 mg tablets:* Bottles of 100 and 1,000 tablets.

500 mg tablets: Bottles of 25 and 100 tablets.

Further information Customary hygienic measures should be adopted to minimise the risk of re-infection, and concurrent use of a topical fungicide may be helpful to minimise any spread of infective material.

Product licence numbers

Grisovin Tablets 125 mg 0004/5060

Grisovin Tablets 500 mg 0004/5061

MYODIL*

Presentation Ampoules containing lophendylate Injection BP, a colourless to pale yellow viscous liquid which darkens on exposure to light. It contains 30% of organically combined iodine, has a density of approximately 1.26 g/ml, and is immiscible with cerebrospinal fluid.

Uses Myelography.

Ventriculography; Visualisation of the third and fourth ventricles and the aqueduct of Sylvius.

Intra-uterine use; To outline the fetus prior to intra-uterine blood transfusion.

Dosage and administration *Myelography:* In general, sufficient Myodil is introduced into the spinal subarachnoid space to allow all the structures under suspicion to be outlined by simple posturing of the patient. Usually 6 to 9 ml are ample, and if complete block is present, a smaller volume is adequate. Occasionally up to 18 ml are necessary if the subarachnoid space is wide. The material should be removed by aspiration after the examination unless it is required for further study.

Ventriculography: Good visualisation of the third and fourth ventricles and the aqueduct of Sylvius can be obtained by use of Myodil. The amount injected into the selected lateral ventricle is usually 1 to 1.6 ml, but the dose can range from 0.5 ml to 2 ml according to circumstances.

Intra-uterine use: 9 ml of Myodil has been injected into the amniotic sac to outline the fetus prior to intra-uterine blood transfusion.

Contra-indications, warnings, etc

Contra-indications: As for simple lumbar puncture, Myodil should not be used when there is a history of reaction to iophendylate or to iodine. The procedure should be postponed if there is blood or bilirubin in the spinal fluid.

Warnings: Myodil should NOT be emulsified with cerebrospinal fluid, as this is reported to increase the frequency of toxic reactions. If Myodil enters the blood stream, it can cause shock and violent coughing.

When myelography has to be performed during pregnancy, the raised maternal serum iodine levels may result in congenital goitre and hypothyroidism in the fetus. Patients with nodular goitre may become thyrotoxic.

Ideally, all-glass syringes should be used, as Myodil may dissolve substances from some plastic syringes and/or their rubber plungers. If a plastic syringe is used, the Myodil should be drawn into it immediately prior to injection to minimise contact with the syringe.

The risk of induced arachnoiditis and aseptic meningitis has been reported to be enhanced in patients with multiple sclerosis.

Precautions: If possible, 10 to 14 days should elapse between lumbar puncture and subsequent myelography. As much Myodil as possible should be removed after the procedure, but when only small amounts are involved, most consider it reasonable not to aspirate if this requires another lumbar puncture. Retention of Myodil may cause prolonged elevation of the serum protein-bound iodine, thus invalidating diagnostic PBI estimations.

Side-effects: Myodil is usually well-tolerated, and provided a suitable technique of injection is used, preferably with video control, serious effects are rare. Myodil usually causes a slight increase in the white cell count and protein of the CSF, and diagnostic examination should therefore precede use of this contrast agent.

Hypersensitivity reactions, probably anaphylactic in type, are rare, but may be severe or even fatal. Immediate withdrawal of the Myodil should be performed if there is indication of such a process. Emergency drugs should always be available to deal with crises. As with simple lumbar puncture, headache is frequent, and after myelography it is sometimes severe, with vomiting and photophobia.

Pyrexia and stiff neck can occur, usually soon after myelography; rarely, they appear some weeks after the examination. Low back pain is not uncommon, and previous symptoms such as sciatica may be exacerbated. Symptoms normally resolve within several days, but if they persist, any residual Myodil should be removed, and where warranted, a suitable dose of hydrocortisone sodium succinate injected intrathecally.

Post-myelography arachnoiditis, which may be severe, occurs in some patients, and adhesions and fibrous exudate may be found on operation in patients who had at some time undergone myelography with iophendylate.

This emphasises the importance of removing as much Myodil as possible at the time of investigation.

Overdosage: Aspirate the Myodil.

Pharmaceutical precautions Protect from light; do not use if discoloured.

Legal category POM.

Package quantities Box of three 3 ml ampoules.

Further information Nil.

Product licence number 0004/5099.

NEO-CYTAMEN®

Presentation Ampoules containing a clear red solution, which provides either 250 mcg (Neo-Cytamer 250) or 1,000 mcg (Neo-Cytamen 1,000) of hydroxocobalamin (vitamin B₁₂) per millilitre. Neo-Cytamen Injection complies with the specification for Hydroxocobalamin Injection BP, BNF.

Uses Addisonian pernicious anaemia.

Prophylaxis and treatment of other macrocytic anaemias associated with vitamin B₁₂ deficiency.

Tobacco amblyopia and Leber's optic atrophy.

Dosage and administration The following dosage schemes are suitable for adults and children:

Addisonian pernicious anaemia and other macrocytic anaemias without neurological involvement: Initially 250–1,000 mcg intramuscularly on alternate days for one to two weeks, then 250 mcg weekly until the blood count is normal.

Maintenance: 1,000 mcg every two or three months.

Addisonian pernicious anaemia and other macrocytic anaemias with neurological involvement: Initially 1,000 mcg on alternate days as long as improvement is occurring.

Maintenance: 1,000 mcg every two months.

Prophylaxis of macrocytic anaemia associated with vitamin B₁₂ deficiency resulting from gastrectomy, some malabsorption syndromes and strict vegetarianism 1,000 mcg every two or three months.

Tobacco amblyopia and Leber's optic atrophy: Initially 1,000 mcg or more daily by intramuscular injection for two weeks, then twice weekly as long as improvement is occurring.

Maintenance: 1,000 mcg monthly.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to hydroxocobalamin.

Precautions: The dosage schemes given above are usually satisfactory, but regular examination of the blood is advisable.

If megaloblastic anaemia fails to respond to Neo-Cytamen, folate metabolism should be investigated.

Side-effects: Sensitisation to hydroxocobalamin is rare but may manifest itself as itching exanthema, and exceptionally, anaphylaxis.

Overdosage: Treatment is unlikely to be needed in case of overdosage.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Ampoules of 1 ml in boxes of 5.

Further information An intramuscular injection of hydroxocobalamin produces higher serum levels than the same dose of cyanocobalamin, and these levels are well maintained.

Product licence numbers

Neo-Cytamen '250' 0004/5025

Neo-Cytamen '1,000' 0004/5026

PREDNESOL* TABLETS

Presentation Small, pink, soluble tablets engraved 'Prednesol Glaxo' on one side and scored on the reverse. Each tablet contains 5 mg prednisolone as the sodium phosphate ester.

Uses Prednisolone is a glucocorticosteroid which is about four times as active as hydrocortisone on a weight-for-weight basis.

Prednisolone sodium phosphate is very soluble in water, and is therefore less likely to cause local gastric irritation than prednisolone alcohol, which is only slightly soluble. This is important when high dosages are required, as in immunosuppressive therapy.

A wide variety of diseases may sometimes require corticosteroid therapy. Some of the principal indications are: asthma, severe allergic disturbances, leukaemia, rheumatoid arthritis, collagen diseases, and various inflammatory skin diseases. Other indications are the nephrotic syndrome, ulcerative colitis, regional ileitis (Crohn's disease), pemphigus, sarcoidosis (especially with hypercalcaemia), rheumatic carditis, ankylosing spondylitis, and various blood dyscrasias, including selected cases of haemolytic anaemia, agranulocytosis and thrombocytopenic purpura.

Dosage and administration Prednesol Tablets are best taken dissolved in water, but they can be swallowed whole without difficulty.

The lowest dosage that will produce an acceptable result should be used; when it is possible to reduce the dosage, this must be accomplished by stages. During prolonged therapy, dosage may need to be increased temporarily during periods of stress or in exacerbations of illness.

Adults: The dose used will depend upon the disease, its severity, and the clinical response obtained. The following regimens are for guidance only. Divided dosage is usually employed.

Short-term treatment: 20–30 mg daily for the first few days, subsequently reducing the daily dosage by 2.5 or 5 mg every two to five days, depending upon the response.

Rheumatoid arthritis: 7.5–10 mg daily. For maintenance therapy the lowest effective dosage is used.

Most other conditions: 10–100 mg daily for one to three weeks, then reducing to the minimum effective dosage.

Children: Fractions of the adult dosage may be used (e.g., 75% at 12 years, 50% at 7 years and 25% at 1 year), but clinical factors must be given due weight.

Contra-indications, warnings, etc

Contra-indications: Systemic infections, unless specific anti-infective therapy is employed.

Precautions: Administration of corticosteroids may impair the ability to resist and counteract infection; in addition clinical signs and symptoms of infection are suppressed.

Corticosteroid treatment is likely to reduce the response of the pituitary-adrenal axis to stress, and relative insufficiency may persist for up to a year after withdrawal of prolonged therapy.

In pregnant animals, systemic administration of corticosteroids can cause abnormalities of fetal development. The relevance of this finding to humans has not been established.

Corticosteroids may worsen diabetes.

Side-effects: Prolonged treatment with corticosteroids in high dosage is occasionally associated with subcapsular cataract and glaucoma, in addition, any of the features of hypercorticism, such as osteoporosis, may occur. Aseptic osteonecrosis, particularly of the femoral head, may occur after prolonged corticosteroid therapy, or after repeated short courses involving high dosage. Peptic ulceration may develop, or be aggravated.

In children, prolonged therapy may retard growth.

Overdosage: Treatment is unlikely to be needed in cases of acute overdosage.

Pharmaceutical precautions None.

Legal category POM.

Package quantities The tablets are strip-packed in cartons of 100.

Further information Prednesol Tablets do not contain carbohydrates.

Product licence number 0004/5091.

PREDSOL* DROPS FOR EYE AND EAR

Presentation Predsol Drops contain prednisolone sodium phosphate 0.5% w/v and benzalkonium chloride 0.02% w/v in a sterilised clear and colourless aqueous solution. The product complies with the specification for Prednisolone Sodium Phosphate Eye Drops BPC, BNF.

Uses Non-infected inflammatory conditions of the eye and ear.

Dosage and administration **Eyes:** 1 or 2 drops instilled into the eye every one or two hours until control is achieved, when the frequency may be reduced.

Ears: 2 or 3 drops instilled into the ear every two or three hours until control is achieved, when the frequency can be reduced.

Contra-indications, warnings, etc

Contra-indications: Viral, fungal, tuberculous or purulent conditions. Hypersensitivity to the preparation. Use in the eye is contra-indicated if glaucoma is present.

Predsol Eye Drops contain benzalkonium chloride as a preservative and therefore should not be used to treat patients who wear soft contact lenses.

Precautions: Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e., in large amounts or for prolonged periods.

Side-effects: Eye Drops containing corticosteroids cause a serious rise in intra-ocular pressure in a small percentage of the population, which includes most of those with a family history of glaucoma. A milder rise may be experienced by a larger proportion of subjects if treatment is continued for longer than a few weeks. Thinning of the

cornea leading to perforation has occurred with use of topical corticosteroids. Cataract is reported to have occurred after unduly prolonged treatment of eye conditions with topical corticosteroids.

Pharmaceutical precautions It is desirable that the contents should not be used more than four weeks after first opening the bottle.

Legal category POM.

Package quantities Plastic dropper bottles containing 5 ml or 10 ml.

Further information Nil.

Product licence number 0004/5092.

PREDSOL* RETENTION ENEMA

Presentation 100 ml disposable plastic bags, each containing 20 mg prednisolone as the sodium phosphate ester in a buffered solution. The product complies with the specification for Prednisolone Sodium Phosphate Enema BPC, BNF.

Uses Predsol Retention Enema provides local corticosteroid activity to the lower part of the colon. It is indicated in the treatment of ulcerative colitis.

Dosage and administration *Adults:* 1 enema used nightly, for two to four weeks. Treatment may be continued in patients showing progressive improvement, but it should not be persisted with if the response has been inadequate. Some patients may relapse after an interval but are likely to respond equally well to a repeated course of treatment.

Predsol Retention Enema as packed is not suitable for use in children.

The enema is used each night on retiring. It may be warmed before administration by placing the bag in a vessel of hot water for a few minutes. When in bed and lying on the left side with knees drawn up, the patient should remove the stopper from the bag, lubricate the nozzle with petroleum jelly and gently insert about half the length of the nozzle into the rectum. The bag should then be slowly rolled up like a tube of toothpaste until it is emptied, taking a minute or two to do so. The nozzle should then be removed, with the bag still rolled up, and the whole unit discarded. The patient should then roll over to lie face down for three to five minutes but may sleep in any comfortable position.

Contra-indications, warnings, etc

Contra-indications: Corticosteroids should not be used in the presence of infection unless effective chemotherapy is also employed.

Precautions: Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e., in large amounts or for prolonged periods.

Side-effects: The consequences of systemic absorption should be considered if Predsol Retention Enema is used over long periods or in high dosage.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Boxes of seven 100 ml disposable bags (instructions to patients enclosed).

Further information The volume of the enema is considered to be the optimum to ensure maximum coverage of the affected area.

Product licence number 0004/5094.

PREDSOL* SUPPOSITORIES

Presentation Predsol Suppositories are white and opaque. Each suppository contains 5 mg prednisolone as the sodium phosphate ester.

Uses Prednisolone is a glucocorticosteroid which is about four times as potent as hydrocortisone on a weight-for-weight basis.

Predsol Suppositories are indicated for the treatment of haemorrhagic and granular proctitis and the anal complications of Crohn's disease.

Dosage and administration One suppository inserted at night and one in the morning after defaecation for adults or children. When the response is good, treatment is usually continued for some months. If symptoms recur later, treatment should be resumed.

Contra-indications, warnings, etc

Contra-indications: Corticosteroids should not be used in the presence of infection unless effective chemotherapy is also employed.

Precautions: Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e., in large amounts or for prolonged periods.

Side-effects: As with all topical corticosteroids, if Predsol Suppositories are used for prolonged periods the consequences of systemic absorption should be considered, especially in children.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Cartonned plastic moulds each containing 10 suppositories.

Further information Nil.

Product licence number 0004/5095.

PREDSOL*-N DROPS FOR EYE OR EAR

Presentation Predsol-N Drops contain prednisolone sodium phosphate 0.5% w/v, neomycin sulphate 0.5% w/v and thiomersal 0.005% w/v in a clear, colourless aqueous solution. Sterile until opened.

Uses *Eye:* Non-infected inflammatory conditions where development of bacterial infection is a possibility.

Ear: Otitis externa (see 'Contra-indications') and other inflammatory conditions where bacterial infection is present or suspected (see 'Contra-indications').

Dosage and administration *Eyes:* 1 or 2 drops instilled into the eye every one or two hours until control is achieved, when the frequency may be reduced.

Ears: 2 or 3 drops instilled into the ear every two or three hours until control is achieved, when the frequency may be reduced.

Contra-indications, warnings, etc

Contra-indications: Viral, fungal or tuberculous conditions; use in the eye is contra-indicated if purulent infection or glaucoma is present.

Hypersensitivity to any component.

Preparations containing neomycin should not be used for treating otitis externa when the ear drum is perforated, because of the risk of ototoxicity.

Precautions: Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e., in large amounts or for prolonged periods.

Side-effects: Eye drops containing corticosteroids cause a serious rise in intra-ocular pressure in a small percentage of the population, which includes most of those with a family history of glaucoma. A milder rise may be experienced by a larger proportion of subjects if treatment is continued for longer than a few weeks. Thinning of the cornea leading to perforation has occurred with use of topical corticosteroids. Cataract is reported to have occurred after unduly prolonged treatment of eye conditions with topical corticosteroids. Sensitivity to neomycin is uncommon, but if it occurs, avoid further use of the antibiotic.

Pharmaceutical precautions It is desirable that the contents should not be used more than four weeks after first opening the bottle.

Legal category POM.

Package quantities Plastic dropper bottles containing 5 ml or 10 ml.

Further information Nil.

Product licence number 0004/5093.

PREGADAY* TABLETS

Presentation Pregaday Tablets are reddish brown, film-coated tablets engraved 'Pregaday' on one face and 'Glaxo' on the reverse. Each tablet contains Ferrous Fumarate BP equivalent to 100 mg ferrous iron and 350 mcg (0.35 mg) anhydrous folic acid.

These tablets comply with the specification for Iron and Folic Acid Tablets BNF.

Uses There is evidence that a daily intake of 100 mg of elemental iron in the ferrous form is adequate to prevent development of iron deficiency in expectant mothers. If a mild iron deficiency is present when Pregaday administration is started, this will be corrected by increased absorption of iron.

The daily folate requirement rises steeply during the final trimester of pregnancy, and evidence of maternal depletion may be found. To ensure normal tissue folate levels in the mother after delivery, a daily supplement of about 300 mcg is required throughout pregnancy. This dose does not obscure the blood picture of Addisonian pernicious anaemia.

Pregaday is indicated throughout pregnancy for prophylaxis against iron deficiency and megaloblastic anaemia of pregnancy. Pregaday is not intended as a treatment for established megaloblastic anaemia of pregnancy.

Dosage and administration One tablet daily by

mouth. When necessary, one tablet may be given twice daily.

Contra-indications, warnings, etc

Contra-indications: Vitamin B₁₂ deficiency.

Precautions: A minority of pregnant women are not protected by physiological doses of folic acid. The development of anaemia despite prophylaxis with Pregaday calls for investigation.

Some post-gastrectomy patients show poor absorption of iron. Care is needed when treating patients with peptic ulceration. Pregaday Tablets should be kept out of the reach of children.

Side-effects: Diarrhoea or constipation is uncommon.

Overdosage: Ingestion of an overdose of iron orally requires emergency treatment along the following lines. Vomiting should be induced immediately, followed as soon as possible by parenteral injection of desferrioxamine mesylate, and then gastric lavage. In the meantime, it is helpful to give milk and/or 5% sodium bicarbonate solution by mouth.

Dissolve 2 g desferrioxamine mesylate in 2 to 3 ml of Water for Injections and give intramuscularly. A solution of 5 g desferrioxamine in 50 to 100 ml of fluid may be left in the stomach. If desferrioxamine is not available, leave 300 ml of 1% to 5% sodium bicarbonate solution in the stomach. Fluid replacement is essential.

Pharmaceutical precautions None.

Legal category POM.

Package quantities Calendar wallet of 28 tablets.

Further information Nil.

Product licence number 0004/5030.

TERTROXIN* TABLETS

Presentation Small, white, uncoated tablets engraved 'Tertroxin Glaxo' on one side and scored on the other. Each tablet contains 20 mcg (0.02 mg) liothyronine sodium and complies with the specification for Liothyronine Tablets BP, BNF.

Uses Liothyronine (L-triiodothyronine) sodium is a naturally occurring thyroid hormone. Its biological action is qualitatively similar to that of thyroxine, but the effect develops in a few hours and disappears within 24–48 hours of stopping treatment.

Tertroxin is particularly suitable for treating severe and acute hypothyroid states because of its rapid, intensive and short-lived effect.

It is indicated in the treatment of: coma due to myxoedema; management of severe chronic thyroid deficiency; hypothyroid states arising in treatment of thyrotoxicosis.

Tertroxin is also used therapeutically in thyrotoxicosis as an adjunct to carbimazole. After six months of this treatment it may be possible to distinguish drug-responsive patients from relapse-prone patients who are better treated with radioiodine or surgery.

Large doses of liothyronine normally suppress the uptake of iodine by the thyroid, but not in thyrotoxicosis, and this forms the basis of a routine test for thyrotoxicosis.

Dosage and administration *Thyroid deficiency:* Treatment of adults may be begun with 10 or 20 mcg daily, increasing by increments of 10 mcg daily every seven days to a total daily dosage of 80 to 100 mcg.

For children and elderly patients it is suggested that the initial dosage should be 5 mcg daily. (To obtain small doses, tablets may be crushed and triturated with lactose for administration as a powder.)

Tertroxin should be given in divided doses two or three times daily.

Myxoedema coma: Initially, 60 mcg may be given by stomach tube, then 20 mcg every eight hours.

Thyrotoxicosis: As a diagnostic test in adults, 80 mcg or more of liothyronine are given daily for seven or eight days. The daily amount should be divided into 3 or 4 doses. Radioiodine is then administered, and uptake by the thyroid can be estimated about 20 minutes later. Failure to suppress the uptake of radioiodine is indicative of thyrotoxicosis.

As therapy for thyrotoxicosis with carbimazole: In adults, 80 mcg of liothyronine daily. In some patients it is possible to discontinue the carbimazole after about a year without subsequent relapse.

Contra-indications, warnings, etc

Contra-indications: Tertroxin is contra-indicated in patients with angina of effort or cardiovascular disorders.

Precautions: In myxoedema, care must be taken to avoid imposing excessive burden on cardiac muscle affected by prolonged severe thyroid depletion.

Side-effects: The following effects are indicative of excessive dosage, and usually disappear on reduction of dosage or withdrawal of treatment for a day or two. Anginal pain, cardiac arrhythmias, palpitation, and cramps in skeletal muscle; also tachycardia, diarrhoea, restlessness, excitability, headache, flushing, sweating, excessive loss of weight and muscular weakness.

Overdosage: Gastric lavage or emesis is required if the patient is seen within several hours of taking the dose. Treatment is symptomatic; tachycardia has been controlled in an adult by 40 mg doses of propranolol given every six hours.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Bottles of 100 tablets.

Further information 20 mcg liothyronine is equivalent in activity to 60–100 mcg thyroxine or to 60 mg Thyroid BP.

Product licence number 0004/5032.

TRIIODOTHYRONINE INJECTION

Presentation A freeze-dried sterile white plug containing 20 mcg sodium triiodothyronine (Liothyronine Sodium, BP) with dextran. The plug is dissolved in Water for Injections for preparation of an intravenous injection (Liothyronine Injection BNF).

Uses Treatment of myxoedema coma, usually in conjunction with other measures, including intravenous injection of a corticosteroid. For lesser degrees of myxoedema and for maintenance therapy, orally administered thyroxine should be used.

Dosage and administration Triiodothyronine injection is usually given by the intravenous route, as the alkalinity of the solution might cause irritation of the tissues if given by deep intramuscular injection. The solution is prepared by adding 1 ml or 2 ml of Water for

Injections and shaking the ampoule gently until the substance has dissolved.

The dosage may be 5 to 20 mcg given by slow intravenous injection and repeated at intervals of 1; hours, or sometimes more frequently. The minimum interval between doses is four hours. Some authorities have advocated an initial dose of 50 mcg intravenously followed by further intravenous injections of 25 mcg every eight hours until improvement occurs. The dosage may then be reduced to 25 mcg intravenously twice daily.

Contra-indications, warnings, etc

Contra-indications: No absolute contra-indication is known.

Precautions: Triiodothyronine must be given with extreme caution in myxoedema coma, as too large a dose can precipitate heart failure, especially in elderly patients; and in those with ischaemic heart disease. Electrocardiographic monitoring can give a useful indicator of impending ischaemia, but the ST changes of hypothyroidism may be confused with ECG evidence of ischaemia.

Use of sedatives may cause respiratory depression.

Side-effects: The following effects are indicative of excessive dosage, and usually disappear on reduction of dosage or withdrawal of treatment for a day or two. Anginal pain, cardiac arrhythmias, palpitation, and/or cramps in skeletal muscle. Also tachycardia, diarrhoea, restlessness, excitability, headache, flushing, sweating and muscular weakness.

Overdosage: Treatment of overdosage is symptomatic. Tachycardia has been controlled in an adult by 40 mg doses of propranolol given every six hours.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Ampoules containing 20 mcg sterile Liothyronine Sodium BP. Boxes of 3 ampoules.

Further information 20 mcg liothyronine are equivalent in activity to 60–100 mcg thyroxine.

Product licence number 0004/5033.

TRIMOVATE* CREAM ▼

Presentation Trimovate Cream is a yellow water-miscible cream, containing clobetasone butyrate 0.05% w/w, oxytetracycline 3.0% w/w as calcium oxytetracycline and nystatin 100,000 units per gram.

Uses Clobetasone butyrate is a topically active corticosteroid which provides an exceptional combination of activity and safety. Topical formulations have been shown to be more effective in the treatment of eczema than 1% hydrocortisone, yet to have little effect or hypothalamic-pituitary-adrenal function.

The combination of the topically active antibiotics nystatin and oxytetracycline, provides a broad spectrum of antibacterial and anticandidal activity against many of the organisms associated with infected dermatoses.

Trimovate is indicated for the treatment and management of steroid-responsive dermatoses where candida or bacterial infection is present, suspected, or likely to occur, and the use of a more potent topical corticosteroid is not required. These include infected eczemas, inter-

trigo, napkin rash, anogenital pruritus and seborrhoeic dermatitis.

Dosage and administration Apply to the affected area up to four times a day.

Suitable for treating infants, children and adults.

Contra-indications, warnings, etc Viral (e.g., herpes simplex) and dermatophyte (tinea/ringworm) infections of the skin, and tuberculous lesions.

Hypersensitivity to the preparation.

Precautions: In infants and children, long-term continuous topical steroid therapy should be avoided where possible, as adrenal suppression can occur even without occlusion. In infants, the napkin may act as an occlusive dressing, and increase absorption.

Any spread of infection requires withdrawal of topical corticosteroid therapy and institution of appropriate systemic chemotherapy.

With all corticosteroids, prolonged application to the face is undesirable.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e., in large amounts or for prolonged periods. Trimovate may cause slight staining of hair, skin or fabric, but this can be removed by washing.

The application may be covered with a simple dressing to protect clothing.

Side-effects: In the unlikely event of signs of hypersensitivity appearing, application should stop immediately.

If large areas of the body were to be treated with Trimovate, it is possible that some patients would absorb sufficient steroid to cause transient adrenal depression despite the low degree of systemic activity associated with clobetasone butyrate.

Local atrophic changes could possibly occur in situations where moisture increases absorption of clobetasone butyrate, but only after prolonged use.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Tubes of 25 grams.

Further information The least potent corticosteroid which will control the disease should be selected. Trimovate Cream does not contain lanolin or parabens.

The low systemic activity of clobetasone butyrate has been demonstrated in adults under conditions of whole body occlusion. In animal and human models, preparations of clobetasone butyrate and of hydrocortisone caused less thinning of the epidermis than the other topical corticosteroids tested.

Product licence number 0004/0266.

TRIMOVATE* OINTMENT ▼

Presentation Trimovate Ointment is a yellow ointment containing clobetasone butyrate 0.05% w/w, chlortetracycline hydrochloride 3.0% w/w and nystatin 100,000 units per gram in soft paraffin base.

Uses Clobetasone butyrate is a topically active corticosteroid which provides an exceptional combination of

activity and safety. Topical formulations have been shown to be more effective in the treatment of eczemas than 1% hydrocortisone, yet to have little effect on hypothalamic-pituitary-adrenal function.

The combination of the topically active antibiotics, nystatin and chlortetracycline hydrochloride, provides a broad spectrum of antibacterial and anticandidal activity against many of the organisms associated with infected dermatoses. Trimovate is indicated for the treatment and management of steroid responsive dermatoses where candidal or bacterial infection is present, suspected or likely to occur and the use of a more potent topical corticosteroid is not required. These include infected eczemas, intertrigo, napkin rash, anogenital pruritus and seborrhoeic dermatitis.

Dosage and administration Apply to the affected area up to four times a day.

Suitable for treating infants, children and adults.

Contra-indications, warnings, etc Viral (e.g., herpes simplex) and dermatophyte (tinea/ringworm) infections of the skin and tuberculous lesions.

Hypersensitivity to the preparation.

Precautions: In infants and children, long-term continuous topical steroid therapy should be avoided where possible, as adrenal suppression can occur even without occlusion. In infants, the napkin may act as an occlusive dressing, and increase absorption. Any spread of infection requires withdrawal of topical corticosteroid therapy and institution of appropriate systemic chemotherapy.

With all corticosteroids, prolonged application to the face is undesirable.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e., in large amounts or for prolonged periods.

Trimovate may cause slight staining of hair, skin or fabric, but this can be removed by washing. The application may be covered with a simple dressing to protect clothing.

Side-effects: In the unlikely event of signs of hypersensitivity appearing, application should stop immediately.

If large areas of the body were to be treated with Trimovate, it is possible that some patients would absorb sufficient steroid to cause transient adrenal depression despite the low degree of systemic activity associated with clobetasone butyrate.

Local atrophic changes could possibly occur in situations where moisture increases absorption of clobetasone butyrate, but only after prolonged use.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Tubes of 25 grams.

Further information The least potent corticosteroid which will control the disease should be selected. Trimovate Ointment does not contain lanolin or parabens.

The low systemic activity of clobetasone butyrate has been demonstrated in adults under conditions of whole body occlusion. In animal and human models, preparations of clobetasone butyrate and of hydrocortisone caused less thinning of the epidermis than the other topical corticosteroids tested.

Product licence number 0004/0265.

TRIPLOPEN*

Presentation Each single-dose vial contains a white, sterile powder consisting of:

Benethamine penicillin	475 mg (500,000 units)
Procaine penicillin	250 mg (250,000 units)
Sodium penicillin	300 mg (500,000 units)

A suspension for intramuscular injection (Benethamine Penicillin Injection Fortified, BPC: Triple Penicillin Injection BNF) is formed on addition of Water for Injections.

Uses The dose of sodium penicillin gives a prompt, high blood level which supplements the lower but more prolonged level of the procaine penicillin. The therapeutic level is further maintained by the benethamine penicillin. Altogether, the effect lasts for two or three days.

Triplopen is of value in the following infections: acute localised infections such as boils, carbuncles and cellulitis; many infections caused by the more sensitive bacteria, e.g., haemolytic streptococci and pneumococci; prophylaxis against infections after accident or surgery; gonorrhoea and syphilis.

Dosage and administration To prepare the suspension for intramuscular administration, inject 1.3 ml Water for Injections into the inverted vial. On shaking, a very fluid suspension is formed which may be injected with a 23 SWG needle.

General infections in adults: Effective treatment can be carried out conveniently by a single injection of Triplopen, which can be repeated every two or three days. Triplopen is given only by deep intramuscular injection, preferably into the thigh or buttocks.

Gonorrhoea: Two vials as a single injection given once.

Syphilis: One vial daily for a week.

General infections in infants and children: Age 0–6 years: A quarter vial, 7–12 years: A half vial. 13 years and over: One vial.

Any suspension remaining after giving a fractional dose should be discarded unless it can be used promptly.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to penicillins.

Precautions: Inadvertent injection into a blood vessel can cause serious reactions. The risk can usually be avoided by attempting to aspirate blood before injecting the antibiotics.

It should be recognised that a patient with a history of allergy, especially to drugs, is more likely to develop a hypersensitivity reaction.

Side-effects: Penicillin hypersensitivity usually takes the form of an urticarial rash which can be treated with systemic antihistamine drugs. Occasionally anaphylactic reactions to penicillin occur, and resuscitative measures, including subcutaneous injection of adrenaline and use of an intravenous corticosteroid should be employed.

Skin sensitisation may occur in persons handling penicillin, and appropriate protective measures should be taken to avoid contact with the substance.

Overdosage: Excessive blood levels of penicillin G can be corrected by haemodialysis.

Pharmaceutical precautions As this product does not contain a bacteriostat, it should be used without undue delay after reconstitution.

Legal category POM.

Package quantities Single-dose vial in box of 10.

Further information If 1.3 ml of water are used to suspend Triplopen, the total volume will be 2.27 ml, but the full amounts of antibiotics are contained in 2 ml of suspension. Each vial contains 27 mg sodium (1.2 mEq).

Product licence number 0004/5076.

ZANTAC* INJECTION ▼

Presentation Zantac Injection: 5 ml ampoules each containing 50 mg ranitidine (as hydrochloride) in 5 ml solution for intravenous administration.

Uses *Indications:* Zantac Injection is indicated for the treatment of duodenal ulcer, benign gastric ulcer, post-operative ulcer, reflux oesophagitis and the Zollinger-Ellison syndrome. For appropriate cases, Zantac Tablets are also available (see separate Data Sheet).

Mode of action: Zantac is a highly effective, rapidly acting histamine H₂-antagonist. It inhibits basal and stimulated secretion of gastric acid, reducing both the volume of secretions and the acid and pepsin content.

Dosage and administration *Adults:* Zantac Injection may be given either as a slow (over one minute) intravenous injection of 50 mg, which may be repeated every six to eight hours; or as an intravenous infusion at a rate of 25 mg per hour for two hours; the infusion may be repeated at six to eight hour intervals.

Children: There has been no experience with Zantac Injection in children.

Contra-indications, warnings, etc There are no known contra-indications to the use of Zantac Injection.

Precautions: Treatment with a histamine H₂-antagonist may mask the symptoms associated with carcinoma of the stomach and therefore may delay diagnosis of this condition. Accordingly, where gastric ulcer is suspected the possibility of malignancy should be excluded before therapy with Zantac is instituted.

Ranitidine is excreted via the kidney and in the presence of severe renal impairment, plasma levels of ranitidine are increased and prolonged. Accordingly, it is recommended in such patients that Zantac be administered in doses of 25 mg.

Like other drugs, Zantac should be used during pregnancy or nursing only if strictly necessary. Zantac is secreted in breast milk in lactating mothers but the clinical significance of this has not been fully evaluated.

Side-effects: No serious adverse side effects have been reported to date in patients treated with Zantac Injection. There has been no clinically significant interference with endocrine, gonadal or liver function, nor has the drug adversely affected the central nervous system even in elderly patients.

Overdosage: Zantac is highly specific in action and accordingly no particular problems are expected following overdosage with the drug. Symptomatic and supportive therapy should be given as appropriate. The drug may be removed from the plasma by haemodialysis.

Pharmaceutical precautions Zantac Injection has been shown to be compatible with the following intravenous infusion fluids: 0.9% Sodium Chloride BP, 5% Dextrose BP, 0.18% Sodium Chloride and 4% Dextrose BP, 4.2% Sodium Bicarbonate BP and Hartmann's Solution. Although compatibility studies have only been undertaken in polyvinyl chloride infusion bags (in glass for Sodium Bicarbonate BP) and a polyvinyl

chloride administration set it is considered that adequate stability would also be conferred by use of a polyethylene infusion bag. All unused admixtures of Zantac Injection with infusion fluids should be discarded 24 hours after preparation.

Store in a cool place. Protect from light.

Legal category POM.

Package quantities Zantac Injection: 5 ml ampoules, boxes of five.

Further information *Drug interactions:* Ranitidine does not inhibit the cytochrome P450-linked mixed function oxygenase enzyme system in the liver and therefore does not interfere with the effects of the many drugs which are metabolised by this enzyme system. For example, there is no interaction with warfarin or diazepam.

Pharmacokinetics: The elimination half-life of ranitidine is approximately two hours. Ranitidine is excreted via the kidneys mainly as the free drug and in minor amounts as metabolites. Its major metabolite is the N-oxide and there are smaller quantities of S-oxide and desmethyl ranitidine. Recovery of free and metabolised ranitidine from the urine after 24 hours is approximately 75% after intravenous administration.

Use in renal transplants: Zantac has been used without adverse effect in patients with renal transplants.

Product licence number 0004/0280.

ZANTAC* TABLETS ▼

Presentation Zantac Tablets: white, film-coated, engraved ZANTAC 150 on one face and GLAXO on the other. Each Tablet contains ranitidine 150 mg (as hydrochloride).

Uses *Indications:* Zantac Tablets are indicated for the treatment of duodenal ulcer, benign gastric ulcer, post-operative ulcer, reflux oesophagitis and the Zollinger-Ellison syndrome. For appropriate cases, Zantac Injection is also available (see separate Data Sheet).

Mode of action: Zantac is a highly effective, rapidly acting histamine H₂-antagonist. It inhibits basal and stimulated secretion of gastric acid, reducing both the volume and the acid and pepsin content of the secretion. Zantac has a relatively long duration of action and so a single dose effectively suppresses gastric acid secretion for twelve hours.

Dosage and administration *Adults:* The usual dosage is one 150 mg tablet twice daily, taken in the morning and before retiring. It is not necessary to time the dose in relation to meals. In most cases of duodenal ulcer, benign gastric ulcer and post-operative ulcer, healing occurs in four weeks. In the small number of patients whose ulcers have not fully healed, healing usually occurs after a further course of treatment. Maintenance treatment at a reduced dosage of one 150 mg tablet at bedtime is recommended for patients who have responded to short-term therapy, particularly those with a history of recurrent ulcer. In the management of reflux oesophagitis, the recommended course of treatment is one 150 mg tablet twice daily for up to 8 weeks.

In patients with Zollinger-Ellison syndrome, the starting dose is 150 mg three times daily and this may be increased, as necessary, to 900 mg per day.

Children: Experience with Zantac Tablets in children is limited and such use has not been fully evaluated in clinical studies. It has however been used successfully in children aged 8–18 years in doses up to 150 mg twice daily without adverse effect.

Contra-indications, warnings, etc *Contra-indications:* There are no known contra-indications to the use of Zantac Tablets.

Precautions: Treatment with a histamine H₂-antagonist may mask symptoms associated with carcinoma of the stomach and may therefore delay diagnosis of the condition. Accordingly, where gastric ulcer is suspected the possibility of malignancy should be excluded before therapy with Zantac Tablets is instituted.

Ranitidine is excreted via the kidney and so plasma levels of the drug are increased and prolonged in patients with severe renal failure. Accordingly, it is recommended that the therapeutic regimen for Zantac in such patients be 150 mg at night for 4 to 8 weeks. The same dose should be used for maintenance treatment should this be deemed necessary. If an ulcer has not healed after treatment for 4 to 8 weeks and the condition of the patient requires it, the standard dosage regimen of 150 mg twice daily should be instituted, followed, if need be, by maintenance treatment at 150 mg at night.

Although the incidence of adverse reactions in clinical trials of one year's duration and longer has been very low and no serious side effects have been reported with Zantac treatment, care should be taken to carry out periodic examinations of patients on prolonged maintenance treatment with the drug as a safeguard against the occurrence of unforeseeable consequences of drug treatment.

Like other drugs, Zantac should be used during pregnancy and nursing only if strictly necessary. Zantac is secreted in breast milk in lactating mothers but the clinical significance of this has not been fully evaluated.

Side-effects: No serious adverse effects have been reported to date in patients treated with Zantac Tablets. There has been no clinically significant interference with endocrine, gonadal or liver function, nor has the drug adversely affected the central nervous system even in elderly patients.

Overdosage: Zantac is very specific in action and accordingly no particular problems are expected following overdosage with the drug. Symptomatic and supportive therapy should be given as appropriate. If need be, the drug may be removed from the plasma by haemodialysis.

Pharmaceutical precautions No special storage conditions are necessary.

Legal category POM.

Package quantities Zantac Tablets (150 mg): Carton of 60 tablets, foil-wrapped.

Further information *Drug interactions:* Ranitidine does not inhibit the cytochrome P450-linked mixed function oxygenase enzyme system in the liver and therefore does not interfere with the effects of the many drugs which are metabolised by this enzyme system. For example, there is no interaction with warfarin or diazepam.

Pharmacokinetics: Absorption of ranitidine after oral administration is rapid and peak plasma concentrations are usually achieved within two hours of administration. Absorption is not impaired by food or antacids. The

elimination half-life of ranitidine is approximately two hours. Ranitidine is excreted via the kidneys mainly as the free drug and in minor amounts as metabolites. Its major metabolite is an N-oxide and there are smaller quantities of S-oxide and desmethyl ranitidine. The 24-hour urinary recovery of free ranitidine and its metabolites is about 40% with orally administered drug.

Use in renal transplants: Zantac has been used without adverse effect in patients with renal transplants.

Product licence number 0004/0279.

ZINACEF*

Presentation Vials containing 250 mg, 750 mg or 1.5 g cefuroxime as cefuroxime sodium.

Cefuroxime is a white to faintly yellow powder to which appropriate amounts of water are added to prepare an off-white suspension for intramuscular use or a yellowish solution for intravenous administration. Variations in the intensity of this colour do not indicate any change in either the efficacy or safety of the product.

Uses Zinacef is a bactericidal cephalosporin antibiotic which is resistant to most β -lactamases and is active against a wide range of Gram-positive and Gram-negative organisms. It is indicated for the treatment of infections before the infecting organism has been identified or when caused by sensitive bacteria. In addition, it is an effective prophylactic against post-operative infection in a variety of operations. Usually Zinacef will be effective alone, but when appropriate, it may be used in combination with an aminoglycoside antibiotic, or in conjunction with metronidazole (orally or by suppository or injection), especially for prophylaxis in colonic surgery (see Pharmaceutical precautions). Indications include:

Respiratory tract infections for example, acute and chronic bronchitis, infected bronchiectasis, bacterial pneumonia, lung abscess and post-operative chest infections.

Ear, nose and throat infections for example, sinusitis, tonsillitis and pharyngitis.

Urinary tract infections for example, acute and chronic pyelonephritis, cystitis and asymptomatic bacteriuria.

Soft-tissue infections for example, cellulitis, erysipelas, peritonitis and wound infections.

Bone and joint infections for example, osteomyelitis and septic arthritis.

Obstetric and gynaecological infections pelvic inflammatory diseases.

Gonorrhoea particularly when penicillin is unsuitable.

Other infections including septicaemia and meningitis.

Prophylaxis against infection in abdominal, pelvic, orthopaedic, cardiac, pulmonary, oesophageal and vascular surgery where there is increased risk from infection.

Bacteriology: Zinacef is highly active against *Staphylococcus aureus*, including strains which are resistant to penicillin (but not the rare methicillin resistant strains), *Staph. epidermidis*, *Haemophilus influenzae*, *Klebsiella* spp., *Enterobacter* spp., *Streptococcus pyogenes*, *Escherichia coli*, *Str. mitis* (viridans group), *Clotridium* spp., *Proteus mirabilis*, *Pr. rettgeri*, *Salmonella typhi*, *S. typhimurium* and other *Salmonella* spp. *Shigella* spp., *Neisseria* spp. (including β -lactamase producing strains

of *N. gonorrhoeae*) and *Bordetella pertussis*. It is also moderately active against strains of *Pr. vulgaris*, *Pr. morganii* and *Bacteroides fragilis*.

In vitro the activities of Zinacef and aminoglycoside antibiotics in combination have been shown to be at least additive with occasional evidence of synergy.

Dosage and administration *General dosage recommendations:* **Adults:** Many infections will respond to 750 mg t.d.s. by i.m. or i.v. injection. For more severe infections, this dose should be increased to 1.5 g t.d.s. i.v. The frequency of i.m. or i.v. injections can be increased to six-hourly if necessary, giving total doses of 3 g to 6 g daily.

Infants and children: Doses of 30 to 100 mg/kg/day, given as three or four divided doses. A dose of 60 mg/kg/day will be appropriate for most infections.

Neonates: Doses of 30 to 100 mg/kg/day, given as two or three divided doses. In the first weeks of life the serum half-life of cefuroxime can be three to five times that in adults.

Other recommendations: *Gonorrhoea:* 1.5 g should be given as a single dose. This may be given as 2 x 750 mg injections into different sites, e.g., each buttock.

Meningitis: Zinacef is suitable for sole therapy of bacterial meningitis due to sensitive strains. The following dosages are recommended.

Infants and children: 200 to 240 mg/kg/day i.v. in three or four divided doses. This dosage may be reduced to 100 mg/kg/day i.v. after three days or when clinical improvement occurs.

Neonates: The initial dosage should be 100 mg/kg/day i.v. A reduction to 50 mg/kg/day i.v. may be made when clinically indicated.

Adults: 3 g i.v. every eight hours. Data are not yet sufficient to recommend a dose for intrathecal administration.

Prophylaxis: The usual dose is 1.5 g i.v. with induction of anaesthesia for abdominal, pelvic and orthopaedic operations, but may be supplemented with two 750 mg i.m. doses eight and sixteen hours later. In cardiac, pulmonary, oesophageal and vascular operations, the usual dose is 1.5 g i.v. with induction of anaesthesia continuing with 750 mg i.m. t.d.s. for a further 24 to 48 hours.

In total joint replacement, 1.5 g cefuroxime powder may be mixed dry with each pack of methyl methacrylate cement monomer before adding the liquid polymer.

Dosage in impaired renal function: Cefuroxime is excreted by the kidneys. Therefore, as with all such antibiotics, in patients with impaired renal function it is recommended that the dosage of Zinacef should be reduced to compensate for its slower excretion. However, it is not necessary to reduce the dose until the creatinine clearance falls below 20 ml/min. In adults with marked impairment (creatinine clearance 10–20 ml/min) 750 mg b.d. is recommended and with severe impairment (creatinine clearance < 10 ml/min) 750 mg once daily is adequate. For patients on dialysis a further 750 mg dose should be given at the end of each dialysis. When continuous peritoneal dialysis is being used, a suitable dosage is usually 750 mg twice daily.

Administration: *Intramuscular:* Add 1 ml Water for Injections to 250 mg Zinacef or 3 ml Water for Injections to 750 mg Zinacef. Shake gently to produce an opaque suspension.

intravenous: Dissolve Zinacef in Water for Injections using at least 2 ml for 250 mg, at least 6 ml for 750 mg, or 15 ml for 1.5 g. For short intravenous infusion (e.g., up to 30 minutes), 1.5 g may be dissolved in 50 ml Water or Injections. These solutions may be given directly into the vein or introduced into the tubing of the giving set if the patient is receiving parenteral fluids.

Zinacef is compatible with the more commonly used intravenous fluids. (See Pharmaceutical precautions.)

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to cephalosporin antibiotics.

Precautions: Cephalosporin antibiotics may in general be given safely to patients who are hypersensitive to penicillins, although cross-reactions have been reported. Special care is indicated in patients who have experienced an anaphylactic reaction to penicillin.

Cephalosporin antibiotics at high dosage should be given with caution to patients receiving concurrent treatment with potent diuretics such as frusemide, as these combinations are suspected of adversely affecting renal function. Clinical experience with Zinacef has shown that this is not likely to be a problem at the recommended dose levels. There is no experimental evidence of embryopathic or teratogenic effects attributable to Zinacef but, as with all drugs, it should be administered with caution during the early months of pregnancy.

Zinacef does not interfere in enzyme-based tests or glycosuria. Slight interference with copper reduction methods (Benedict's, Fehling's, Clinitest) may be observed. However, this should not lead to false-positive results, as may be experienced with some other cephalosporins.

Zinacef may cause false-negative results in the ferricyanide test for glucose. This antibiotic does not interfere in the alkaline picrate assay for creatinine.

Side-effects: Adverse reactions to Zinacef have occurred relatively infrequently and have been generally mild and transient in nature. Effects reported include rashes and gastro-intestinal disturbance. As with other antibiotics, prolonged use may result in the overgrowth of non-susceptible organisms, e.g., *Candida*.

The principal changes in haematological parameters seen in some patients have been of decreased haemoglobin concentration and of eosinophilia. A positive 'Coombs' test has been found in some patients treated with cefuroxime – this phenomenon can interfere with the cross-matching of blood.

Although there are sometimes transient rises in serum liver enzymes or serum bilirubin, particularly in patients with pre-existing liver disease, there is no evidence of hepatic involvement.

There may also be some variation in the results of biochemical tests of renal function, but these do not appear to be of clinical importance. As a precaution, renal function should be monitored if this is already impaired.

Transient pain may be experienced at the site of intramuscular injection. This is more likely to occur with higher doses. However, it is unlikely to be a cause for discontinuation of treatment.

Verdosage: Serum levels of cefuroxime are reduced by dialysis.

Pharmaceutical precautions Protect from light.

Zinacef should not be mixed in the syringe with aminoglycoside antibiotics.

Suspensions of Zinacef for intramuscular injection and aqueous solutions for direct intravenous injection retain their potency for five hours if kept below 25°C and for 48 hours if refrigerated. More dilute solutions, i.e., 1.5 g plus 50 ml Water for Injections, retain satisfactory potency for 24 hours if kept below 25°C and for 72 hours if refrigerated.

Some increase in the colour of prepared solutions and suspensions of Zinacef may occur on storage.

1.5 g Zinacef constituted with 15 ml Water for Injections may be added to metronidazole injection (500 mg/100 ml) and both retain their activity for up to 24 hours below 25°C. 1.5 g Zinacef is compatible with azlocillin 1 g (in 15 ml) or 5 g (in 50 ml) for up to 24 hours at 4°C or 6 hours below 25°C.

Zinacef (5 mg/ml) in 5% w/v or 10% w/v xylitol injection may be stored for up to 24 hours at 25°C.

Zinacef is compatible with the more commonly used intravenous infusion fluids. It will retain potency for up to 24 hours at room temperature in Sodium Chloride Injection BP 0.9% w/v, 5% Dextrose Injection BP 0.18% w/v, Sodium Chloride plus 4% Dextrose Injection BP, and Compound Sodium Lactate Injection BP (Hartmann's solution). The pH of 2.74% w/v Sodium Bicarbonate Injection BP considerably affects the colour of the solution and therefore this solution is not recommended for the dilution of Zinacef. However, if required, for patients receiving Sodium Bicarbonate Injection by infusion the Zinacef may be introduced into the tube of the giving set. The stability of Zinacef in Sodium Chloride Injection BP 0.9% w/v and in 5% Dextrose Injection is not affected by the presence of hydrocortisone sodium phosphate.

Zinacef is also compatible with aqueous solutions containing up to 1% lignocaine hydrochloride.

Legal category POM.

Package quantities Vials containing 250 mg or 750 mg cefuroxime as the sodium salt (for use by intramuscular or intravenous injection) in packs of 5.

Vials containing 1.5 g cefuroxime as the sodium salt (for use by intravenous injection), packed singly.

Vials containing 1.5 g cefuroxime as the sodium salt (for use by intravenous infusion), packed singly.

Further information Peak levels of cefuroxime are achieved within 30 to 45 minutes after intramuscular administration. The serum half-life after either intramuscular or intravenous injection is approximately 70 minutes. Concurrent administration of probenecid prolongs the excretion of the antibiotic and produces an elevated peak serum level. There is almost complete recovery of unchanged cefuroxime in the urine within 24 hours of administration, the major part being eliminated in the first six hours. Approximately 50% is excreted through the renal tubules and approximately 50% by glomerular filtration. Concentrations of cefuroxime in excess of the minimum inhibitory levels for common pathogens can be achieved in bone, synovial fluid and aqueous humour. Cefuroxime passes the blood-brain barrier when the meninges are inflamed.

Each 750 mg vial contains 42 mg sodium (1.8 mEq). When dissolved, the contents of a 750 mg vial displace 0.53 ml on average.

Product licence number 0004/0263.

***Trade Mark**

Hoechst UK Limited

Pharmaceutical Division

Hoechst House, Salisbury Road
Hounslow, Middlesex TW4 6JH



DANERAL* SA TABLETS

Presentation Daneral SA Tablets each contain 75 mg Pheniramine Maleate BP in a sustained release formulation. Daneral SA is presented as unmarked pink, sugar-coated tablets 10.3 mm in diameter.

Uses All allergic conditions. Examples of its use include hay fever, vasomotor rhinitis, acute rhinitis, urticaria, allergic dermatoses, pruritus.

Dosage and administration One tablet at bedtime will be sufficient for most patients. In more severe cases two tablets may be taken at night or one tablet night and morning. The tablet should be swallowed whole and not sucked or chewed.

Children: This formulation is not suitable for children.

Contra-indications, warnings, etc Daneral SA tablets may cause drowsiness. Those affected should not drive or operate machinery.

In common with all antihistamines, the sedative effect of other central nervous system depressant agents, e.g. alcohol may be potentiated.

In infants and children antihistamines may act as central stimulants.

Overdosage: The primary symptom is sedation. Following doses of 300–1,800 mg cerebral stimulation, convulsions and hyperpyrexia may occur. If an overdose has been taken recently by mouth the stomach should be emptied by aspiration and lavage. Peritoneal dialysis is not effective. The patient should be kept quiet, diazepam i.v. may be given to prevent paroxysms and excessive hyperkinesia.

Precautions: There is little evidence of the safety of Daneral SA in human or animal pregnancy, although the drug has been in wide, general use for many years without apparent ill consequence.

Pharmaceutical precautions Daneral SA Tablets should be stored in a cool dry place, protected from light, in containers similar to those of the manufacturer.

Legal category P.

Package quantities Daneral SA Tablets are available in packs of 50.

Further information Nil.

Product licence number 0086/5001.

DAONIL* TABLETS SEMI-DAONIL* TABLETS

Presentation Daonil Tablets each contain 5 mg Glibenclamide BP. Daonil is presented as white oblong tablets, scored in the middle, one half bearing the Hoechst insignia, the other bearing the letters LDI. The tablet is 10 mm in length and 5 mm wide.

Semi-Daonil Tablets each contain 2.5 mg Glibenclamide

BP. Semi-Daonil is presented as white circular biplanar tablets, 6 mm in diameter, one side bearing the Hoechst insignia, the other scored and bearing the letter: LBG on either side of the score mark.

Uses Daonil is a hypoglycaemic agent, indicated for the oral treatment of patients with non-insulin dependent diabetes who respond inadequately to dietary measure alone.

Dosage and administration

1. *Treatment of previously untreated diabetics:* Stabilisation can be started with one 5 mg tablet of Daonil daily or, in debilitated or aged patients, one Semi-Daonil tablet. The dose should be taken by mouth, with or immediately after breakfast or the first main meal. When control is satisfactory, 1 tablet is continued as the maintenance dose. If control is unsatisfactory, the dose can be adjusted by increments of 2.5 or 5 mg at weekly intervals. The total daily dosage rarely exceeds 15 mg and increasing the daily dosage above this does not generally produce any additional effect. The total daily requirement should normally be administered as a single dose at breakfast, or with the first main meal; due consideration should be given to the patient's dietary habits and daily activity in apportioning the dosage.

2. *Change-over from other oral anti-diabetics:* The change over to Daonil from other drugs with a similar mode of action can be carried out without any break in therapy.

Daonil treatment should be started with one 5 mg tablet daily and adjusted by increments of 2.5–5 mg to achieve control. For patients not adequately controlled on other oral agents, treatment is commenced with the equivalent dose of Daonil, without exceeding an initial dose of 10 mg. If response is inadequate, the dose can be raised in a stepwise fashion to 15 mg daily. One 5 mg tablet of Daonil is approximately equivalent to 1 mg tolbutamide or glymidine, 250 mg chlorpropamide, 1 mg tolazamide, 500 mg acetohexamide, 25 mg glibornuride or 5 mg glipizide.

3. *Change-over from biguanides:* Daonil treatment should be started with 1 tablet of Semi-Daonil (2.5 mg) and the biguanide withdrawn. The dosage should then be adjusted by increments of 2.5 mg to achieve control.

Combination with biguanides: If adequate control is not possible with diet and 15 mg of Daonil, control can often be re-established by combined administration of Daonil and a biguanide derivative.

4. *Change-over from insulin:* While it is appreciated that most patients who are on insulin therapy will continue to need it, there may be a few patients, particularly those on low daily doses, who will remain stabilised if transferred from insulin to Daonil.

The tablets should always be taken with, or immediately after, the first main meal.

Children: As non-insulin dependent diabetes is not

usually a disease of childhood, Daonil is generally considered unsuitable for use in children.

Contra-indications, warnings, etc

Contra-indications: Daonil should not be used in patients who have or have ever had diabetic ketoacidosis or those who have insulin-dependent diabetes mellitus, serious impairment of renal, hepatic or adrenocortical function, or in circumstances of unusual stress, e.g. surgical operations or during pregnancy, when insulin is preferable.

Warnings: Debilitated or aged patients may be more liable to hypoglycaemia. The hypoglycaemic effect of glibenclamide may be enhanced by dicoumarol, monoamine oxidase inhibitors, beta-adrenergic blocking agents, sulphonamides, phenylbutazone, chloramphenicol, cyclophosphamide and salicylates or diminished by adrenaline, corticosteroids, oral contraceptives or thiazide diuretics.

There is no information on the use of Daonil in human pregnancy but it has been in wide, general use for many years without apparent ill consequence. Animal studies have shown no hazard.

Nursing mothers: It has not yet been established whether glibenclamide is transferred to human milk. However, other sulphonylureas have been found in milk and there is no evidence to suggest that glibenclamide differs from the group in this respect.

Overdosage: Hypoglycaemia may be treated in the conscious patient by the administration of glucose, or three to four lumps of table sugar with water. This may be repeated as necessary.

If the patient is comatose, glucose should be administered as an intravenous infusion. Bolus glucose injections are not recommended because of the possibility of rebound hypoglycaemia. Alternatively, glucagon may be administered in a dose of 1 mg subcutaneously or intramuscularly to produce consciousness.

Side-effects: Adverse reactions serious enough to warrant discontinuation of treatment are uncommon, but mild gastro-intestinal or allergic skin reactions have occurred. Reversible leucopenia and thrombocytopenia have been reported but are rare. Transient changes in liver function tests have been observed during treatment with Daonil, but are not known to be directly attributable to the drug. Hypoglycaemic symptoms have occasionally been reported when the dose has been administered without due regard to the patients' dietary habits.

Pharmaceutical precautions Daonil Tablets should be stored in a cool, dry place protected from light and in containers similar to those of the manufacturer.

Legal category POM.

Package quantities Daonil and Semi-Daonil Tablets are available in blister packs of 100.

Further information Orally administered Daonil is rapidly absorbed. It is substantially metabolised prior to its excretion in urine and bile. Some of the metabolites have hypoglycaemic activity, markedly reduced in comparison with the parent compound and usually without clinical significance.

Product licence numbers

Daonil Tablets 5 mg	0086/5002
Semi-Daonil Tablets 2.5 mg	0086/0068

FACTOR XIII CONCENTRATE

Presentation Factor XIII Concentrate is presented in clear glass vials, each containing approximately 85 mg lyophilised concentrate, having Factor XIII activity equivalent to at least 250 ml fresh pooled citrated plasma. Each vial is provided with an ampoule containing 4 ml Water for Injections for reconstitution of the lyophilisate.

Uses Factor XIII Concentrate is indicated for replacement therapy in congenital Factor XIII deficiency.

Dosage and administration The contents of one vial should be dissolved in 4 ml of Water for Injections and the solution should be administered by slow intravenous injection.

When reconstituted, the dosage for congenital Factor XIII deficiency is as follows:

1. For substitution therapy, the normal adult dose is 8 ml (about 170 mg) intravenously every four weeks. The interval between doses should be decreased if spontaneous bleeding occurs.

2. For prophylaxis prior to surgery, 8–16 ml (about 170–340 mg) i.v. in the immediate pre-operative period followed by 8–12 ml (about 170–255 mg) i.v. on each of the following five days.

3. For therapy in severe bleeding or massive haematoma 8–16 ml (about 170–340 mg) i.v. daily until the bleeding stops.

Children: In children under the age of 14 years, the dose is normally half the adult dose.

Contra-indications, warnings, etc Factor XIII Concentrate is contra-indicated for patients with fresh thrombosis because of its fibrin-stabilising effect.

No side effects have been observed.

Pharmaceutical precautions Factor XIII Concentrate should be stored at 4°C. Prepared solutions of Factor XIII Concentrate should be used immediately and any remainder discarded. No additives or diluents should be used other than pyrogen-free Water for Injections.

Legal category POM.

Package quantities The product is supplied as single vials each with an ampoule containing Water for Injections.

Further information Factor XIII Concentrate is a purified standardised and concentrated preparation of human coagulation factor XIII, fibrin-stabilising factor. The method of production of Factor XIII Concentrate has been shown to remove experimental artificial contamination with Australia Antigen; thus, there is little risk of transmission of hepatitis from the concentrate. In addition, every batch is routinely tested for freedom from HB_sAg.

Product licence number 0086/0047.

HAEMACCEL® INFUSION SOLUTION

Presentation 3.5% colloidal infusion solution for plasma substitution.

Composition:

<i>Haemacel contains</i>	<i>Per 500 ml bottle</i>	<i>Per 1,000 ml</i>
Polygeline (degraded and modified gelatin of average molecular weight 35,000)	17.50 g	35.00 g
Cations		
Na ⁺	72.50 mmol	145.00 mmol
K ⁺	2.55 mmol	5.10 mmol
Ca ⁺⁺	3.13 mmol	6.25 mmol
Anions		
Cl ⁻	72.50 mmol	145.00 mmol
PO ₄ ⁻⁻⁻ and SO ₄ ⁻⁻⁻	traces	traces

Isoionic equilibrium is made up by the polypeptides. There are no preservatives.

Physico-Chemical Properties:

Electrophoretic mobility	$\alpha_2 - \beta$
Viscosity ratio	1.7–1.8
Dynamic viscosity (at 38°C)	1.15–1.20 kPa.s (cP)
The iso-electric point is at	pH 4.7 ± 0.3
pH of the infusion solution	7.2–7.3
Colloid osmotic pressure (at 37°C)	3.432–3.824 kPa (350–390 mmH ₂ O)
Gel point	below +3°C
Appearance	straw-coloured
Nitrogen equivalent of polygeline	3.15 g

Uses As a plasma volume substitute in cases of:

1. Hypovolaemic shock due to:
 - (a) Haemorrhage (visible or concealed)
 - (b) Burns, peritonitis, pancreatitis, crush injuries
 - (c) Water and electrolyte loss from persistent vomiting and diarrhoea, diseases of the kidneys and adrenals, portal vein thrombosis, ileus, diabetic coma.
2. Fluid replacement in plasma exchange.
3. Extra-corporeal circulation.
4. Isolated organ perfusion.
5. As a carrier solution for insulin.

Dosage and administration Haemacel should be administered intravenously in a volume approximately equal to the estimated blood loss.

In common with all intravenous infusion solutions, Haemacel should, if possible, be warmed to body temperature before use. However, in emergencies, it may be infused at ambient temperatures.

Infusion rate: The rate of infusion is determined by the condition of the patient. Normally 500 ml will be infused in not less than 60 minutes, but in emergencies Haemacel can be rapidly infused. Losses of up to 25% of the blood volume can be replaced by Haemacel alone.

Plastic infusion bottle: It is advisable to disinfect the bottle top then pull out the plastic ring. A hole will be exposed through which the piercing needle of an infusion set can be pushed. There is no need to disinfect the cap further.

Hypovolaemic shock: 500–1,000 ml Haemacel should be infused intravenously initially. Up to 1,500 ml blood loss can be replaced entirely by Haemacel. For between 1,500 ml and 4,000 ml blood loss, fluid replacement

should be with equal volumes of Haemacel and blood, given separately (see Pharmaceutical precautions). For losses over 4,000 ml the separate infusions should be in the ratio of two parts blood to one part Haemacel. The haematocrit should not be allowed to fall below 25%.

Burns: It is suggested that at least 1 ml Haemacel be infused per kg body weight, multiplied by the % of body surface burned for each 24 hours for two days, e.g. if a 70 kg person has burns covering 10% of body surface, then the dosage of Haemacel should be at least 1 (ml) × 70 (kg) × 10 (%) = 700 ml/24 hours. Additional crystalloid solutions should be given to cover the normal fluid loss, i.e. about 2,000 ml per 24 hours. In severe burns, additional protein and vitamin therapy may be required. The volume of colloid and crystalloid given should be varied according to the clinical response of the patient, the urine volume, its specific gravity and osmolality, etc.

Plasma exchange: Haemacel should be given either alone or in combination with other replacement fluids in a volume adequate to replace the plasma removed. Up to 2 litres have been given as sole replacement fluid.

Contra-indications, warnings, etc There are no absolute contra-indications to the use of Haemacel. However, caution should be used in infusing Haemacel in any patient likely to develop circulatory overloading (e.g. severe congestive cardiac failure). Inappropriately rapid administration of Haemacel, especially to normovolaemic patients, may cause the release of vasoactive substances. The exact mechanism of such histamine release has not been clearly defined. Histamine release may be especially hazardous in patients with known allergic conditions such as asthma. In the event of histamine release, the infusion should be discontinued and appropriate action taken with antihistamines, etc. Haemacel contains calcium ions and caution should be observed in patients being treated with cardiac glycosides.

Pharmaceutical precautions There are no special storage requirements. Haemacel will gel below 3°C; however, warming will reverse this. Freezing does not alter its physico-chemical characteristics in any way. Haemacel contains no preservatives; any unused fluid should be discarded once a bottle has been opened.

Haemacel may be mixed with other infusion solutions (e.g. saline, dextrose, Ringer's solution, etc.) or with heparinised blood. Sterility must be maintained. Compatible water-soluble drugs may be infused in Haemacel, e.g. insulin, streptokinase, etc. Any additive should be injected into the bottle through the small hole located next to the pull-ring.

Citrated blood should *not* be mixed with Haemacel since the calcium ions present in Haemacel may cause recalcification. However, citrated blood may be infused before or after Haemacel provided that there is adequate flushing of the infusion set.

Do not use Haemacel if the seal has been broken or if the contents are cloudy.

Haemacel is stable for eight years at room temperature, five years in tropical conditions.

Legal category POM.

Package quantities Available in 500 ml plastic bottles.

Further information Haemacel is of particular value as a volume replacement as it promotes a demonstrable osmotic diuresis, thereby protecting the kidneys. Provided that the recipient's red cells are suspended in saline

rather than serum it does not interfere with subsequent blood grouping and cross matching, nor does it interfere with the coagulation system. It is non-immunogenic and does not induce antibody formation.

Product licence number 0086/0040.

LASIKAL* TABLETS ▼

Presentation Lasikal Tablets each contain 20 mg Frusemide BP and 750 mg (10 mmol K⁺) slow-release potassium chloride. They are presented as film-coated, biconvex, twin-layered tablets, 12.5 mm in diameter, marked 'LK' on one side. The frusemide layer is white and the slow-release potassium chloride layer is yellow.

Uses Lasikal contains a short-acting diuretic and a slow-release potassium supplement. It is intended for the treatment of oedema in patients who require potassium supplementation.

Dosage and administration The recommended initial adult dose is 2 tablets (40 mg frusemide and 20 mmol K⁺) to be taken each morning. This may be increased to four tablets daily, to be taken as 2 tablets each morning and evening, or may be decreased to 1 tablet each morning, according to clinical response.

Lasikal tablets must be swallowed whole.

Children: Lasikal tablets cannot be sub-divided and are unsuitable for paediatric use.

Contra-indications, warnings, etc

Contra-indications: Lasikal is contra-indicated in hyperkalaemia, precomatose states associated with liver cirrhosis, Addison's disease and in patients taking potassium-sparing diuretics.

Warnings: Patients with prostatic hypertrophy or impairment of micturition have an increased risk of developing acute retention.

The dosage of concurrently administered cardiac glycosides or antihypertensive agents may require adjustment.

Cephaloridine nephrotoxicity may be increased by concomitant administration of potent diuretics such as frusemide.

Latent diabetes may become manifest or the insulin requirements of diabetic patients may increase.

Care should be exercised when treating patients with renal insufficiency because of the risk of hyperkalaemia.

In common with other diuretics, serum lithium levels may be increased when lithium is given concomitantly with frusemide, necessitating adjustment of the lithium dosage.

Certain non-steroidal anti-inflammatory agents have been shown to antagonise the action of diuretics such as frusemide.

Precautions: Results of animal work, in general, show no hazardous effect of Lasix in pregnancy. There is clinical evidence of safety of the drug in the third trimester of human pregnancy; however, there is no evidence of the safety of Lasix in early pregnancy.

Nursing mothers: As Lasix may inhibit lactation, it should be used with caution in nursing mothers.

Overdosage: In cases of overdose there is a danger of dehydration and electrolyte depletion due to excessive diuresis. Treatment should therefore be aimed at fluid replacement and correction of the electrolyte imbalance.

Side-effects: Lasikal is generally well tolerated. Side-effects of a minor nature such as nausea, malaise or

gastric upset may occur but are not usually severe enough to necessitate withdrawal of treatment.

The incidence of allergic reactions, such as skin rashes, is very low, but when these occur treatment should be withdrawn.

In common with other sulphonamide-based diuretics, hyperuricaemia may occur and, in rare cases, clinical gout may be precipitated.

Bone marrow depression has been reported as a rare complication and necessitates withdrawal of treatment.

Pharmaceutical precautions Lasikal should be stored in a cool dry place, protected from light, in the original containers or in containers similar to those of the manufacturer. Lasikal tablets should be dispensed in moisture-tight containers which offer protection from light.

Legal category POM.

Package quantities Lasikal is available in containers of 100 and 250 tablets.

Further information Lasix produces a prompt and effective diuresis which lasts for approximately four hours following oral administration. The potassium chloride in Lasikal tablets is contained in an inert matrix which allows slow release of potassium ions, thereby helping to avoid high local K⁺ ion concentrations in the intestine.

Ghost tablets may appear in the patient's faeces.

Product licence number 0086/0060.

LASILACTONE* CAPSULES ▼

Presentation Lasilactone Capsules each contain 20 mg of Frusemide BP and 50 mg Spironolactone BP. They are presented as hard gelatin capsules with a light blue opaque cap and white opaque body.

Uses Lasilactone contains a short-acting diuretic and a long-acting aldosterone antagonist. It is indicated in the treatment of resistant oedema where this is associated with secondary hyperaldosteronism; conditions include chronic congestive cardiac failure and hepatic cirrhosis.

Treatment with Lasilactone should be reserved for cases refractory to a diuretic alone at conventional dosage.

This fixed ratio combination should only be used if titration with the component drugs separately indicates that this product is appropriate.

The use of Lasilactone in the management of essential hypertension should be restricted to patients with demonstrated hyperaldosteronism. It is recommended that in these patients also, this combination should only be used if titration with the component drugs separately indicates that this product is appropriate.

Dosage and administration In accordance with the recommendations on usage given above the dosage of Lasilactone will normally be in the range of 1 to 4 capsules daily (20–80 mg Lasix and 50–200 mg spironolactone).

Children: The product is not suitable for use in children.

Contra-indications, warnings, etc

Contra-indications: Lasilactone should not be given in acute renal insufficiency, anuric states, hyperkalaemia or Addison's disease.

Warnings: Patients with prostatic hypertrophy or impairment of micturition have an increased risk of developing acute retention. Caution should also be exercised in the presence of liver disease as hepatic coma may be precipitated in susceptible cases. Administration of Lasilactone should be avoided in the presence of a raised serum potassium. Concomitant administration of triamterene, amiloride or potassium supplements is not recommended as hyperkalaemia may result.

The dosage of concurrently administered cardiac glycosides or hypotensive agents may require adjustment.

Cephaloridine nephrotoxicity may be potentiated by concurrent administration of potent diuretics such as frusemide.

Latent diabetes may become manifest; the insulin requirements of diabetic patients may increase.

In common with other diuretics, serum lithium levels may be increased when lithium is given concomitantly with frusemide, necessitating adjustment of the lithium dosage.

Carcinogenicity: Spironolactone has been shown to produce tumours in rats when administered at high doses over a long period of time. The significance of these findings with respect to clinical use is not certain. However, the long-term use of spironolactone in young patients requires careful consideration of the benefits and the potential hazard involved.

Precautions: Caution should be observed in patients liable to electrolyte deficiency.

Results of animal work, in general, show no hazardous effect of frusemide in pregnancy. There is clinical evidence of the safety of the drug in the third trimester of human pregnancy; however, there is no evidence of the safety of frusemide in early pregnancy.

Spironolactone or its metabolites may cross the placental barrier.

Nursing mothers: As frusemide may inhibit lactation it should be used with caution in nursing mothers. Canrenone, a metabolite of spironolactone appears in breast milk. If use of spironolactone is considered essential, an alternative method of infant feeding should be instituted.

Overdosage: In cases of overdosage with Lasilactone there is a danger of severe electrolyte disturbance and dehydration due to excessive diuresis. Signs of overdosage may include drowsiness, mental confusion, nausea, vomiting, dizziness or diarrhoea. Electrolyte disturbances such as hyperkalaemia, hypokalaemia and hyponatraemia may be induced. Hyperkalaemia may be manifested clinically by paraesthesia, weakness, flaccid paralysis or muscle spasm and may be difficult to distinguish from hypokalaemia. Electrocardiographic changes are the earliest signs of potassium disturbances.

Treatment should be aimed at the replacement of fluid and the correction of any electrolyte imbalance.

Side-effects: Lasix is generally well tolerated. Side-effects of a minor nature such as nausea, malaise or gastric upset may occur but are not usually severe enough to necessitate withdrawal of treatment.

The incidence of allergic reactions, such as skin rashes, is very low, but when these occur treatment should be withdrawn.

In common with other sulphonamide-based diuretics, the administration of Lasix may induce a rise in serum uric acid; in rare cases, clinical gout may be precipitated.

Bone marrow depression has been reported as a rare

complication of Lasix therapy and necessitates withdrawal of treatment.

Spironolactone has been reported to induce gastrointestinal intolerance and also drowsiness, headache, ataxia and mental confusion. Reversible gynaecomastia may occur. Maculopapular or erythematous cutaneous eruptions have been reported rarely, as have mild androgenic manifestations such as hirsutism and menstrual irregularities.

Pharmaceutical precautions Lasilactone should be stored in a cool dry place, protected from light, in the original container or in containers similar to those of the manufacturer.

Legal category POM.

Package quantities Lasilactone is available in blister strips packed in cartons of 50 capsules.

Further information Lasix is an effective short-acting diuretic; diuresis usually commences within one hour and lasts for four to six hours.

Spironolactone is a competitive inhibitor of aldosterone and thus increases sodium excretion whilst reducing potassium loss at the distal renal tubule. It has a slow and prolonged action, maximum response being usually attained after 2-3 days' treatment.

Product licence number 0086/0039.

LASIX* TABLETS 20 mg

LASIX* TABLETS 40 mg

Presentation Lasix Tablets 20 mg each contain 20 mg Frusemide BP. They are presented as white, circular, biplanar tablets, 6 mm in diameter, one side bearing the Hoechst insignia, the other scored and bearing the letters DLF on either side of the score mark.

Lasix Tablets 40 mg each contain 40 mg Frusemide BP. They are presented as white, circular, biplanar tablets, 8 mm in diameter, one side bearing the Hoechst insignia, the other scored and bearing the letters DLI on one side of the score mark and '40' on the other.

Uses Lasix is a diuretic recommended for use in all indications when a prompt and effective diuresis is required. Indications for Lasix Tablets 40 mg include cardiac, pulmonary, hepatic and renal oedema, peripheral oedema due to mechanical obstruction or changes in the walls of the veins, ascites, toxemia of pregnancy, hypertension and miscellaneous conditions such as acute barbiturate poisoning.

Lasix Tablets 20 mg are indicated for the maintenance therapy of mild oedema of any origin.

Dosage and administration Lasix has an exceptionally wide therapeutic range, the effect being proportional to the dosage. Lasix is best given as a single dose either daily, on alternate days, or on three successive days of the week.

The usual initial daily dose is 40 mg. This may require adjustment until the effective dose is achieved. In mild cases, 20 mg daily or 40 mg on alternate days may be sufficient, whereas in cases of resistant oedema, daily doses of 80 mg and above may be used.

Children: Oral doses for children range from 1 to 3 mg/kg body weight daily.

Contra-indications, warnings, etc

Contra-indications: Lasix is contra-indicated in electro-

lyte deficiency and pre-comatose states associated with liver cirrhosis.

Warnings: Patients with prostatic hypertrophy or impairment of micturition have an increased risk of developing acute retention.

The dosage of concurrently administered cardiac glycosides or anti-hypertensive agents may require adjustment.

Cephaloridine nephrotoxicity may be increased by concomitant administration of potent diuretics such as frusemide.

Latent diabetes may become manifest or the insulin requirements of diabetic patients may increase.

In common with other diuretics, serum lithium levels may be increased when lithium is given concomitantly with frusemide, necessitating adjustment of the lithium dosage.

Certain non-steroidal anti-inflammatory agents have been shown to antagonise the action of diuretics such as frusemide.

Precautions: Caution should be observed in patients liable to electrolyte deficiency.

Results of animal work, in general, show no hazardous effect of Lasix in pregnancy. There is clinical evidence of safety of the drug in the third trimester of human pregnancy; however, there is no evidence of the safety of Lasix in early pregnancy.

Nursing mothers: As Lasix may inhibit lactation it should be used with caution in nursing mothers.

Overdosage: In cases of overdose there is a danger of dehydration and electrolyte depletion due to excessive diuresis. Treatment should therefore be aimed at fluid replacement and correction of the electrolyte imbalance.

Side-effects: Lasix is generally well tolerated. Side-effects of a minor nature such as nausea, malaise or gastric upset may occur but are not usually severe enough to necessitate withdrawal of treatment.

The incidence of allergic reactions, such as skin rashes, is very low, but when these occur treatment should be withdrawn.

In common with other sulphonamide-based diuretics, hyperuricaemia may occur and, in rare cases, clinical gout may be precipitated.

Bone marrow depression has been reported as a rare complication and necessitates withdrawal of treatment.

Pharmaceutical precautions Lasix tablets should be stored in a cool dry place, protected from light, in containers similar to those of the manufacturer.

Legal category POM.

Package quantities Lasix Tablets 20 mg are available in packs of 60 and 600. Lasix Tablets 40 mg are available in packs of 250 and 1,000.

Further information Lasix produces a prompt and effective diuresis which lasts for approximately four hours following oral administration. Therefore the time of administration can be adjusted to suit the patient's requirements.

Product licence numbers

Lasix Tablets 20 mg 0086/0017

Lasix Tablets 40 mg 0086/5011

LASIX* INJECTION 20 mg/2 ml
LASIX* INJECTION 50 mg/5 ml ▼

Presentation Lasix Injection 20 mg contains 20 mg

Frusemide BP in 2 ml. Lasix Injection 50 mg contains 50 mg Frusemide BP in 5 ml.

Uses Lasix is a diuretic recommended for use when a prompt and effective diuresis is required. The intravenous formulation is appropriate for use in emergencies or when oral therapy is precluded. Indications include cardiac, pulmonary, hepatic and renal oedema.

Dosage and administration Lasix injection *must* always be given slowly. The diuretic effect of Lasix is proportional to the dosage. Doses of 20–50 mg intramuscularly or intravenously may be given initially. If larger doses are required, they should be given by slow infusion and titrated according to the response. In such cases the use of Lasix 250 mg ampoules should be considered.

Children: Parenteral doses for children range from 0.5–1.5 mg/kg body weight daily.

Contra-indications, warnings, etc Intravenous injections of Lasix *must* always be given slowly.

Contra-indications: Lasix is contra-indicated in electrolyte deficiency and pre-comatose states associated with liver cirrhosis.

Warnings: Patients with prostatic hypertrophy or impairment of micturition have an increased risk of developing acute retention.

The dosage of concurrently administered cardiac glycosides or antihypertensive agents may require adjustment.

Cephaloridine nephrotoxicity may be increased by concomitant administration of potent diuretics such as frusemide.

Latent diabetes may become manifest or the insulin requirements of diabetic patients may increase.

In common with other diuretics, serum lithium levels may be increased when lithium is given concomitantly with frusemide, necessitating adjustment of the lithium dosage.

Certain non-steroidal anti-inflammatory agents have been shown to antagonise the action of diuretics such as frusemide.

Precautions: Caution should be observed in patients liable to electrolyte deficiency.

Results of animal work, in general, show no hazardous effect of Lasix in pregnancy. There is clinical evidence of safety of the drug in the third trimester of human pregnancy; however, there is no evidence of the safety of Lasix in early pregnancy.

Nursing mothers: As Lasix may inhibit lactation it should be used with caution in nursing mothers.

Overdosage: In cases of overdose there is a danger of dehydration and electrolyte depletion due to excessive diuresis. Treatment should therefore be aimed at fluid replacement and correction of the electrolyte imbalance.

Side-effects: Lasix is generally well tolerated. Side-effects of a minor nature such as nausea, malaise or gastric upset may occur but are not usually severe enough to necessitate withdrawal of treatment.

The incidence of allergic reactions, such as skin rashes, is very low but, when these occur, treatment should be withdrawn.

In common with other sulphonamide-based diuretics hyperuricaemia may occur and, in rare cases, clinical gout may be precipitated.

Bone marrow depression has been reported as a rare complication and necessitates withdrawal of treatment.

Pharmaceutical precautions Lasix injections should be stored in a cool dry place, protected from light. Injections of Lasix should not be mixed with any other preparations. Opened ampoules should be used immediately and any remainder discarded.

Legal category POM.

Package quantities Lasix ampoules 20 mg are available in packs of 25×2 ml. Lasix ampoules 50 mg are available in packs of 5×5 ml.

Further information Lasix 20 mg and 50 mg injections contain approximately $0.14 \text{ mmol Na}^+/\text{ml}$.

Product licence numbers

Lasix injection 20 mg 0086/5012

Lasix injection 50 mg 0086/0054

LASIX* TABLETS 500 mg

Presentation Lasix Tablets 500 mg each contain 500 mg of Frusemide BP. They are presented as yellow, circular, biplanar, uncoated tablets, 13 mm in diameter, one side bearing the Hoechst insignia; the other is quarter-scored bearing the letters DLX, one in each of three of the four quarters.

Uses Lasix 500 mg is a diuretic for the management of oliguria due to acute or chronic renal insufficiency with a GFR below 20 ml/minute.

Dosage and administration In patients with chronic renal insufficiency, an initial daily dose of 250 mg ($\frac{1}{2}$ tablet) is employed. If a satisfactory diuresis is not produced then the dose may be increased in steps of 250 mg at four to six hourly intervals up to a maximum dose of 2,000 mg (4 tablets) as a single dose.

In cases of acute renal failure which have been initially controlled using Lasix Injection 250 mg, oral therapy may be substituted for parenteral therapy, regarding one 500 mg tablet as approximately equal to one 250 mg ampoule. Appropriate dosage adjustments may then be made according to the observed clinical response.

Children: Lasix Tablets 500 mg are unlikely to be suitable for use in children.

Contra-indications, warnings, etc During treatment with high-dosage forms of Lasix, fluid balance should be carefully controlled. In the particular case of patients with shock, steps should be taken to correct the blood pressure and circulating blood volume before commencing therapy. Regular checks of plasma electrolytes, particularly sodium, potassium, chloride and bicarbonate, should be carried out and electrolyte replacement therapy instituted accordingly.

Contra-indications: Lasix Tablets 500 mg are contra-indicated in renal failure as a result of poisoning by nephrotoxic or hepatotoxic agents and in renal failure associated with hepatic coma.

Warnings: The dosage of concurrently administered cardiac glycosides or antihypertensive agents may require adjustment.

Cephaloridine nephrotoxicity may be increased by concomitant administration of potent diuretics such as frusemide.

Latent diabetes may become manifest or the insulin requirements of diabetic patients may increase.

In common with other diuretics, serum lithium levels may be increased when lithium is given concomitantly

with frusemide, necessitating adjustment of the lithium dosage.

Certain non-steroidal anti-inflammatory agents have been shown to antagonise the action of diuretics such as frusemide.

Precautions: There is little evidence of safety of high-dose Lasix in human pregnancy, although the results of animal work, in general, show no hazardous effects.

Nursing mothers: As Lasix may inhibit lactation it should be used with caution in nursing mothers.

Overdosage: In cases of overdosage there is a danger of dehydration and electrolyte depletion due to excessive diuresis. Treatment should therefore be aimed at fluid replacement and correction of the electrolyte imbalance.

Side-effects: Lasix Tablets 500 mg are generally well tolerated. Side-effects of a minor nature such as nausea, malaise or gastric upset may occur but are not usually severe enough to necessitate withdrawal of treatment.

The incidence of allergic reactions, such as skin rashes, is very low but, when these occur, treatment should be withdrawn.

In common with other sulphonamide-based diuretics, hyperuricaemia may occur and, in rare cases, clinical gout may be precipitated.

Bone marrow depression has been reported as a rare complication and necessitates withdrawal of treatment.

Pharmaceutical precautions Lasix tablets should be stored in a cool dry place, protected from light, in the original containers or in containers similar to those of the manufacturer.

Legal category POM.

Package quantities Lasix Tablets 500 mg are available in packs of 100.

Further information Diuresis commences within one hour of taking the tablets and the effect lasts for approximately four hours.

Product licence number 0086/5013.

LASIX* INJECTION 250 mg/25 ml

Presentation Lasix 250 mg ampoules contain 250 mg Frusemide BP in 25 ml.

Uses Lasix Injection 250 mg is a diuretic for the management of oliguria due to acute or chronic renal insufficiency with a GFR below 20 ml/minute.

Dosage and administration Lasix 250 mg should be administered by intravenous injection at a rate not exceeding 4 mg/minute.

The recommended initial dose is one 25 ml ampoule (250 mg) diluted in approximately 225 ml Sodium Chloride Injection BP or Ringer's Solution for Injection administered over one hour. This gives an approximate drip rate of 80 drops/minute, ensuring that the infusion is at the level of 4 mg/minute.

If a satisfactory increase in urine output, such as 40-50 ml/hour, is not attained within the next hour, a second infusion of two 25 ml ampoules (500 mg) in an appropriate infusion fluid should be given, the total volume of the infusion being governed by the patient's state of hydration. If a satisfactory output is still not achieved within one hour of the end of the second infusion, a third infusion consisting of four 25 ml ampoules (1,000 mg) can be given. The rate of infusion should not exceed 4 mg/minute.

If the third infusion using the maximum intravenous dose of 1,000 mg over four hours is not effective, then dialysis will probably be required.

In oliguric or anuric patients with significant fluid overload, it may not be practicable to administer high-dose Lasix injection by the method suggested above. Under these circumstances, the use of a constant-rate infusion pump (e.g. Sage pump) with micrometer screw-gauge adjustment may be considered for direct administration of the injection into the vein. The rate of administration should not exceed 4 mg/minute.

If the Lasix infusion produces a satisfactory response of 40–50 ml/hour, then the effective dose (up to 1,000 mg) can be repeated every 24 hours. Alternatively, maintenance therapy can be continued with oral Lasix 500 mg Tablets when one 500 mg tablet may be regarded as being approximately equal to one 250 mg ampoule. Appropriate dosage adjustments may then be made according to the observed clinical response.

Children: Doses for children can only be determined on the basis of the severity of the renal insufficiency and clinical response to initial doses.

Contra-indications, warnings, etc During treatment with high-dosage forms of Lasix, fluid balance should be carefully controlled. In the particular case of patients with shock, steps should be taken to correct the blood pressure and circulating blood volume before commencing therapy. Regular checks of plasma electrolytes, particularly sodium, potassium, chloride and bicarbonate, should be carried out, and electrolyte replacement therapy instituted accordingly.

Intravenous injections of Lasix *must* be given slowly.

If the recommended infusion rate of 4 mg/minute is exceeded, transient deafness may occur.

Contra-indications: Lasix Injection 250 mg is contra-indicated in renal failure as a result of poisoning by nephrotoxic or hepatotoxic agents and in renal failure associated with hepatic coma.

Warnings: The dosage of concurrently administered cardiac glycosides or antihypertensive agents may require adjustment.

Cephaloridine nephrotoxicity may be increased by concomitant administration of potent diuretics such as frusemide.

Latent diabetes may become manifest or the insulin requirements of diabetic patients may increase.

In common with other diuretics, serum lithium levels may be increased when lithium is given concomitantly with frusemide, necessitating adjustment of the lithium dosage.

Certain non-steroidal anti-inflammatory agents have been shown to antagonise the action of diuretics such as frusemide.

Precautions: There is little evidence of safety of high-dose Lasix in human pregnancy although the results of animal work, in general, show no hazardous effects.

Nursing mothers: As Lasix may inhibit lactation it should be used with caution in nursing mothers.

Overdosage: In cases of overdose there is a danger of dehydration and electrolyte depletion due to excessive diuresis. Treatment should therefore be aimed at fluid replacement and correction of the electrolyte imbalance.

Side-effects: Lasix injection 250 mg is generally well tolerated. Side-effects of a minor nature such as nausea, malaise or gastric upset may occur but are not usually severe enough to necessitate withdrawal of treatment.

The incidence of allergic reactions, such as skin rashes, is very low but, when these occur, treatment should be withdrawn.

In common with other sulphonamide-based diuretics, hyperuricaemia may occur and, in rare cases, clinical gout may be precipitated.

Bone marrow depression has been reported as a rare complication and necessitates withdrawal of treatment.

Transient ototoxicity has also been reported; it is generally only associated with rapid intravenous administration.

Pharmaceutical precautions Lasix Injection 250 mg should be stored in a cool place protected from light. Frusemide may precipitate in solutions of low pH and therefore dextrose solutions are not suitable infusion fluids for Lasix injections. The injection solution should not be mixed with other drugs in the infusion bottle.

Opened ampoules should be used immediately and any remainder of either the ampoule content or the prepared infusion solution should be discarded.

Legal category POM.

Package quantities Lasix Injections 250 mg are available in packs of 10 × 25 ml.

Further information Diuresis should commence within a few minutes and last for approximately two hours. A diuretic effect is seen during the infusion and its duration is related to the infusion time.

Lasix Injection 250 mg contains approximately 0.04 mmol Na⁺/ml.

Product licence number 0086/5014.

LASIX* + K COMBINATION PACK

Presentation Lasix Tablets 40 mg each contain 40 mg of Frusemide BP. They are presented as white, circular, biplanar tablets measuring 8 mm in diameter. On one side they bear the Hoechst insignia. The other side is scored and bears the letters DLI on one side of the score mark and '40' on the other.

The potassium chloride slow-release tablets each contain 750 mg (10 mmol) of potassium chloride. They are presented as yellow, circular, biconvex tablets, 12 mm in diameter, and have no superficial markings.

These tablets are presented together in a calendar pack as Lasix + K.

Uses Lasix + K contains a short-acting diuretic and a slow-release potassium supplement. The calendar pack is designed for patients who require a fixed dose comprising 40 mg of Lasix (1 tablet) and 20 mmol of potassium (2 tablets) each day. It is not intended for patients who require individual titration of dosage.

Dosage and administration Lasix + K is supplied in calendar packs bearing directions for use. The instructions state that the Lasix 40 mg tablet is taken in the morning, that one potassium chloride tablet is taken at noon, and one in the evening. This ensures that the release of the latter occurs outside the diuretic phase, at a time when conditions are optimal for absorption and retention.

Children: Lasix + K is not suitable for paediatric use.

Contra-indications, warnings, etc

Contra-indications: Lasix + K is contra-indicated in hyperkalaemia, precomatose states associated with liver

cirrhosis and Addison's disease, and in patients taking potassium-sparing diuretics.

Warnings: Patients with prostatic hypertrophy or impairment of micturition have an increased risk of developing acute retention.

The dosage of concurrently administered cardiac glycosides or antihypertensive agents may require adjustment.

Cephaloridine nephrotoxicity may be increased by concomitant administration of potent diuretics such as frusemide.

Latent diabetes may become manifest or the insulin requirements of diabetic patients may increase.

Care should be exercised when treating patients with renal insufficiency because of the risk of hyperkalaemia. In common with other diuretics, serum lithium levels may be increased when lithium is given concomitantly with frusemide, necessitating adjustment of the lithium dosage.

Certain non-steroidal anti-inflammatory agents have been shown to antagonise the action of diuretics such as frusemide.

Precautions: Results of animal work, in general, show no hazardous effect of Lasix in pregnancy. There is clinical evidence of safety of the drug in the third trimester of human pregnancy; however, there is no evidence of the safety of Lasix in early pregnancy.

Nursing mothers: As Lasix may inhibit lactation it should be used with caution in nursing mothers.

Overdosage: In cases of overdose there is a danger of dehydration and electrolyte depletion due to excessive diuresis. Treatment should therefore be aimed at fluid replacement and correction of the electrolyte imbalance.

Side-effects: Lasix + K is generally well tolerated. Side-effects of a minor nature such as nausea, malaise or gastric upset may occur but are not usually severe enough to necessitate withdrawal of treatment.

The incidence of allergic reactions, such as skin rashes, is very low, but when these occur treatment should be withdrawn.

In common with other sulphonamide-based diuretics hyperuricaemia may occur and, in rare cases, clinical gout may be precipitated.

Bone marrow depression has been reported as a rare complication and necessitates withdrawal of treatment.

Pharmaceutical precautions Lasix + K should be stored in a cool dry place, protected from light, in the original container or in containers similar to those of the manufacturer.

Legal category POM.

Package quantities Lasix + K is packed in blister strips, each containing 10 Lasix tablets and 20 potassium chloride tablets. It is supplied in boxes of three blister strips.

Further information Lasix produces a prompt and effective diuresis which lasts for approximately four hours following oral administration. The potassium chloride is contained in an inert matrix allowing sustained release over a period of six to eight hours.

If the prescribing instructions are followed, this ensures potassium release outside the diuretic phase at a time when conditions are optimal for absorption and retention.

Ghost tablets may appear in the patient's faeces.

Product licence number 0086/0037.

LASIX* PAEDIATRIC LIQUID ▼

Presentation Lasix Paediatric Liquid is presented as a granulate for reconstitution. The granulate is reconstituted with distilled water to produce a solution containing 1 mg/ml Frusemide BP in a volume of 150 ml.

Uses Lasix Paediatric Liquid is a diuretic which is indicated for the treatment of oedema in children. It may also be used in elderly patients or other patients unable to take solid oral dose forms of Lasix.

Dosage and administration The recommended daily dose of Lasix Paediatric Liquid for children is 1–3 mg/kg body weight (1–3 ml/kg as the reconstituted liquid).

When Lasix Paediatric Liquid is used as a substitute for tablet therapy in adults, the normal dose range is 20–80 mg (20–80 ml) daily (see 'Side-effects' section).

Reconstitution: Lasix Paediatric Liquid is supplied in a 150 ml bottle containing granules for reconstitution. The granules are reconstituted by the addition of 142 ml distilled water to the bottle which is then shaken vigorously to dissolve the granulate before oral administration.

Contra-indications, warnings, etc

Contra-indications: Lasix Paediatric Liquid is contra-indicated in electrolyte deficiency and pre-comatose states associated with liver cirrhosis.

Warnings: Patients with prostatic hypertrophy or impairment of micturition have an increased risk of developing acute retention.

The dosage of concurrently administered cardiac glycosides or hypotensive agents may require adjustment.

Cephaloridine nephrotoxicity may be increased by concomitant administration of potent diuretics such as frusemide.

Latent diabetes may become manifest or the insulin requirements of diabetic patients may increase.

In common with other diuretics, serum lithium levels may be increased when lithium is given concomitantly with frusemide, necessitating adjustment of the lithium dosage.

Certain non-steroidal anti-inflammatory agents have been shown to antagonise the action of diuretics such as frusemide.

Precautions: Caution should be exercised in patients liable to electrolyte deficiency.

Results of animal work, in general, show no hazardous effect of Lasix in pregnancy. There is clinical evidence of safety of the drug in the third trimester of human pregnancy; however, there is no evidence of the safety of Lasix in early pregnancy.

Nursing mothers: As Lasix may inhibit lactation it should be used with caution in nursing mothers.

Overdosage: In cases of overdose there is a danger of dehydration and electrolyte depletion due to excessive diuresis. Treatment should therefore be aimed at fluid replacement and correction of the electrolyte imbalance.

Side-effects: Lasix is generally well tolerated. Side-effects of a minor nature such as nausea, malaise or gastric upset may occur but are not usually severe enough to necessitate withdrawal of treatment.

Flatulence, abdominal distension or diarrhoea may occur following the ingestion of large quantities of Lasix Paediatric Liquid, due to its sorbitol content.

The incidence of allergic reactions, such as skin rashes

s very low but, when these occur, treatment should be withdrawn.

In common with other sulphonamide-based diuretics, hyperuricaemia may occur and, in rare cases, clinical gout may be precipitated.

Bone marrow depression has been reported as a rare complication and necessitates withdrawal of treatment.

Pharmaceutical precautions Lasix Paediatric Liquid granulate should be stored in a cool dry place, protected from light, in the original container.

The granulate should be reconstituted only with 142 ml of distilled water. When reconstituted the liquid should be stored in a cool place, preferably in a refrigerator at 5°C, protected from light.

Under these conditions, reconstituted Lasix Paediatric liquid may be used for up to 30 days, after which any remaining solution must be discarded.

The shelf-life of the granulate prior to reconstitution is three years. The use of sterile distilled water is recommended when the product is intended for administration to neonates.

Legal category POM.

Package quantities Lasix Paediatric Liquid is available in 150 ml bottles.

Further information Lasix produces a prompt and effective diuresis which lasts for approximately four hours following oral administration. Therefore, the time of administration can be adjusted to suit the patient's requirements. Lasix Paediatric Liquid does not contain sucrose.

Product licence number 0086/0063.

METENIX* 5 TABLETS

Representation Metenix 5 Tablets each contain 5 mg metolazone. They are presented as blue flat uncoated round tablets, 7 mm in diameter, marked with a figure '5' on one side and the Hoechst insignia on the other side.

Uses Metenix 5 is a diuretic for use in the treatment of mild and moderate hypertension. Metenix 5 may be used in conjunction with non-diuretic antihypertensive agents and, in these circumstances, it is usually possible to achieve satisfactory control of blood pressure with a reduced dose of the non-diuretic agent. Patients who have become resistant to therapy with these agents may respond to the addition of Metenix 5 to their antihypertensive regimen.

Metenix 5 may also be used for the treatment of cardiac, renal and hepatic oedema, ascites or toxæmia of pregnancy.

Dosage and administration

Hypertension: The recommended initial dose in mild and moderate hypertension is 5 mg daily. After three to four weeks, the dose may be reduced if necessary to 5 mg on alternate days as maintenance therapy.

Oedema: In oedematous conditions, the normal recommended dose is 5–10 mg daily, given as a single dose. In resistant conditions, this may be increased to 20 mg daily or above. However, no more than 80 mg should be given in any 24-hour period.

Children: There is insufficient knowledge of the effects of Metenix 5 in children for any dosage recommendations to be made.

Contra-indications, warnings, etc

Contra-indications: Metenix 5 is contra-indicated in electrolyte deficiency states, anuria, coma or pre-comatose states associated with liver cirrhosis; also in patients with known allergy or hypersensitivity to metolazone.

Warnings: The dosage of concurrently administered cardiac glycosides may require adjustment. Metenix 5 may aggravate the increased potassium excretion associated with steroid therapy or diseases such as cirrhosis or severe ischaemic heart disease.

Latent diabetes may become manifest or the insulin requirements of diabetic patients may increase.

Precautions: Because of the antihypertensive effects of metolazone the dosage of concurrently administered non-diuretic antihypertensive agents may need to be reduced.

Caution should be exercised during Metenix 5 therapy in patients liable to electrolyte deficiency. Fluid and electrolyte balance should be carefully monitored during therapy especially if Metenix 5 is used concurrently with other diuretics. In particular, Metenix 5 may potentiate the diuresis produced by frusemide and, if the two agents are used concurrently, patients should be carefully monitored. This combination of drugs has been used in the treatment of resistant oedema. Prolonged therapy with Metenix 5 may result in hypokalaemia. Serum potassium levels should be determined at regular intervals and, if necessary, potassium supplementation should be instituted. Chloride deficit, hyponatraemia and a low salt syndrome may also occur, particularly when the patient is also on a diet with restricted salt intake. Hypomagnesaemia has been reported as a consequence of prolonged diuretic therapy.

There is little evidence of safety of the drug in human pregnancy, but it has been in wide, general use for many years without apparent ill consequence, animal studies having shown no hazard.

Nursing mothers: If Metenix 5 is given to nursing mothers, metolazone may be present in the breast milk.

Overdosage: In cases of overdose there is a danger of dehydration and electrolyte depletion. Treatment should therefore be aimed at fluid replacement and correction of the electrolyte imbalance.

Side-effects: Metenix 5 is generally well tolerated. There have been occasional reports of headache, anorexia, vomiting, abdominal discomfort, muscle cramps and dizziness. There have been isolated reports of urticaria, leucopenia, tachycardia, chills and chest pain.

Hyperuricaemia or azotaemia may occur during treatment with Metenix 5, particularly in patients with impaired renal function. On rare occasions, clinical gout has been reported.

Pharmaceutical precautions Metenix 5 Tablets should be stored in a cool dry place, protected from light, in the original containers or in containers similar to those of the manufacturer.

Legal category POM.

Package quantities Metenix 5 Tablets are available in blister strips packed in cartons of 100 tablets.

Further information Metolazone is a substituted quinazolinone diuretic.

Diuresis and saluresis begin within one hour of administration of Metenix 5 Tablets, reaching a maximum

in two hours and continuing for 12–24 hours according to dosage.

Product licence number 0086/0056.

PRESSIMMUNE* INJECTION

Presentation Pressimmune (Antilymphocyte Immunoglobulin (Horse), ALG, AHLG) is a sterile, pyrogen-free, isotonic solution for injection, which contains 50 mg equine immunoglobulin (IgG + IgT) in each ml. It contains no preservatives.

Uses Pressimmune is an immunosuppressive agent indicated in organ and tissue transplantation.

Pressimmune may be used to reduce the need for other immunosuppressive therapy, thereby minimising the incidence of those side-effects associated with such therapy.

A combination of Pressimmune with steroids has been reported to produce a synergistic effect in experimental studies.

Dosage and administration

General rules for the use of Pressimmune:

1. Test for sensitivity to equine protein using an immunoglobulin solution containing 10 mg globulin/ml. Test methods (see below):

- (a) intracutaneous test,
- (b) conjunctival test.

2. Do not use cloudy solutions or preparations past their date of expiry.

3. Strictly evaluate the indications for every administration of immunoglobulins, especially if the patient is allergic.

4. During infusion, observe the patient closely for symptoms of incipient shock.

Test methods:

1. **Intracutaneous test:** Inject 0.1 ml of equine immunoglobulin (10 mg/ml) intracutaneously into the anterior aspect of the forearm. If a marked wheal with erythema appears at the injection site within 15 minutes, the patient is hypersensitive to equine protein. If there is a history of allergy, use only 0.05 ml of a 1:100 dilution (i.e. 5 mcg globulin) as a precautionary measure.

2. **Conjunctival test:** Instil 1 drop of equine immunoglobulin (10 mg/ml) on to the conjunctival sac. If itching, lacrimation, oedema of the lid, and conjunctival injection develop within 15 minutes, the test is positive, indicating hypersensitivity.

The results of both tests should be checked by applying an identical dose of saline to the other arm or eye, using the same technique. (See 'Contra-indications').

Renal transplantation

1. Prophylaxis of rejection:

Pressimmune must be given by intravenous infusion. The total amount to be administered in any one day should be made up in about 250–500 ml saline and infused slowly, intravenously, over about one to two hours under constant medical supervision.

If Pressimmune is given before transplantation, an initial dose of 20–30 mg of globulin per kg of body weight, combined with 2×80 mg of methylprednisolone, is recommended.

If Pressimmune is given after transplantation in combination with, for example, 6-mercaptopurine and corticosteroids for immunosuppression, a dose of 20–

30 mg of globulin per kg of body weight should be infused daily for at least three weeks. Clinical work has suggested that the dosage should be reduced gradually after the three-week period to minimise the chance of precipitating a rejection crisis.

The necessity of continuing Pressimmune therapy is determined by the function of the transplanted kidney during the first three months and depends upon the number of rejection crises that occur during this period.

2. Treatment of rejection crises:

In threatened rejection crisis the dose of Pressimmune is 20–30 mg of globulin per kg of body weight daily. Once rejection is successfully suppressed, the dosage of Pressimmune can gradually be reduced.

If Pressimmune, together with other immunosuppressive medication (e.g. 6-mercaptopurine, corticosteroids etc.), is administered only when a rejection crisis sets in a daily dose of 10–30 mg of globulin per kg body weight is recommended. After the crisis has been overcome Pressimmune therapy should be continued for three to four weeks with a daily dose of 10 mg of globulin per kg of body weight.

Contra-indications, warnings, etc If the tests for sensitivity are positive (see 'Dosage'), Pressimmune should be administered only if special precautionary measures are taken. Since Pressimmune is always administered over a long period of time, the patient's serum should be regularly examined for antibodies against equine globulin. An increase in the antibody titre as shown by the passive haemagglutination test, indicates the possibility that anaphylactic reactions may appear.

Pre-treatment testing is especially important in those patients who have previously received equine serum e.g. tetanus antitoxin, or who have an allergic diathesis.

Side-effects: The most frequent local adverse reaction to Pressimmune is thrombophlebitis following intravenous administration. This can usually be avoided by the use of a subclavian catheter.

Systemic reactions are associated with fever and shivering, and commonly occur 10–30 minutes after the end of infusion. These are likely to be of greater severity during the first days of treatment and are more likely to take place if the Pressimmune is administered too rapidly; they may be accompanied by nausea, tachycardia and hypotension.

The desired lymphocytopenia may be accompanied chiefly during the initial phase of treatment, by a relative thrombocytopenia or leucopenia.

Anaphylactic reactions, serum sickness (including serum nephritis), urticaria and pruritus may occur on rare occasions.

Treatment of adverse reactions:

1. **Shock (anaphylaxis and allergy):** Inject 1 ml (0.5 ml for children) of adrenaline 1:1,000 intramuscularly, and repeat injection of the same dose every 30 minutes until blood pressure has returned to normal. At the same time slowly inject 500 mg of methylprednisolone intravenously, and antihistamines intramuscularly. In extremely severe cases, 0.2–0.5 ml of adrenaline 1:10,000 can be slowly injected intravenously and up to 30 mg/kg methylprednisolone given by slow intravenous injection. Oral treatment with antihistamines should be continued for 10 days, in order to prevent the possible appearance of delayed allergic complications.

2. **Serum sickness:** Calcium Gluconate Injection B

should be administered intravenously and antihistamines orally. Intense pruritus can be alleviated immediately, but only temporarily, by subcutaneous injection of 1.0 ml of adrenaline 1:1,000.

Pharmaceutical precautions Pressimmune should be stored at 2–6°C in the manufacturer's containers. For administration, it should be diluted in physiological saline. Any solution prepared for infusion, but not administered, should be discarded.

Legal category POM.

Supply is restricted to those hospitals and specialist centres with the facilities for the transplantation of human organs. Centres wishing to use Pressimmune for applications other than transplantation should apply to the manufacturer.

Package quantities Pressimmune is supplied in the following quantities:

Packs of 10 ampoules of 5 ml (250 mg globulin/5 ml).
Packs of 10 ampoules of 10 ml (500 mg globulin/10 ml).

Further information Pressimmune is a pure immunoglobulin (IgG + IgT) obtained from the blood of horses immunised with human lymphocytes. It is routinely tested for freedom from antibodies against erythrocytes, platelets, human plasma proteins and glomerular basement membrane, and is tested for *in-vitro* activity (lympholysis and rosette inhibition) and *in-vivo* immunosuppressive activity (survival time of monkey skin grafts).

Pressimmune is an immunosuppressive agent which suppresses cell-mediated immunity but does not greatly affect antibody production or resistance to bacterial infection.

Product licence number 0086/0036.

RASTINON* TABLETS 500 mg

Presentation Rastinon Tablets each contain 500 mg Tolbutamide BP. They are presented as uncoated white, circular, scored tablets, 13 mm in diameter, one side bearing the Hoechst insignia, the other bearing the marks 'Rastinon' and '0.5' on either side of the score mark.

Uses Rastinon is a hypoglycaemic agent, indicated for the oral treatment of patients with non-insulin dependent diabetes who respond inadequately to dietary treatment alone. Rastinon is particularly suitable for elderly patients.

Dosage and administration

1. *Treatment of previously untreated diabetics:* Treatment may be initiated by administering 6 tablets on the first day, 4 on the second and 2 on the third. Stabilisation can also be achieved by commencing with 2–3 tablets daily. The subsequent dosage must depend on the patient's individual response. The average daily dose is 1–3 tablets which can be taken as a single dose or divided into 2 or 3 doses as required. Generally, patients who do not respond to 4 tablets (2 g) daily will not respond to higher doses.

2. *Change-over from other oral antidiabetics:* The change-over to Rastinon, from other drugs with a similar mode of action, can be carried out without any break in therapy, even with chlorpropamide despite the long persistence of this agent in the body.

Where existing control is satisfactory, stabilisation can be achieved commencing with 2–3 tablets daily, sub-

sequent dosage depending on the patient's individual response. For patients not adequately controlled on other oral agents, Rastinon treatment may be initiated by administering 6 tablets on the first day, 4 on the second and 2 on the third, adjusting the dose subsequently according to the patient's response.

3. *Combination with biguanides:* If adequate control is not possible with diet and 4 tablets of Rastinon daily, control can often be re-established by combined administration of Rastinon and a biguanide derivative.

4. *Change-over from insulin:* Some cases of non-insulin dependent diabetes, previously treated with insulin, can be changed to Rastinon. Low insulin doses (less than 20 units) can be replaced immediately. With higher doses a gradual change is advisable by giving insulin and Rastinon concurrently and reducing the dose of insulin.

The tablets may be taken by mouth as a single dose with or immediately after the first main meal of the day, or as a divided dose.

Children: As non-insulin dependent diabetes is not usually a disease of childhood, Rastinon is generally considered unsuitable for use in children.

Contra-indications, warnings, etc

Contra-indications: Rastinon should not be used in patients who have or have ever had diabetic ketoacidosis, who have insulin-dependent diabetes mellitus, serious impairment of renal, hepatic, adrenocortical or thyroid function or in circumstances of unusual stress, e.g. surgical operations or during pregnancy, when insulin is preferable.

Rastinon should not be used during the first trimester of pregnancy. There is some evidence of harmful effects in pregnancy in animals and isolated reports which suggest a hazard in human pregnancy.

Nursing mothers: Tolbutamide has been detected in breast milk in small quantities; the effect of this low dose on the neonate is unknown.

Warnings: Debilitated or aged patients may be more liable to hypoglycaemia. The hypoglycaemic effect of tolbutamide may be enhanced by dicumarol, monoamine oxidase inhibitors, beta-adrenergic blocking agents, sulphonamides, phenylbutazone, chloramphenicol, cyclophosphamide and salicylates, or diminished by adrenaline, corticosteroids, oral contraceptives or thiazide diuretics.

Overdosage: Hypoglycaemia may be treated in the conscious patient by the administration of glucose or 3–4 lumps of table sugar with water. This may be repeated as necessary.

If the patient is comatose, glucose should be administered as an intravenous infusion. Bolus glucose injections are not recommended because of the possibility of rebound hypoglycaemia. Alternatively, glucagon may be administered in a dose of 1 mg subcutaneously or intramuscularly to produce consciousness.

Side-effects: Adverse reactions serious enough to warrant discontinuation of treatment are uncommon but mild gastro-intestinal and allergic skin reactions have occurred. There have been reports of anaemia, pancytopenia and transient changes in liver enzyme concentrations and liver function tests during treatment with tolbutamide, but these effects are not known to be directly attributable to the drug. Hypoglycaemic symptoms have occasionally been reported when the dose has been administered without due regard to the patient's dietary habits.

Pharmaceutical precautions Rastinon tablets should be stored in a cool dry place, protected from light, in the original containers or in containers similar to those of the manufacturer.

Legal category POM.

Package quantities Rastinon tablets are available as loose tablets packed in tubs of 100 and 500.

Further information Rastinon is an orally active hypoglycaemic agent which reduces blood sugar concentration without affecting glucose tolerance. It probably acts by stimulating insulin secretion as it has no action on muscle-glucose metabolism when given alone. It is only effective in the presence of functioning islet tissue.

Product licence number 0086/5016.

RASTINON* INJECTION 1 g/20 ml

Presentation Each ampoule contains the equivalent of 1 g of tolbutamide (as the sodium salt) in 20 ml of solution.

Uses Rastinon Injection is used primarily as an aid to the diagnosis of diabetes mellitus, but is also useful in investigation of impaired glucose tolerance of hepatic origin and islet cell adenoma.

Dosage and administration

1. *Diagnosis of mild diabetes:* Tolbutamide stimulates release of insulin from the pancreas and thus indicates the activity of beta-cells in the islet tissue. In healthy adults, intravenous injection of tolbutamide produces a rapid marked fall in blood sugar but in patients with diabetes the fall is smaller and more prolonged.

Fasting blood glucose is determined before starting the test. 1 g of tolbutamide (20 ml of Rastinon Injection) is then given by slow intravenous injection over three minutes. Children receive 25 mg/kg body weight (i.e. 0.5 ml of solution per kg). Blood samples are withdrawn at 20 and 30 minutes for measurement of blood glucose. Patients should be given carbohydrate after the 30-minute sample has been collected.

Blood glucose should be measured by a specific procedure (e.g. glucose oxidase).

In the normal subject, the blood glucose level 20 minutes after injection is 74% or less of the fasting value. Probable diabetes is defined by a 20-minute value of 85–89% of the fasting level. Definite diabetes is shown by a 20-minute level of 90% or more and/or a 30-minute value 77% or more of the fasting value.

2. *Impaired glucose tolerance of hepatic origin:* Patients with chronic liver disease sometimes have disturbed carbohydrate metabolism. In these patients, the oral glucose tolerance test may provoke hyperglycaemia even though there is adequate beta-cell activity in the pancreas.

Patients should be tested by both an oral glucose tolerance test and the tolbutamide injection test described above. Patients who show abnormal results in both tests may be diagnosed as diabetic. Where the oral GTT is abnormal but the tolbutamide injection produces the normal rapid fall in blood sugar, the decreased glucose tolerance is not due to beta-cell deficiency.

3. *Islet cell adenoma:* Patients with active insuloma show a characteristic deep, prolonged hypoglycaemia

after tolbutamide injection, which can be readily distinguished from the much shorter effect seen in functional or hepatogenic hyperinsulinism or adrenocortical insufficiency.

Fasting blood glucose is determined before starting the test. 1 g of tolbutamide (20 ml of Rastinon Injection) is then given by slow intravenous injection over three minutes. Blood is taken for blood-sugar estimations at 15-minute intervals for the first hour and then at 30-minute intervals for the next two hours. Patients should be watched closely for signs of hypoglycaemia during the test and should be given ample carbohydrate after taking the last blood sample.

In functional or hepatogenic hyperinsulinism there is a rapid fall in blood sugar to 25–60% of the resting value within 20–45 minutes, and the levels return to near normal over the next 90–180 minutes.

In patients with insuloma there is also a rapid fall, usually significantly greater, followed by a characteristic sustained hypoglycaemia which persists over three hours. Patients with adrenal insufficiency may show a similar degree of fall but the hypoglycaemia rapidly recovers. Patients with severe liver disease sometimes mimic the insuloma pattern and must be differentially diagnosed on other grounds.

Contra-indications, warnings, etc Patients should be given carbohydrates after the last withdrawal of blood. Hypoglycaemic reactions are rare and occur almost exclusively in normal subjects. In the case of a severe reaction the test may be interrupted at any time by administration of glucose. Some patients note a transient sensation of heat in the region of the brachial vein if the injection is given too quickly. Allergic reactions are rare. The test should not be carried out during pregnancy or where pregnancy is suspected.

Nursing mothers: Tolbutamide has been detected in breast milk in small quantities; the effect of this low dose on the neonate is unknown.

Pharmaceutical precautions Store in a cool place, protected from light. Opened ampoules should be used immediately and any remainder discarded.

Legal category POM.

Package quantities Rastinon Injection is available as single ampoules of 20 ml.

Further information Nil.

Product licence number 0086/5017.

RELEFACT* LH-RH INJECTION ▼

Presentation Each ampoule contains 100 mcg Gonadorelin BP (luteinizing hormone releasing hormone) in 1 ml aqueous solution.

Uses Intravenous injection of Relefact LH-RH causes release of LH (luteinizing hormone) and FSH (follicle-stimulating hormone) from the pituitary gland. It provides a means of assessing the reserve of LH and FSH in the pituitary glands of patients with suspected pituitary impairment. In addition, Relefact LH-RH may be of value in the differential diagnosis of delayed puberty and hypogonadism.

Dosage and administration Relefact LH-RH should be administered intravenously to adults or children as single dose of 100 mcg. The test is based upon the pituitary response to this dose measured as serum LH

and FSH levels. Qualitative data may be obtained from a single test but each laboratory must establish its own normal range for values of serum LH and FSH to obtain quantitative assessment of pituitary reserve.

Test procedure:

1. Obtain venous blood sample for control value of LH and, if facilities are available for its measurement, FSH.
2. Rapid intravenous injection of 100 mcg Relefact LH-RH.
3. Obtain venous blood sample 20 minutes after injection for measurement of LH/FSH response.

Interpretation of results:

1. **Normal response:** Following the administration of Relefact LH-RH there is a rise in serum LH within two minutes of injection; the response is dose-dependent. Peak levels are achieved 20–30 minutes after injection and baseline levels are approached six hours after a dose of 100 mcg. The FSH response is similar but of lesser magnitude (except (a) prior to puberty when, in girls, the FSH response is higher than the LH response and (b) in some patients with hypothalamic-pituitary dysfunction, e.g. anorexia nervosa). The normal female response to Relefact LH-RH shows cyclical variation, the response in the luteal phase being about twice that seen in the early follicular phase.

It is important for each laboratory to establish its own normal ranges of LH and FSH according to the time of the menstrual cycle before attempting to obtain quantitative results.

2. **Assessment of pituitary function:** Relefact LH-RH is a very sensitive index of pituitary function. Consequently, many patients with pituitary tumours, who do not respond to other dynamic tests of pituitary function (such as the growth hormone response to hypoglycaemia), will show a normal response to Relefact LH-RH; others will show an impaired or absent response. A normal response to the Relefact LH-RH test in clinically hypogonadal patients with pituitary abnormalities indicates that their pituitary glands are capable of producing LH and FSH in response to therapy. Similar responses may be seen in patients with hypothalamic tumours such as craniopharyngiomas.

3. **Assessment of primary and secondary hypogonadism:** Patients with primary hypogonadism resulting from gonadal failure or gonadal dysgenesis will have an exaggerated response to Relefact LH-RH. The majority of these patients will also have elevated basal values. The test is of particular value in those cases where basal levels are normal.

The majority of patients with congenital hypogonadotrophic hypogonadism with or without hyposmia (Kallman's syndrome) show a normal or impaired response to single doses of Relefact LH-RH.

These results indicate that, in most cases of isolated pituitary gonadotrophin deficiency, there is a reduced output of hypothalamic hormone releasing factor. An absent response to a single injection, however, is not necessarily indicative of pituitary failure, as more than one injection may be required in order to produce a response.

4. **Assessment of delayed puberty:** In simple delayed puberty the LH and FSH responses are within the normal range, whereas patients with hypogonadotrophic hypogonadism or hypopituitarism have an absent or impaired response. Patients with primary gonadal failure will have an exaggerated response.

Contra-indications, warnings, etc Relefact LH-RH should not be administered in pregnancy. There is a theoretical possibility of induction of ovulation following the administration of LH-RH.

Side-effects: Side-effects of any description are rare, but the following reactions have been reported in isolated cases in healthy women: abdominal pain, nausea, headache and increased menstrual bleeding.

Overdosage: Overdosage with Relefact LH-RH has never been reported and is unlikely to be a problem.

Pharmaceutical precautions Store in a cool dark place. Do not dilute or administer with any additive.

Legal category POM.

Package quantities Relefact LH-RH is available in packs of 10 ampoules.

Further information Relefact LH-RH (luteinizing hormone-releasing hormone) is a synthetic decapeptide. It has also been referred to in the literature as LRF (luteinizing hormone-releasing factor), as LH/FSH-RH (luteinizing hormone/follicle stimulating hormone-releasing hormone) and as luliberin.

Product licence number 0086/0019.

RELEFACT* LH-RH/TRH INJECTION ▼

Presentation Each ampoule contains 100 mcg Gonadorelin BP (luteinizing hormone-releasing hormone) and 200 mcg protirelin (thyrotrophin-releasing hormone) in 1 ml aqueous solution.

Uses Intravenous injection of Relefact LH-RH/TRH causes the release of LH (luteinizing hormone), FSH (follicle-stimulating hormone) and TSH (thyroid-stimulating hormone) from the pituitary gland. In addition, TRH is also known to cause the release of prolactin.

The use of a combined releasing hormone preparation provides a means of simultaneous assessment of anterior pituitary reserve of these hormones in patients with suspected pituitary impairment.

Dosage and administration The contents of 1 ampoule of LH-RH/TRH should be administered intravenously to adults and children as a single dose (100 mcg LH-RH and 200 mcg TRH). The test is based upon the pituitary response to this dose measured as serum TSH, LH and FSH levels. Qualitative data may be obtained from a single combined test but each laboratory must establish its own normal range for the serum level of these hormones to obtain a quantitative assessment of pituitary function.

Test procedure:

1. Obtain venous blood sample for control measurements of TSH, LH and, if required, FSH.
2. Rapid intravenous injection of one ampoule LH-RH/TRH.
3. Obtain venous blood sample 20 minutes after injection to give peak LH, FSH and TSH values.
4. A further venous blood sample may be taken at 60 or 90 minutes to detect a delayed or prolonged response.

Interpretation of results:

LH-RH

1. **Normal response:** Following the administration of LH-RH there is a rise of serum LH within two minutes of injection; the response is dose-dependent. Peak levels are achieved 20–30 minutes after injection and baseline

levels are approached six hours after a dose of 100 mcg. The FSH response is similar but of lesser magnitude (except (a) prior to puberty when, in girls, the FSH response is higher than the LH response and (b) in some patients with hypothalamic-pituitary dysfunction, e.g. anorexia nervosa). The normal female response to LH-RH shows cyclical variation, the response in the luteal phase being about twice that seen in the early follicular phase.

It is important for each laboratory to establish its own normal ranges of LH and FSH according to the time of the menstrual cycle before attempting to obtain quantitative results.

2. *Assessment of pituitary function:* LH-RH response is a very sensitive index of pituitary function. Consequently, many patients with pituitary tumours who do not respond to other dynamic tests of pituitary function (such as the growth hormone response to hypoglycaemia) will show a normal response to LH-RH; others will show an impaired or absent response. A normal response to the LH-RH test in clinically hypogonadal patients with pituitary abnormalities indicates that their pituitary glands are capable of producing LH and FSH in response to therapy. Similar response may be seen in patients with hypothalamic tumours such as craniopharyngiomas.

3. *Assessment of primary and secondary hypogonadism:* Patients with primary hypogonadism resulting from gonadal failure or gonadal dysgenesis will have an exaggerated response to LH-RH. Most of these patients will also have elevated basal values. The test is of particular value in those cases where basal levels are normal.

The majority of patients with congenital hypogonadotrophic hypogonadism with or without hyposmia (Kallman's syndrome) show a normal or impaired response to single doses of LH-RH.

These results indicate that, in most cases of isolated pituitary gonadotrophin deficiency, there is a reduced output of hypothalamic hormone-releasing factor. An absent response to a single injection, however, is not necessarily indicative of pituitary failure, as more than one injection may be required in order to produce a response.

4. *Assessment of delayed puberty:* In simple delayed puberty the LH and FSH responses are within the normal range, whereas patients with hypogonadotrophic hypogonadism or hypopituitarism have an absent or impaired response. Patients with primary gonadal failure will have an exaggerated response.

TRH

1. *Normal response:* In normal subjects, intravenous injection of TRH causes a prompt rise (within five minutes) in serum TSH. This increases to a maximum at about 20 minutes and is declining at 60 minutes. Basal levels are reached about four hours after TRH administration.

2. *Thyroid disease: Hyperthyroidism.* Diagnosis is based upon the measurement of two parameters.

- the increase in TSH values from basal levels, 20 minutes after TRH administration (Δ TSH).
- the ratio of 20 minute TSH value to its basal value (TSH_{20}/TSH_0).

The usual hyperthyroid response is as follows:

- increase in TSH 20 minutes after injection will be less than 2 mcU/ml (Δ TSH < 2).

- the ratio of 20 minute TSH to its basal value will be equal to or less than 1.5 ($TSH_{20}/TSH_0 \leq 1.5$).

Primary hypothyroidism. Primary hypothyroidism is characterised by a high basal TSH level and an exaggerated and prolonged rise in serum TSH following the administration of TRH.

3. *Hypothalamic or pituitary disease: Pituitary disease.* An absent or impaired TSH response indicates a reduction in pituitary reserve (although failure to respond to TRH is also found in patients with hyperthyroidism, this will not usually cause diagnostic difficulty).

Hypothalamic disease. Patients with hypothyroidism caused by hypothalamic disease may have a normal TSH response to TRH. However, more usually, a delayed response is found.

Note: The administration of TRH together with LH-RH may cause slightly greater FSH release in males than that caused by LH-RH alone.

Contra-indications, warnings, etc Relfact LH-RH/TRH should not be used in patients with bronchial asthma or obstructive airways disease. Care should be exercised in patients with myocardial ischaemia.

LH-RH/TRH should not be administered in pregnancy; there is a theoretical possibility of induction of ovulation following the administration of LH-RH/TRH.

Side-effects: The following minor transient side-effects have been reported in patients given TRH: desire to micturate, sensation of heat, slight dizziness and a peculiar taste. There have been isolated reports of transient amaurosis and severe headache.

LH-RH administration has been associated with the following reactions in isolated cases in healthy women: abdominal pain, nausea, headache and increased menstrual bleeding.

Overdosage: Overdosage with LH-RH/TRH should be treated symptomatically.

Pharmaceutical precautions Store in a cool dark place; do not dilute or administer with any additive.

Legal category POM.

Package quantity Relfact LH-RH/TRH is available in packs of 10 ampoules.

Further information LH-RH, TRH and insulin have been administered at the same time for a full and rapid assessment of anterior pituitary function. Such combined administration does not appreciably affect the various hormone responses (LH, FSH, TSH, growth hormone, ACTH, corticosteroids and prolactin).

Note: The mixing of insulin and LH-RH/TRH in the same syringe is not recommended.

Product licence number 0086/0059.

STREPTASE* INJECTION

Presentation Streptase is presented as a freeze-dried powder in vials containing 100,000 Units, 250,000 Units and 750,000 Units of purified streptokinase.

Uses Streptase is a fibrinolytic agent which will produce intravascular dissolution of thrombi and emboli in: extensive deep venous thrombosis pulmonary embolism acute occlusion of peripheral arteries

Isolated:

- rethrombosis after vascular surgery
- thrombosis of vascular prostheses
- clotting in external arteriovenous shunts of patients on haemodialysis
- renal vein thrombosis
- central retinal venous or arterial thrombosis

Dosage and administration Streptase should be given by intravascular infusion in physiological saline or laemacel.

Loading dose: Since human exposure to streptococci is common, antibodies to streptokinase (streptokinase resistance) are found normally. Thus, a loading dose of streptase sufficient to neutralize the resistance is required. A dose of 250,000 Units of Streptase infused into a peripheral vein over 30 minutes has been found appropriate in over 90% of patients.

Maintenance dose: A maintenance dose infusion of 100,000 Units/hour is given following the loading dose. Administer the maintenance dose of 100,000 Units per hour for 72 hours for the treatment of deep vein thrombosis, for 24 hours for the treatment of pulmonary embolism (up to 72 hours if concurrent deep vein thrombosis is suspected) and for 24–72 hours for the treatment of arterial thrombosis. If the thrombin time or any other parameter of lysis after 4 hours of therapy is less than approximately $1\frac{1}{2}$ times the normal control value, discontinue Streptase as excessive resistance to streptokinase is present.

Children: In children, in whom it is always advisable to estimate the initial dose by means of the streptokinase resistance test (see 'Warnings' section), the correct maintenance dose per hour is 20 Units/ml blood volume.

Patient monitoring: Before commencing thrombolytic therapy, it is desirable to obtain a thrombin time (TT), prothrombin time (PT), haematocrit and platelet count to obtain the haemostatic status of the patient. If heparin has been given it should be discontinued, and the TT should be less than twice the normal control value before thrombolytic therapy is started.

During the infusion, decreases in the plasminogen and fibrinogen level and an increase in the level of fibrin degradation products (FDP) (the latter two serving to prolong the clotting times of coagulation tests) will generally confirm the existence of a lytic state. Therefore, therapy can be monitored by performing the TT or PT approximately 4 hours after initiation of therapy.

Following the infusion, before (re-)instituting heparin, the TT should be less than twice the normal control value.

Anticoagulation after terminating intravenous streptokinase treatment: At the end of Streptase therapy, treatment with heparin by continuous intravenous infusion is recommended to prevent recurrent thrombosis. Heparin treatment (without a loading dose) should not begin until the thrombin time has decreased to less than twice the normal control value (approximately 3 to 4 hours). (See manufacturer's prescribing information for proper use of heparin.) This should be followed by oral anticoagulation in the conventional manner.

A variable dosage of Streptase and frequent laboratory monitoring have been recommended. However, since experience shows that these do not seem to increase the efficacy or safety of streptase therapy, they are no longer recommended.

Contra-indications, warnings, etc

Contra-indications: Manifest or recent haemorrhage, haemorrhagic diathesis (with the exception of consumptive coagulopathy), severe hypertension, streptococcal infections and subacute bacterial endocarditis are contra-indications to Streptase therapy.

Drug-induced coagulation defects represent a temporary contra-indication. The effect of heparin can be rapidly neutralised with protamine sulphate or protamine chloride. In patients who have been receiving coumarin drugs, the time at which Streptase therapy may be commenced must be decided in the light of the coagulation status. It is advisable to carry out the appropriate tests at shorter intervals than usual.

Drugs affecting platelet function, such as acetylsalicylic acid, phenylbutazone and dipyridamole should be discontinued at least 3 days before Streptase therapy commences because of a possible increased risk of bleeding.

Recent surgery is a relative contra-indication to Streptase therapy. In cases of embolism, the indication for earlier treatment may be very strong. After careful consideration of all the risks, Streptase may be given 6 days after the operation. The danger of bleeding from the operative area must, of course, be taken into account. In cases of severe pulmonary embolism, the use of Streptase might be considered earlier, the risks, however, should be weighed against the benefits.

Warnings: Caution is necessary in patients with recent cavitating tuberculous lesions of the lungs, gastrointestinal ulceration or serious liver disease accompanied by a bleeding tendency.

Precautions: The use of Streptase before the sixteenth week of pregnancy and, again, immediately post-partum, involves a risk which should be carefully assessed before therapy is instituted. If the patient has just recovered from a streptococcal infection or if it is urgently necessary to give a further course of Streptase within three months of the first course, the streptokinase resistance test must be used to estimate the correct initial dose and corticosteroid cover is essential.

Treatment with streptokinase causes a marked increase in the level of streptokinase antibodies. This normally precludes repeated therapy within 3 months.

Titrated initial dose: The determination of the initial dose by the streptokinase resistance test is recommended in the following circumstances:

- (a) in children
- (b) when there is a history of recent streptococcal infection
- (c) when the patient has previously received streptokinase therapy.

However low the titre determined, the initial dose must not be less than 100,000 Units of Streptase.

As streptokinase is an antigen it is advisable to cover the initial dose of Streptase by prophylactic administration of a corticosteroid, e.g. hydrocortisone hemisuccinate 100 mg i.v., so as to preclude any possibility of allergic reactions.

Side-effects: A mild rise in temperature, usually of short duration, may be noted in some cases. With the prophylactic administration of a corticosteroid before commencing treatment, pyrexia should not be encountered. Allergic-anaphylactic reactions are possible but very rare. Such reactions are more liable to occur if Streptase is injected too rapidly. Should a major reaction be encountered, discontinue Streptase and initiate

therapy with adrenaline, corticosteroids and antihistamines as appropriate.

Overdose: Haemorrhage, considered the main potential complication of streptokinase therapy, is uncommon with the recommended dosage technique. Bleeding episodes are usually confined to oozing from sites of venepuncture and do not require the discontinuation of therapy. Intramuscular therapy can cause formation of local haematomas.

Should serious haemorrhage occur, Streptase therapy should be stopped and tranexamic acid (10 mg/kg) should be administered by slow intravenous injection.

The use of tranexamic acid is not advised during pregnancy when aprotinin should be administered. In only a very few cases will substitution therapy with fibrinogen be necessary.

A transient increase in serum enzymes has been reported following Streptase therapy. This is due to a stimulation of the kallikrein system and not to a hepatotoxic effect.

Pharmaceutical precautions Streptase is stable for at least 3 years when stored at room temperature (<25 °C).

Solutions prepared for infusion but left over or not used should be discarded.

Legal category POM.

Package quantities Available in vials in the following packs:

1 × 100,000 Units and 10 × 100,000 Units

1 × 250,000 Units and 10 × 250,000 Units

1 × 750,000 Units and 10 × 750,000 Units

Streptase for diagnostic use is also supplied in packs of 4 × 5,000 Units.

Further information Streptase activates the intrinsic fibrinolytic system by the formation of a linkage compound between streptokinase and the proactivator-plasminogen molecule. This complex possesses activator properties and brings about the conversion of plasminogen into the fibrinolytic enzyme plasmin. Plasminogen adsorbed on the fibrin clot is also activated, therefore lysis can take place internally as well as externally.

Product licence numbers

Streptase 100,000 Units 0086/5018

Streptase 250,000 Units 0086/5020

Streptase 750,000 Units 0086/5021

SYNADRIN® TABLETS 60 mg

Presentation Synadrin tablets each contain 76 mg Prenylamine Lactate BP, equivalent to 60 mg free base. They are presented as bi-convex, pink, sugar-coated tablets having a diameter of 11 mm.

Uses Synadrin is a catecholamine-depleting agent indicated in the long-term management of angina pectoris.

Dosage and administration One tablet three times daily is adequate for the majority of patients. This can be increased to 1 tablet four or five times daily in patients who do not respond within fourteen days. Reduction in the frequency of anginal attacks should be observed within two weeks, after which a lower maintenance dose, adjusted to individual requirements, is sufficient. The tablet should be swallowed whole.

Children: As angina pectoris is not a disease of childhood, Synadrin is not likely to be of use in children.

Contra-indications, warnings, etc Synadrin is contra-indicated where serious impairment of hepatic or renal function, defects of cardiac conduction or severe uncompensated heart failure are present.

Synadrin may have a slight hypotensive action and the dosage of concurrently administered hypotensive agents may require adjustment.

Synadrin should not be administered concurrently with negative inotropic drugs, e.g. beta-adrenergic receptor blocking agents, quinidine, procainamide, amiodarone or lignocaine. Reports indicate that such combinations are capable of producing paroxysmal ventricular tachycardia or fibrillation. Synadrin should be used with caution in combination with diuretics, laxatives or other drugs likely to cause potassium deficiency. It is recommended that serum potassium concentrations be determined at regular intervals and, if necessary, potassium supplementation should be instituted. If the ECG shows a marked increase in the duration of the QS or QT interval above the rate-adjusted norm, it is recommended that Synadrin treatment be withdrawn.

Some caution should be observed in patients requiring the administration of cardio-depressive inhalation anaesthetics, as there is a theoretical risk of some potentiation of their negative inotropic effects.

There is no information on the use of Synadrin in pregnancy but no untoward effects have been found in animal studies.

Nursing mothers: There is no information on the use of Synadrin in nursing mothers.

Overdosage: In cases of overdosage gastric lavage is indicated, even after some considerable time, as there is a delay in absorption of large doses of Synadrin due to its relative insolubility. Treatment is symptomatic: if convulsions occur i.v. diazepam should be considered. Muscle relaxants may also be given, and artificial respiration may be necessary. If there is a severe fall in blood pressure (collapse) an i.v. drip may be set up. *Avoid* giving adrenaline, noradrenaline or isoprenaline because of the risk of ventricular fibrillation.

Side-effects: Synadrin is well tolerated. Gastro-intestinal upsets have been reported infrequently. Some degree of sedation has been reported following the administration of high doses. In susceptible patients, catecholamine depletion can lead to the onset of extrapyramidal signs. Isolated cases of mild intention tremor have been reported. Hypersensitivity reactions such as skin rashes have occurred.

Pharmaceutical precautions Synadrin tablet should be stored in a cool dry place in the original containers or in containers similar to those of the manufacturer.

Legal category POM.

Package quantities Synadrin tablets are available in blister packs of 100 and loose in tubs of 500.

Further information Synadrin depletes myocardial catecholamine stores and slows calcium transport through the endoplasmic reticulum, thus reducing myocardial oxygen demand in stress situations and thereby reducing the incidence of anginal attacks.

Product licence number 0086/5019.

TRENTAL* TABLETS 100 mg
TRENTAL* INJECTION 100 mg/5 ml ▼

Presentation Trental Tablets each contain 100 mg oxpentifylline. They are presented as biconvex, pink, sugar-coated tablets 8 mm in diameter. Trental Injection contains 100 mg oxpentifylline in 5 ml aqueous solution.

Uses Trental is indicated in the treatment of peripheral vascular disease, including intermittent claudication, Raynaud's syndrome, chilblains, rest pain and night cramps.

Dosage and administration Depending upon the condition being treated, Trental may be given orally, as a combined oral/parenteral treatment or as parenteral treatment alone.

The preferred parenteral route is by infusion.

Oral administration: The recommended initial dose is 2 tablets (200 mg) three times a day until clinical improvement is observed. The recommended maintenance dose is 1 tablet (100 mg) three times a day.

Parenteral administration: Intravenous infusion: It is recommended that an initial dose of 100 mg in 250–500 ml of fluid be infused intravenously over 90–180 minutes. This dose may be increased by 50 mg per day up to a maximum daily dosage of 400 mg. Trental is compatible with 0.9% sodium chloride, 5% laevulose or glucose infusion solutions.

Intra-arterial infusion: 100–300 mg (1–3 ampoules) daily intra-arterially in 20–50 ml of 0.9% sodium chloride infused over 10–30 minutes.

Intravenous injection: This can be used for the initial therapy of peripheral vascular disorders; the recommended dose is 100 mg i.v. The injection **must** be given slowly with the patient lying down. It is best to start a course of intravenous injections with a preliminary dose of 50 mg to 100 mg diluted in 5 ml of 0.9% sodium chloride and injected over several minutes.

Larger doses can be given by intravenous infusion.

Children: As peripheral vascular disease is not generally a disease of childhood, Trental is unlikely to be of use in children.

Contra-indications, warnings, etc

Contra-indications: Trental is contra-indicated in cases where there is known hypersensitivity to the active constituent oxpentifylline.

Warnings: In diabetic patients stabilised on insulin or oral antidiabetic agents, high dose parenteral administration of Trental may intensify the hypoglycaemic activity of the antidiabetic agent concerned. In such cases the dose of insulin or oral antidiabetic agent should be reduced.

Trental may potentiate the effect of antihypertensive agents and the dosage of the latter may need to be reduced.

In patients with hypotension or severe coronary artery disease, Trental should be used with caution, as a transient hypotensive effect is possible and, in isolated cases, might result in a reduction in coronary artery perfusion.

Precautions: There is no information on the use of Trental in pregnancy but no untoward effects have been found in animal studies.

Nursing mothers: There is no information on the use of Trental in nursing mothers.

Overdosage: The treatment of overdosage should be symptomatic.

Side-effects: Trental is generally well tolerated. Nausea, malaise, gastric upset, vertigo and flushing may occur but these are generally mild and transient. In cases where gastric upset does occur, Trental tablets should be given with or immediately after food.

Pharmaceutical precautions Trental should be stored in a cool dry place in the original containers or in containers similar to those of the manufacturer.

Legal category POM.

Package quantities

Trental tablets are available in packs of 100 tablets. Trental injection is available in packs of 5 × 5 ml.

Further information Investigations have shown that Trental has no effect on the bleeding or clotting time of blood. No interaction with anticoagulants has been reported.

Trental injection is compatible with 0.9% sodium chloride, 5% laevulose or glucose infusion solutions.

Trental injection contains 0.12 mmol Na⁺ per ml of solution.

Product licence numbers

Trental Tablets	0086/0021
Trental Injection	0086/0022

TRENTAL* 400 ▼

Presentation Trental 400 Tablets each contain 400 mg oxpentifylline in a slow-release formulation. They are presented as oblong, pink, sugar-coated tablets, 17.5 mm long, 8.75 mm wide and 6 mm thick.

Uses Trental 400 is indicated in the treatment of peripheral vascular disease, including intermittent claudication, Raynaud's syndrome, chilblains, rest pain and night cramps.

Dosage and administration The recommended initial dose is 1 tablet (400 mg) three times daily; two tablets daily may prove sufficient in some patients, particularly for maintenance therapy.

Children: As peripheral vascular disease is not generally a disease of childhood, Trental 400 is unlikely to be of use in children.

Contra-indications, warnings, etc

Contra-indications: Trental 400 is contra-indicated in cases where there is known hypersensitivity to the active constituent, oxpentifylline.

Warnings: High doses of Trental injection have been shown, in rare cases, to intensify the hypoglycaemic action of insulin and oral hypoglycaemic agents. However, no effect on insulin release has been observed with Trental following oral administration.

Trental 400 may potentiate the effect of anti-hypertensive agents and the dosage of the latter may need to be reduced.

In patients with hypotension or severe coronary artery disease, Trental 400 should be used with caution, as a transient hypotensive effect is possible and, in isolated cases, might result in a reduction in coronary artery perfusion.

Precautions: There is no information on the use of Trental in pregnancy but no untoward effects have been found in animal studies.

Nursing mothers: There is no information on the use of Trental 400 in nursing mothers.

Overdosage: The treatment of overdosage should be symptomatic.

Side-effects: Trental 400 is generally well tolerated. Nausea, malaise, gastric upset, vertigo and flushing may occur but these are generally mild and transient. In cases where gastric upset does occur, Trental 400 should be given with or immediately after food.

Pharmaceutical precautions Trental 400 should be stored in a cool dry place in the original containers or in containers similar to those of the manufacturer.

Legal category POM.

Package quantities Trental 400 tablets are available in packs of 100 and 250.

Further information Investigations have shown that Trental has no effect on the bleeding or clotting time of blood. No interaction with anticoagulants has been reported.

Product licence number 0086/0058.

**Trade Mark*

Hough, Hoseason & Company Limited

Chapel Street

Levenshulme

Manchester M19 3PT

MANUSEPT*

Presentation A clear, blue coloured solution containing 70% v/v Isopropyl Alcohol BP, 0.5% w/v Triclosan.

Uses For the disinfection of intact skin.

(i) For preoperative disinfection of physically clean hands.

(ii) For skin disinfection prior to surgery, injection or venepuncture.

Dosage and administration

(i) For the disinfection of physically clean hands: Dispense approximately 5 ml of Manusept into the palm of one hand. Rub both hands, wrists and forearms together vigorously, paying particular attention to the area around the fingernails. Continue rubbing until dry. Repeat this procedure once more.

(ii) For the disinfection of intact skin before surgery, injection or venepuncture: Apply a quantity of Manusept with a sterile swab. Rub vigorously until dry. Repeat this procedure once more.

Contra-indications, warnings, etc *Treatment of overdose:* If swallowed, gastric aspiration and lavage avoiding pulmonary aspiration. Apomorphine should not be used.

Avoid contact with eyes.

Pharmaceutical precautions Store at or below normal ambient temperatures. Do not use in the vicinity of naked flames.

Legal category GSL.

Package quantities 500 ml, 250 ml and 5 Litre.

Further information Triclosan is compatible with soap, which can be used to obtain physically clean hands.

Product licence number 0423/0008.

STER-ZAC* BATH CONCENTRATE

Presentation A clear solution containing 2% Triclosan.

Uses Ster-zac Bath Concentrate has an antibacterial effect in bath water.

For the prevention of cross-infection and secondary infection.

Dosage and administration *Baths:* Add 28.5 ml of Ster-zac Bath Concentrate to a bathful of water (approx. 140 litres) immediately prior to the patient entering the water.

For washing: Add 1 ml of Ster-zac Bath Concentrate to 5 litres of water prior to use.

Contra-indications, warnings, etc Avoid contact with the eyes.

Pharmaceutical precautions For external use only. Store in a cool dry place.

Legal category P.

Package quantities 28.5 ml, 500 ml and 2 litres.

Further information Nil.

Product licence number 0423/5001.

STER-ZAC* DC SKIN CLEANSER

Presentation A white cream. Contains 3% Hexachlorophane BP.

Uses Ster-Zac DC has an antibacterial effect and is used for the pre-operative preparation of the hands.

Indications For the pre-operative disinfection of the hands of surgical personnel.

Dosage and administration For external use only. Apply 3 ml to 5 ml to pre-moistened hands and wash for up to three minutes. Rinse and repeat.

Contra-indications To be administered to children under two years of age on medical advice only. Do not use for whole body bathing. Do not apply to burns or badly damaged skin.

Pharmaceutical precautions No special requirements.

Legal category POM.

Package quantities 150 ml 4.5 litres.

Further information Ster-Zac DC skin cleanser is resistant to contamination in use.

Product licence number 0423/0007.

STER-ZAC* POWDER

Presentation An antibacterial powder containing hexachlorophane in a sterilised powder base.

Hexachlorophane BPC	0.33%
Zinc Oxide BP	3.00%
Sterilised Purified Talc BPC	88.67%
Starch BP sterilised	8.00%

Uses For the prevention of neo-natal staphylococcal cross infection.

For the treatment of furunculosis.

For geriatric use, particularly when incontinence is encountered and for the prevention of bed sores.

For the routine treatment of cord stumps and for ward use in maternity hospitals and in domiciliary midwifery.

Dosage and administration For the prevention of neo-natal staphylococcal cross infection – immediately after ligature, dust the cord and surrounding area and apply the powder liberally to the perineum, buttocks and axillae. Repeat at each napkin change.

For the treatment of furunculosis – dust the affected area and surrounds regularly.

For geriatric use – the powder should be applied to those areas prone to pressure sores.

Contra-indications, warnings, etc This product is to be administered to children under two years of age on medical advice only.

Pharmaceutical precautions No special requirements.

Legal category P.

Package quantities Sprinkler tins of 30 g and 225 g.

Further information Nil.

Product licence number 0423/5000.

TERPOIN*

Presentation A yellow, clear, syrupy, solution with a predominant menthol odour and taste. Each 5 ml contains:

Codeine Phosphate BP	15.0 mg
Guaiphenesin	50.0 mg
Terpin Hydrate BPC	9.15 mg

Eucalyptol BPC	4.15 mg
Menthol BP	18.3 mg

Uses Terpin is an antitussive preparation designed specifically to control unproductive cough.

Indications Terpin is indicated in the treatment of persistent cough.

Dosage and administration *Adults:* 5 to 10 ml in a little water (if necessary) every three hours.

Children: Up to 5 ml, according to age.

Contra-indications, warnings, etc Severe respiratory depression.

Pharmaceutical precautions No special requirements.

Legal category POM.

Package quantities Plastic bottles of 225 ml and 2.25 litres.

Further information Nil.

Product licence number 0423/5005.

*Trade Mark

Immuno Ltd
Arctic House, Rye Lane
Dunton Green, Nr. Sevenoaks,
Kent, TN14 5HB



GAMMABULIN*

Normal Immunoglobulin Injection BP.

Presentation Gammabulin is a concentrate of antibodies present in the IgG fraction of human plasma and is available in liquid or lyophilised forms. It is produced from pooled human plasma obtained from suitable human donors† whose donations are shown by RIA to be free from HB_sAg. Pooled plasma and the final product are also tested for freedom from HB_sAg.

Gammabulin liquid is a clear solution varying in colour from pale yellow to light brown, it contains:

Protein	16.5 ± 1.5%
Gamma Globulin	> 90%
Glycine	2.25%
Merthiolate	0.01%

Gammabulin lyophilised is a white to slightly yellowish powder or solid friable mass completely soluble in Water for Injections BP.

When the lyophilised powder is dissolved with the amount of Water for Injections BP indicated on the label, it contains:

Protein	16.5 ± 1.5%
Gamma Globulin	> 90%
Glycine	6.0%
Merthiolate	0.01%

Uses Gammabulin is used in the treatment of:

Antibody deficiency syndrome and recurring bacterial infections in dys-, hypo- and agammaglobulinaemia.

Hepatitis A prophylaxis.

Prevention or modification of measles infection.

Treatment of susceptible pregnant women exposed to Rubella infection who will not consider therapeutic abortion.

Dosage and administration Gammabulin must be administered by the intramuscular route.

All recommendations and doses given below refer to the 16% solution and are expressed in ml.

Antibody deficiency syndrome in dys-, hypo- and agammaglobulinaemia: By intramuscular administration of Gammabulin antibody concentrate the frequency and severity of recurring bacterial infections can be reduced. For treatment of gamma globulin deficiency, it is necessary to achieve and maintain a gamma globulin level of approximately 200 mg per 100 ml serum.

Initial dosage: 1.8 ml per kg bodyweight e.g. in three single administrations of 0.6 ml/kg bodyweight each in intervals of 24 hours.

Maintenance dose: 0.6 ml per kg bodyweight, monthly.

Hepatitis A: Gammabulin is an efficient agent for the prevention or modification of hepatitis A. It must be pointed out that after gamma globulin administration an anicteric course of hepatitis has been observed. Because of this, regular monitoring of transaminase levels may be warranted.

† Human donors as described in the British Pharmacopoeia 1980 Vol. II under Albumin

Dosage for children: 0.02–0.04 ml per kg bodyweight. If exposure continues, repeat the dose after 4–6 months.

Dosage for adults: 0.08–0.12 ml per kg bodyweight. If exposure continues, repeat the dose after 4–6 months.

Note: No benefit may be expected if administered after the onset of clinical symptoms.

Measles: Gammabulin should be given as soon as possible at a dose of 0.25 ml/kg to prevent or modify measles in a susceptible person exposed less than six days previously. Gammabulin may be especially indicated for susceptible household contacts of measles patients, particularly with children under one year of age or children who are immunosuppressed or have an immune deficiency disease and should not receive measles vaccine or any other live viral vaccine.

Prophylaxis: 0.2 ml per kg bodyweight with continued or repeated exposure repeat after 3 weeks.

Mitigation without influence on the immunising effect: 0.04 ml per kg bodyweight.

Rubella: (German Measles) The routine use of Gammabulin prophylaxis of Rubella in early pregnancy is of dubious value and cannot be justified. Some studies suggest that the use of Gammabulin in exposed, susceptible women can lessen the likelihood of infection and foetal damage, therefore, 20 ml of Gammabulin may benefit those women who will not consider a therapeutic abortion.

Contra-indications, warnings, etc Gammabulin is generally well tolerated without reactions. On very rare occasions (e.g. in special forms of a- or hypogammaglobulinaemia) anaphylactoid reactions may occur in patients who have antibodies against Immune Globulin A (IgA) or who have shown atypical reaction after blood transfusion or following administration of blood derivatives.

Gammabulin must not be administered intravenously.

Pharmaceutical precautions Gammabulin liquid should be stored between +2° and +10°C when it will have a shelf life of 3 years.

Gammabulin lyophilised should be stored at room temperature (+2° to +25°C) when it will have a shelf life of 5 years.

Both preparations should be protected from the light.

Legal category POM.

Package quantities *Gammabulin liquid:* Rubber capped vials containing 2 ml, 5 ml or 10 ml.

Gammabulin lyophilised: Rubber capped vial containing 320 mg lyophilised powder. A 2 ml ampoule of Water for Injections BP is also enclosed.

Further information Nil.

Product licence numbers liquid 0215/0018
lyophilised 0215/0019.

HEPARIN – INJECT 5,000 BP IMMUNO

Presentation Heparin-Inject 5,000 BP is a sterile solution of 5,000 i.u. Heparin Sodium (mucous) dissolved in 0.3 ml Water for Injections BP. It is a clear liquid varying from colourless to straw coloured. Each pre-loaded syringe contains 2.7 mg of Sodium Chloride in 0.3 ml of injection.

Uses Prevention of thrombosis following surgery.

Dosage and administration Heparin – Inject 5,000 BP must be administered by the subcutaneous route preferably through the adipose tissue of the abdominal wall. The following dosage is recommended:

Pre-operative administration: 1 pre-loaded syringe containing Heparin – Inject 5,000 BP to be given two hours before surgery.

Post-operative administration: 1 pre-loaded syringe containing Heparin – Inject 5,000 BP to be given at intervals of 8–12 hours up to the 7th–12th day.

Contra-indications, warnings, etc Heparin should not be used in patients with the following conditions:

1. Heparin allergy.
2. Surgery carried out on the central nervous system and the eye.
3. Haemorrhagic diatheses including haemophilia, thrombocytopenia and when linked with endocarditis.
4. Advanced stages of kidney, liver or pancreatic disease.
5. Post-operative seeping haemorrhage.

Precautions are necessary in patients with potential bleeding sites such as peptic ulcer, ulcerative colitis etc. also in pregnancy and in patients with persistent hypertension or cerebral thrombosis; also during simultaneous administration of Warfarin, Aspirin or other salicylates and medicaments having an impact on blood coagulation. Experience indicates that Heparin can be used with very little risk in the prophylaxis of thrombosis. If, however, bleeding complications occur during or after an operation, the patient's thrombin time or partial thromboplastin time should be determined. If the results of these tests are within the normal range it is unlikely that heparinisation is the cause.

It must, however, be borne in mind that on very rare occasions Heparin can cause thrombocytopenia and could therefore be the cause of the haemorrhage.

If neutralisation must be carried out following the injection of Heparin – Inject 5,000 BP 'Immuno', Protamine Sulphate Injection BP 10 mg in 1 ml must be given by slow (10 min) intravenous injection. Ideally, the dose required should be accurately determined by titration. If there is insufficient time to titrate the dose, the following dosage scale is recommended:

Time interval following dose of 5,000 i.u. Heparin	Dose of Protamine Sulphate injection 10 mg in 1 ml
Immediately after	5.0 ml
Half an hour after	2.5 ml
One hour after	1.25 ml

Pharmaceutical precautions It should be stored at a temperature not exceeding 25°C when it will have a shelf life of three years.

Legal category POM.

Package quantities Pre-loaded syringes containing 0.3 ml solution of 5,000 i.u. Heparin Sodium supplied in packs of 10 and 100 pre-loaded syringes.

Further information An increased tendency towards haemorrhage must be carefully avoided during the operation period and any error of dosage excluded.

Heparin – Inject 5,000 BP is packed in a pre-loaded syringe which enables an accurate dose to be administered. The hazard of overdosage can therefore be avoided.

Product licence number 0215/0017

HUMAN ALBUMIN 20% BP IMMUNO

Presentation Human Albumin 20% BP Immuno is a solution in water of human albumin containing a low proportion of salt and is described as Salt Poor Albumin. It is a clear liquid varying in colour from amber to orange-brown and is presented as a solution for intravenous injection or infusion to human beings. It is prepared from the plasma of suitable human donors whose transaminase levels are constantly checked and whose donations are shown by RIA to be free from HB_sAg. Pooled plasma and the final product are also tested by RIA for freedom from HB_sAg. It contains 20% of protein of which at least 97% is albumin, the rest being thermostable alpha and beta globulins.

It is stabilised with 20 mEq/litre Sodium Caprylate and 20 mEq/litre Sodium Acetyltryptophanate.

There is no preservative added to the solution.

Uses For treating hypoalbuminaemia, oedema, hyperbilirubinaemia, eclampsia, septic shock and shock due to endotoxins, Human Albumin 20% BP Immuno is administered as an injection or an infusion.

For the treatment of the acute phase of burns or haemorrhagic shock Human Albumin 20% BP Immuno is diluted with 3 parts of dextrose, fructose or electrolyte solutions and the resulting 5% solution administered by infusion.

Dosage and administration *Hypoalbuminaemia and oedema:* Adults 100 to 400 ml Human Albumin 20% BP Immuno given slowly daily. Children and infants 1.5 to 6 ml Human Albumin 20% BP Immuno per kg body-weight given slowly daily. In oedema Human Albumin 20% BP Immuno is used in combination with diuretics.

Hyperbilirubinaemia: 5 to 10 ml Human Albumin 20% BP Immuno can be injected or transfused into the newly born or added to a blood transfusion if exchange is being carried out.

Eclampsia: Fluid balance disturbance during pregnancy, together with increased vascular permeability, may lead to pre-eclamptic symptoms. Restoration of the circulatory disorder to normal with Human Albumin 20% BP Immuno effectively lessens the danger of eclampsia. Recommended dosage: 50 ml Human Albumin 20% BP Immuno (10 g) daily.

Septic shock and shock due to endotoxins: Cases of shock with a high packed cell volume resulting from hypovolaemia due to loss of fluid into the extravascular compartments should be treated with Human Albumin

† Human donors as described in the British Pharmacopoeia 1980 Vol II under Albumin

20% BP Immuno to ensure the return of fluid into the circulation.

Dosage: adults 50 to 200 ml Human Albumin 20% BP Immuno. Children 1 to 2 ml Human Albumin 20% BP Immuno per kg bodyweight. The initial dose should be infused over a period of 5 to 15 minutes.

Burns: In the acute phase of extensive and severe burns Human Albumin 20% BP Immuno is diluted with dextrose, fructose or electrolyte solutions to provide a 5% solution.

Dosage: Adults 800 to 1600 ml Human Albumin 5%. Children 16 ml Human Albumin 5% per kg bodyweight. The total dosage over the first 24 hours should be in accordance with the formula 2 ml times bodyweight in kg times percentage of surface burned plus 1500 ml. Any resulting hypoproteinaemia can be corrected by the following dosage. Adults 50 ml Human Albumin 20% BP Immuno twice daily. Children 1 ml Human Albumin 20% BP Immuno per kg bodyweight twice daily.

Haemorrhagic shock: Shock due to blood loss should be treated with blood, if available, or with Human Albumin 20% BP Immuno diluted to 5%. Dosage: adults 200 to 800 ml Human Albumin 5%. Children 4 to 8 ml Human Albumin 5% per kg of bodyweight. An initial dose of 400 ml of 5% solution should be infused rapidly and repeated if shock is not controlled.

Contra-indications, warnings, etc Human Albumin 20% BP Immuno must only be used if the solution is clear. Once the cap has been pierced by a needle, the contents must be used within 4 hours.

Caution is indicated in the administration of Human Albumin 20% BP Immuno to patients suffering from hypertension or in cases of latent or manifest cardiac insufficiency. The single doses should be reduced to relatively small amounts and the infusion given slowly. A careful watch must be kept for the possible development of pulmonary oedema. If pulmonary oedema occurs the infusion must be stopped immediately.

In all cases of considerable blood loss, whole blood or erythrocyte concentrate must be given in addition to Human Albumin 20% BP Immuno. Careful selection and testing of donors and donations and the inclusion of filtration and heating at 60°C for 10 hours in the preparation of the product have virtually eliminated the risk of serum hepatitis. As with all blood products, however, this risk cannot be absolutely excluded. Intolerance reactions are extremely rare with Human Albumin 20% BP Immuno.

Pharmaceutical precautions Human Albumin 20% BP Immuno should be stored between +2°C and +25°C. It must be protected from light. The shelf life is 3 years.

Legal category POM.

Package quantities Human Albumin 20% BP Immuno is supplied in rubber capped vials of 10 ml, 50 ml and 100 ml.

Further information Human Albumin 20% BP Immuno is processed in such a way that removal of all antibodies, particularly isoagglutinins, is achieved. It can therefore be given to patients regardless of their blood group or rhesus factor. It will not interfere with subsequent blood investigations.

Product licence number 0215/0009.

KRYOBULIN* - DRIED HUMAN ANTI-HAEMOPHILIC FRACTION BP

Presentation Dried Human Antihæmophilic Fraction BP is a white to yellowish amorphous powder or friable solid without any characteristic odour.

It is prepared from the plasma of suitable human donors whose transaminase levels are constantly checked and whose donations are shown by RIA to be free from HBsAg. Pooled plasma and the final product are also tested for freedom from HBsAg.

It is packed in vials each containing approximately 250, 500 or 1,000 International Units of Factor VIII. Separate vials of solvent are also provided, these being Water for Injections BP.

1 International Unit is the amount of Factor VIII activity contained in 12.745 mg of the 2nd International Standard for Blood Coagulation Factor VIII Human. It is approximately equivalent to the Factor VIII activity in 1 ml of average normal plasma.

Uses Kryobulin corrects Factor VIII deficiency, and is used in the treatment of bleeding due to such deficiency in:

Haemophilia A
von Willebrand's disease
Haemophilia complicated by Factor VIII inhibitors.

Dosage and administration Frequent tests of the patient's plasma level of Factor VIII must be made to allow correction of the deficiency by administration of Kryobulin, but for guidance an estimation of the required dosage can be made by the following calculation:

To achieve an increase of Factor VIII concentration of 1% it is necessary to administer 1 i.u. of Kryobulin per kg bodyweight, both for adults and children.

Initial treatment requires doses to be given at shorter intervals than in maintenance therapy, to provide an initial high level of activity and to replenish the extravascular compartment.

Bleeding from skin, nose and oral mucous membrane: Initial dose should be 10 i.u./kg at intervals of 6 to 12 hours.

Haemarthrosis: The initial dose should be approximately 10 i.u./kg and the maintenance dose 5 to 10 i.u. per kg at intervals of 6 to 12 hours. Combined with immobilisation of the affected joint for several days, the treatment should be sufficient to restore function.

Bruising: In most cases a single dose of 10 i.u./kg is sufficient. For widespread bruising, repeated administration of 5 to 10 i.u./kg at intervals of 6 to 12 hours may be required.

Heavy bleeding into muscles: Immediate treatment is required to prevent permanent deformity and loss of function, and initial immobilisation of the affected area is important. An initial dose of 15 to 20 i.u./kg should be given, the maintenance dose to be 10 i.u./kg at intervals of 6 hours from the first to the second day, and at intervals of 12 hours from the third to the fifth day.

Haematuria: The initial dose should be 15 to 20 i.u./kg, and the maintenance dose 10 i.u./kg at intervals of 12 hours.

Major surgery on hæmophilic patients: The initial dose should be at least 25 to 50 i.u./kg, and the maintenance

* Human donors as described in the British Pharmacopocia 1980 Vol II under Albumin.

dose 20 to 40 i.u./kg at intervals of 4 hours from the first to the fourth day, of 8 hours from the fifth to the eighth day, and of 12 hours until all wounds are healed.

The effect of treatment must be checked daily. Factor VIII activity should not be allowed to fall below 50% of the normal 100% average value. It is important that treatment be continued until all wounds have healed completely, as the risk of haemorrhage persists till then.

In addition to monitoring Factor VIII activity, tests for the development of Factor VIII inhibitors should also be made.

Dental extractions: The required dosage depends on the number and type of teeth to be extracted, and on the severity of the haemophilia. If *one or two teeth* are to be extracted from a patient with severe haemophilia, an initial dose of 10 to 20 i.u./kg should be given.

Maintenance treatment with this dosage at intervals of 6 hours from the first to the third day, and 8 hours from the fourth to the eighth day after extraction, should be given. If *more than two teeth are to be extracted from patients with severe haemophilia* a minimum initial dose of 20 to 30 i.u./kg should be given, and a maintenance dose of 10 to 20 i.u./kg at intervals of 6 hours from the first to the third day, and of 8 hours for twelve more days. The plasma concentration of Factor VIII should not be allowed to fall below 10% of the normal 100% average value.

Factor VIII assays should be used to monitor the effectiveness of treatment, as partial thromboplastin time gives a less accurate value when large quantities of Kryobulin are being used.

Solutions of Kryobulin must be administered intravenously, at a rate not exceeding 10 ml in 3 minutes.

Contra-indications, warnings, etc Although the danger of volume overload is small with Kryobulin, during major surgery monitoring of the patient's central venous pressure and blood pressure, and serial chest X-rays, may be advisable.

In disseminated intravascular coagulation associated with low Factor VIII levels Heparin should be given to interrupt intravascular coagulation before therapy with Kryobulin is started.

A low incidence of adverse reactions is experienced with Kryobulin, but the following may occur:

1. **Allergic reactions:** All forms of allergic reaction from mild and transient urticaria to severe anaphylactic shock are possible when human plasma derivatives are administered. If such reactions occur, treatment with Kryobulin must be interrupted at once. Allergic reactions should be controlled with antihistamines and corticosteroids and routine treatment given for anaphylactic shock.

Monitoring of pulse rate and blood pressure is essential. If the pulse rate increases and/or blood pressure falls transfusion of 5% Dextrose should be started.

2. **Hepatitis:** Despite the precautions taken in the selection and testing of donors and donations, the risk of transmitting hepatitis cannot be entirely excluded.

3. **Factor VIII Inhibitors:** The appearance of a circulating Factor VIII inhibitor is possible. Its appearance cannot be predicted as it does not relate to the amount of Kryobulin administered, nor to the frequency of administration. As far as is known neither corticosteroids nor immunosuppressive agents significantly influence the formation of inhibitors.

Pharmaceutical precautions Kryobulin must be stored between +2°C and +6°C, and protected from the

light. It then has a shelf-life of two years. When stored between +20°C and +30°C it has a life of six months.

Legal category POM.

Package quantities

Kryobulin Home Treatment Pack (Standard)

Each pack contains:

1 rubber capped vial containing 250 or 500 i.u.

Dried Human Antihaemophilic Fraction BP

1 rubber capped vial containing Water for Injections BP

This pack also contains a syringe I/V needles, winged adaptor needle, filter needle, venting needle and swabs.

Kryobulin Home Treatment Pack (Multipack):

Each pack contains:

5 rubber capped vials containing 250 or 500 i.u. Dried Human Antihaemophilic Fraction BP.

5 rubber capped vials containing Water for Injections BP

The equipment is packed in a separate box and consists of: Syringes, I/V needles, winged adaptor needles, filter needles, venting needles and swabs.

There is sufficient equipment for reconstituting 5 packs of Kryobulin (1 multipack).

Kryobulin Hospital Pack

Each pack contains:

1 rubber capped vial containing 1,000 i.u. Dried Human Antihaemophilic Fraction BP

1 rubber capped vial containing Water for Injections BP.

The pack also contains a filter needle and venting needle.

Further information Kryobulin is especially suitable for Home Treatment. Packs contain all requirements and can be stored in a domestic refrigerator for two years and for up to six months at room temperatures not exceeding 30°C.

Product licence number 0215/0003.

PLASMA PROTEIN FRACTION BP 4.3% IMMUNO (Human Albumin Fraction (Saline) BP 4.3%)

Presentation Plasma Protein Fraction BP 4.3% Immuno is a clear amber liquid, presented as a solution for intravenous administration to human beings. It is prepared from the plasma of suitable human donors whose transaminase levels are constantly checked and whose donations are shown by RIA to be free from HB,Ag. Pooled plasma and the final product are also tested by RIA for freedom from HB,Ag.

Plasma Protein Fraction BP 4.3% Immuno contains 4.3% protein of which at least 97% is albumin, the rest being heat stable alpha - and beta - globulins. As stabilisers sodium caprylate and sodium acetyltryptophanate have been added, both at a concentration of 4.3 mEq/litre.

Uses Plasma Protein Fraction BP 4.3% Immuno is indicated for volume replacement in hypovolaemic shock (e.g. following crush injury, severe trauma, surgery, burns and abdominal emergency) and for use whenever a predominant loss of plasma fluid has occurred.

† Human donors as described in the British Pharmacopoeia 1980 Vol II under Albumin.

Dosage and administration Adult dosage of Plasma Protein Fraction BP 4.3% Immuno for hypovolaemic shock is in the range of 250 to 500 ml. A flow rate of up to 16 ml/min (1 litre/hr) has been well tolerated in adults. The rate of infusion, which can be increased in emergency treatment, depends on response. In hypoproteinaemia the usual dosage range is 1,000 to 1,600 ml daily (equivalent to 43 to 70 g plasma protein), but larger amounts can be given in severe hypoproteinaemia with continuing loss. The flow rate should not exceed 5 to 3 ml/min.

Dosage for infants and young children in whom Plasma Protein Fraction BP 4.3% Immuno is indicated or shock due to dehydration or infection, should be in the range of 20 to 30 ml/kg bodyweight, infused at a rate of 10 ml/min. The infusion rate should be adjusted in accordance with the clinical response. Administration is by intravenous infusion. A site should be chosen away from the area of injury or infection.

Contra-indications, warnings, etc Careful monitoring of the patient's clinical condition is necessary so that hypervolaemia is not caused. Signs to be watched for are dyspnoea, pulmonary oedema, rise of blood pressure and central venous pressure.

Careful selection of donors and the inclusion of filtration and heating at 60°C for 10 hours in the preparation of the product have virtually eliminated the risk of Serum Hepatitis. As with all blood products, however, this risk cannot be absolutely excluded.

A turbid solution must not be given. Once set up, the entire contents of the infusion bottle should be administered within 4 hours.

Pharmaceutical precautions Plasma Protein Fraction BP 4.3% Immuno can be stored at +2°C to +25°C. It must be protected from light. The shelf life is 5 years.

Legal category POM.

Package quantities Plasma Protein Fraction BP 4.3% Immuno is supplied in 50 ml, 100 ml, 250 ml, and 400 ml infusion bottles.

Further information Plasma Protein Fraction BP 4.3% Immuno is processed in such a way that removal of all isoagglutinins and other antibodies is achieved. It can therefore be given without restriction to patients, regardless of blood group. It will not interfere with subsequent blood investigations.

Product licence number 0215/0002.

***ROTHROMPLEX* Partial Prothrombin Complex (Human)**

Presentation Prothromplex contains coagulation Factors II, IX and X and is a white, amorphous freeze-dried powder or friable solid without any characteristic odour. It is packed in rubber-capped vials containing 200 units or 500 units each of Factor II, IX & X.

It is prepared from the plasma of suitable human donors whose transaminase levels are constantly checked and whose donations are shown by RIA to be free from HBsAg. Pooled plasma and the final product are also tested by RIA for freedom from HBsAg. Prothromplex is also tested to discount the likelihood of causing disseminated intravascular coagulation.

Uses Treatment of cases of Factor IX deficiency (Haemophilia B).

By administering an appropriate dose of Prothromplex, it is possible to achieve a prompt and sufficient rise of Factor IX in the patient's plasma.

The effectiveness of treatment can be checked by simple laboratory tests. The activity of Factor IX is assayed through determination of the Partial Thromboplastin Time (PTT), however the most reliable results are obtained by quantitative activity assays of Factor IX.

Dosage and administration Immediately before use Prothromplex must be dissolved in 10 ml of the solvent provided.

After sterilising the cap of the solvent bottle remove 10 ml using the disposable syringe and one of the needles provided. Next sterilise the cap of the Prothromplex bottle and introduce the solvent using the second disposable needle. Reconstitute by gently shaking to and fro, thus avoiding frothing. Withdraw the reconstituted Prothromplex, then remove the syringe from the needle and attach the third disposable needle.

Prothromplex is now ready for slow intravenous injection taking about ten minutes.

Only general directions can be given for the dosage of Prothromplex. It is dependent upon the severity of the coagulation defect and the degree of the traumatic and haemorrhagic tissue damage. The suggested dosage for the treatment of Factor IX deficiency is given in the guide below.

Dosage guide for the treatment of severe and semi-severe cases of Factor IX deficiency: Formula for the calculation of the necessary quantity of Factor IX:

One unit of Factor IX/kg bodyweight = 1% increase of Factor IX in the patient's plasma.

Prothromplex dosage table (Factor IX)

<i>Clinical Manifestation</i>	<i>Therapeutically wanted minimum level</i>	<i>Initial dose in units per kg bodyweight</i>	<i>Maintenance dose at intervals of 6 to 12 (24) hours in units per kg bodyweight</i>
Surface bleeding from the skin and mucosae Superficial or deep haematoma Haemarthroses Slight bleeding following injuries Uncomplicated dental extractions Severe muscle haematoma	5–10%	15 U	7–15 U
Moderate bleeding following injuries Gastric and intestinal haemorrhages Bone fractures Cerebral bleeding Haematuria Complicated dental extractions Minor surgery	15–30%	20–30 U	15–30 U
Major surgery	more than 50%	75 U	50–75 U

It is suggested that a high initial dosage be chosen to ensure a rapid and sufficient increase of Factor IX thus achieving a reliable cessation of bleeding. Here, as well

† Human donors as described in the British Pharmacopoeia 980 Vol II under Albumin.

as with the subsequent maintenance therapy the initial short half-life of the coagulation factors has to be considered. Depending on the in-vivo half-life of Factor IX, which is approx 12–30 hours, a successful result will be achieved by repeated administration of Prothromplex at intervals of 6–12 hours. To assure absolute control of treatment, determination of the PTT should be made and, where possible, quantitative assays of Factor IX activity. Treatment should be maintained up to the resorption of the tissue haemorrhage or until the wounds have healed completely, thus ensuring a complication-free post-operative course. The special advantage of Prothromplex lies in the fact that by application of small volumes of fluid and a low amount of protein a high concentration of circulating coagulation Factor IX is achieved. The danger of volume or protein overloading of the patient is avoided even with the administration of high doses.

Contra-indications, warnings, etc With patients suffering from disseminated intravascular coagulation, (DIC), Prothromplex should not be given unless consumption of the coagulation factors has been previously interrupted by Heparin.

Side-effects are rarely observed during treatment with Prothromplex though the following reactions may occur:

1. **Allergic reactions:** All forms of allergic reactions from mild and temporary urticarial rashes to severe anaphylactic shock are possible when human plasma derivatives are administered. If these occur, treatment with Prothromplex must be interrupted at once. Allergic reactions should be controlled with antihistamines and glucocorticoids and routine shock-treatment given for anaphylactic shock. Careful and frequent recording of pulse rate and blood pressure is essential. If the pulse rate increases and/or the blood pressure falls a transfusion of 5% Dextrose should be started.

2. Despite the precautions taken in the checking of donors, donations and the final product, the transmission of hepatitis cannot be entirely excluded following the administration of coagulation factors. This should be

taken into account before using Prothromplex to control haemorrhage in non life saving situations in liver disease patients and those undergoing anticoagulant therapy.

3. During every type of therapy involving blood or coagulation factor concentrates, the occurrence of a circulating coagulation factor inhibitor is a possibility. The time at which such an inhibitor is produced cannot be predicted and depends neither on the amount of the plasma preparation administered nor on the frequency of the administration. As far as is known neither corticosteroids nor immunosuppressive agents significantly influence the formation of inhibitors.

Pharmaceutical precautions Prothromplex has a shelf life of one and a half years when stored between +2°C and +6°C, and should be protected from light.

Legal category POM.

Package quantities 200 units or 500 units of Factors II, IX and X in each container.

1 rubber-capped vial containing lyophilised Prothromplex.

1 rubber-capped vial containing 10 ml Water for Injections BP.

1 10 ml disposable syringe.

3 disposable needles.

Further information Prothromplex can be stored in a domestic refrigerator, and can therefore be kept available for home treatment.

Prothromplex can be given in small volume injections, and is therefore suitable for home treatment.

Prothromplex can be moved in insulated containers to a refrigerator at some other location, giving a patient a greater degree of mobility.

Product licence number

0215/0006 – 200 U

0215/0007 – 500 U

***Trade Mark**

Imperial Chemical Industries PLC

Pharmaceuticals Division

Alderley Park

Macclesfield, Cheshire SK 10 4TF



ATROMID-S

Presentation Atromid-S is presented as red, soft gelatine capsules, each containing 500 mg Clofibrate BP.

Uses

Atromid-S is indicated in the treatment of severe hyperlipoproteinaemia where full investigation has been performed to define the abnormality. It should be used in conjunction with appropriate dietary measures and after diet alone has failed to produce an adequate response. Other risk factors such as hypertension and smoking should be dealt with. Examples of abnormal lipid patterns are:

<i>Fredrickson type</i>	<i>Lipoprotein elevated</i>	<i>Major lipid elevations</i>
1 (very rare)	Chylomicra	Triglycerides
11a	β (LDL)	Cholesterol
11b	pre- β + β (LDL+VLDL)	Chol+ Triglycerides
111 (rare)	abnormal β (LDL)	Chol.+TG
IV	pre- β (VLDL)	Triglycerides
V (rare)	Chylomicrons + pre- β (VLDL)	Triglycerides + Cholesterol

'Atromid-S' is effective in patients with Type III hyperlipidaemia and in patients with severe hypertriglyceridaemia found in some patients in Types IIb, IV and V.

Dosage and administration A dose of 20–30 mg/kg body weight is given daily, this should be divided into 2 or 3 doses after meals. The effective dose level must be maintained. Examples of dosage:

Patients over 65 kg: 2 g daily (4 × 500 mg capsules).

Patients 50–65 kg: 1.5 g daily (3 × 500 mg capsules).

The biochemical response to clofibrate is variable, and it is not always possible to predict from the lipoprotein type or other factors which patients will obtain favourable results. It is essential that lipid levels be measured and that the drug be discontinued in any patient in whom lipids do not show significant improvement within three months of initiating therapy.

Contra-indications, warnings, etc Due to its action on cholesterol metabolism, Atromid-S may increase the lithogenicity of bile and there is an increased frequency of gall stones. Accordingly, clofibrate should not be used in patients with a history of, or existent gallbladder disease, or stones.

Also, it is contra-indicated in patients with impairment of renal or hepatic function (e.g. biliary cirrhosis).

In patients with low serum albumin levels, for example those with nephrotic syndrome, high levels of unbound drug may give rise to myalgia with raised serum creatinine kinase levels. Caution is advised in treating such patients.

Patients taking anticoagulants and Atromid-S together should have their dose of anticoagulant halved and adjusted later as necessary.

Clofibrate has been shown to produce liver tumours in rats and mice. The liver changes found in rodents have not been seen in other species, including sub-human primates and man. The relevance of this finding to man has not been established.

Pregnancy: It is considered advisable on theoretical grounds not to give Atromid-S during pregnancy.

Side-effects: Atromid-S has been in clinical use since 1963 and has been subjected to many long-term studies. Side-effects are seldom seen but include transient slight upper abdominal discomfort, nausea and looseness of the bowels. It is usually unnecessary to discontinue treatment. Very occasionally myalgia has been reported. Due to its action on bile there is an increased incidence of gallstones (see 'Contra-indications and warnings' above).

Liver function: At therapeutic doses Atromid-S does not enter the liver cell. In some cases slight and usually transient increases in serum transaminase levels have been observed. It is considered that these reflect adaptive responses of the liver. In large, long-term studies, even transient increases in transaminase levels have seldom been reported. Atromid-S has not been shown to affect serum bilirubin or bromosulphthalein tests. Serial liver biopsy studies in patients undergoing long-term treatment have confirmed the absence of hepatotoxicity in man.

Cardiovascular system: There has been a published report of ventricular arrhythmia associated with Atromid-S treatment. However, the patient had an unstable rhythm prior to treatment.

Blood: Atromid-S normally has no effect on the blood picture. Isolated cases of adverse effects include slight fluctuation in haemoglobin values and occasional reduction in white cell counts. There is no evidence of marrow toxicity, but one case of agranulocytosis has been reported in a patient undergoing multiple drug therapy which included Atromid-S.

Overdosage: No adverse biochemical or clinical effects have been observed upon overdosage with Atromid-S, but should these occur, symptomatic treatment should be administered.

One case of a 15-year-old boy has been recorded who took 12.25 g of Atromid-S with no resulting adverse effects.

Pharmaceutical precautions Protect from heat, light and moisture.

Legal category POM.

Package quantities Containers of 50, 250 and 500 capsules.

Further information Nil.

Product licence number 0029/5022.

AVLOCLOR*

Presentation Avloclor is presented as white, biconvex tablets, each with a bisecting line and bearing the ICI roundel. The tablets each contain 250 mg Chloroquine Phosphate BP, equivalent to 155 mg chloroquine base.

Uses Avloclor is an antimalarial agent highly active against the erythrocytic forms of *Plasmodium falciparum*, *Plasmodium vivax* and *Plasmodium malariae*. It also possesses amoebicidal properties and is useful in treating chronic discoid and systemic lupus erythematosus and rheumatoid arthritis.

It is indicated for treatment and suppression of malaria, and the treatment of amoebic hepatitis and abscess, lupus erythematosus and rheumatoid arthritis.

Dosage and administration

Treatment of malaria:

Children:

Age (years)	Initial dose	Second dose 6 hrs after first	Dose on each of the two subsequent days
1-4	1 tablet	$\frac{1}{2}$ tablet	$\frac{1}{2}$ tablet
4-8	2 tablets	1 tablet	1 tablet
8-12	3 tablets	$1\frac{1}{2}$ tablets	$1\frac{1}{2}$ tablets

Adults: A three-day course is sufficient to effect disappearance of symptoms and parasitaemia as follows: initial dose 4 Avloclor tablets, followed by 2 tablets six hours later, then 2 tablets a day for two days.

Overt attacks of Vivax and Quartan malaria are treated with a single dose consisting of 4 Avloclor tablets, followed by a course of treatment with Primaquine Phosphate BP (15 mg of base daily for 14 days).

Prophylaxis and suppression of malaria:

Children:

Once a week the dose appropriate to the age group should be taken on the same day each week and for 6 weeks after leaving a malarious area.

1-4 years: $\frac{1}{2}$ tablet.

4-8 years: 1 tablet.

8-12 years: $1\frac{1}{2}$ tablets.

Children over 12 years are dosed as described for adults.

Adults: A dose of 2 Avloclor Tablets is taken on the same day each week during exposure to risk, and for 6 weeks after leaving a malarious area. Except in cases of known resistance, this will prevent malaria due to *Plasmodium falciparum*, but relapses may be treated by the Avloclor/primaquine treatment described above.

Amoebic hepatitis: The initial dose is 4 Avloclor Tablets daily for two days followed by 1 tablet twice daily for two or three weeks.

Lupus erythematosus: The initial dose is 1 tablet of Avloclor twice daily for one to two weeks followed by a maintenance dose of 1 tablet daily.

Rheumatoid arthritis: The usual dose is 1 tablet of Avloclor daily, at bedtime.

Contra-indications, warnings, etc Caution is necessary when giving chloroquine to patients with porphyria who also have hepatic dysfunction or cirrhosis as the drug may precipitate severe constitutional symptoms and an increase in the amount of porphyrins excreted in

the urine. This reaction is especially apparent in alcoholics.

Patients receiving Avloclor continuously at higher dose levels for periods longer than 12 months should undergo ophthalmic examination at three monthly intervals. This also applies to patients receiving chloroquine at weekly intervals for a period of more than 3 years as a prophylactic against malarial attacks, or if the total consumption exceeds 1.6 g/kg.

Pregnancy: As with all drugs, the use of Avloclor during pregnancy should be avoided if possible, unless in the case of life threatening infections, in the judgement of the physician, potential benefit outweighs the risk. There is evidence to suggest that Avloclor given to women in high doses throughout pregnancy can give rise to foetal cochlear damage.

Overdosage: In the event of gross overdosage with Avloclor prompt measures will be required to counteract the depressant effect of the drug on the cardiovascular and respiratory systems. Vomiting should be induced or gastric lavage carried out as soon as possible, followed by appropriate resuscitative measures, such as tracheal intubation with artificial respiration and the administration of vasopressor agents or intravenous fluids. Intravenous molar sodium lactate solution 30-50 ml has been used to counteract the quinidine-like action of chloroquine on the myocardium. To promote excretion of the drug, the administration of enteric-coated ammonium chloride tablets 0.5 g every eight hours is also recommended.

Side-effects: When used at the standard dosage regimes recommended for the control of malaria, Avloclor is well tolerated, and side-effects such as headache and gastrointestinal disturbances which may occur are not of a serious nature. In the treatment of lupus erythematosus and rheumatoid arthritis, however, where prolonged high dosage is required the side-effects can be of greater severity and patients may develop skin eruptions occasional depigmentation or loss of hair, difficulty in accommodation, blurring of vision, corneal opacities and, less often, retinal degeneration. The defects in visual accommodation may occur on first taking chloroquine and patients should be warned regarding driving or operating machinery. Corneal opacities disappear completely when the drug is stopped, but the most serious toxic hazard of prolonged therapy with high doses is the occasional development of irreversible retinal damage. For this reason considerable caution is needed in the use of Avloclor for long-term high dosage therapy and such use should only be considered when no other drug so effective is available. Rarely thrombocytopenia, agranulocytosis and aplastic anaemia have been reported.

Pharmaceutical precautions Nil.

Legal category POM.

P. for prevention of malaria.

Package quantities Containers of 100 tablets.

Further information Nil.

Product licence number 0029/5053R.

CETAVLEX* CREAM

Presentation Cetavlex Cream is a water-miscible cream containing 0.5% w/w Cetrimide PhEur.

Uses For application to minor wounds and abrasions napkin rash and skin disorders.

Dosage and administration Apply topically.

For adults and children: Apply liberally to the affected area of skin. In some cases it may be necessary to cover the wound or burn with a clean dressing.

Accidental administration: The toxicity hazard of Cetavlex arises from the content of cetrimide (Cetavlon®). It seems unlikely that systemic toxicity is likely to occur from accidental ingestion of the cream. The specific antidotes to cetrimide (a quaternary ammonium, cationic detergent) are common soap or anionic surfactants.

General measures: No alcohol to be given. Stomach wash out and administration of egg whites, milk, gelatine or mild soap may be helpful.

Contra-indications, warnings, etc Cetavlex is for topical use only. It must be kept away from the eyes, and should not come into contact with the brain, meninges, middle ear, or be used as an enema.

Side effects: True sensitivity to Cetavlon preparations is very rare. The clinical appearance of the skin conforms to that of any chemical sensitisation reaction. Should a reaction occur, then Cetavlex should not be applied again.

Pharmaceutical precautions Cetavlex Cream should be used undiluted.

Legal category GSL.

Package quantities Tubes of 50 g and jars of 500 g.

Further information Nil.

Product licence number 0029/5015.

CETAVLON® PC

Presentation Cetavlon PC (pro-capite) is a perfumed imber liquid containing 17.5% w/v Cetrimide PhEur.

Uses For the treatment and control of seborrhoea, pityriasis capitis and allied conditions of the scalp.

Administration: Apply topically.

For adults and children: dilute 5 ml of Cetavlon PC with 10 ml of water. Wet hair thoroughly, apply the diluted solution to the scalp and massage thoroughly. Rinse and repeat the process. Finally, rinse thoroughly with clean water. Any tendency to matting of the hair can usually be overcome by further washing with Cetavlon PC.

As with similar preparations, keep the solution out of the eyes with a dry towel or face flannel.

Weekly hair washing with Cetavlon PC is generally sufficient, but the preparation may be used more frequently if necessary.

Accidental administration: *Accidental oral or rectal administration:* Fatal poisoning can result even when the only pathological signs are visceral congestion, cloudy swelling, mild pulmonary oedema or varying degrees of gastro-intestinal irritation. Severe CNS depression, sometimes preceded by excitement and convulsions, can cause death from respiratory paralysis.

Accidental intra-uterine administration: This may lead to haemolysis and pulmonary embolism.

Accidental intravenous transfusion: This will cause massive haemolysis (blood transfusions may be required).

Specific antidotes: Soap, anionic surfactants.

General measures: Do not give alcohol in any form. If cetrimide has been swallowed give large quantities of, or

wash out stomach with, milk, egg whites, gelatine or mild soap. Central paralysis cannot be countered by curare antagonists or CNS stimulants but sympathomimetic drugs have been given.

Mechanically assisted ventilation with oxygen may be necessary. Persistent convulsions may be controlled with cautious doses of a short-acting barbiturate.

Contra-indications, warnings, etc Cetavlon is for topical use only. It must be kept away from the eyes and should not come into contact with the brain, meninges, middle ear, or be used as an enema.

Side effects: Although sensitivity to Cetavlon preparations is very rare there have been very occasional reports of severe burn-like reactions to concentrated solutions such as Cetavlon PC. The clinical appearance of the skin conforms to that of a chemical sensitisation reaction. Should such a reaction occur, treat as a chemical burn and avoid further exposure to products containing the sensitising agent.

Pharmaceutical precautions Cetavlon PC must be used diluted with water.

Legal category GSL.

Package quantities Bottles of 125 ml.

Further information Nil.

Product licence number 0029/5055.

CETAVLON® SOLUTION 40%

(Strong Cetrimide Solution BP)

Presentation Cetavlon Solution 40% is a colourless to pale straw coloured aqueous solution containing 40% w/v cetrimide.

Uses Cetavlon Solution 40% contains Cetrimide PhEur, a powerful bactericidal agent which also has useful detergent properties.

Cetavlon Solution 40% when diluted is used as an aqueous or alcoholic solution in wound and burn therapy, skin disinfection, removing ointments, scabs, crusts, etc. in skin diseases, seborrhoeic dermatitis, and medication of infant's napkins to prevent napkin rash. Cleansing and storage of sterile instruments.

Dosage and administration Cetavlon preparations are all applied topically. The concentrations given are applicable both to adults and children.

Cetavlon Solution 40% is diluted and used as follows:

Wound and burn therapy: A 0.1% aqueous solution of Cetavlon is used. In cases involving contamination with dirt or grease a 0.5–1.0% solution may be used.

Skin disinfection: A 1% aqueous solution of Cetavlon may be used for the preoperative 'scrub-up' of the surgeon's or obstetrician's hands. A rapid and prolonged disinfection of the skin is produced by swabbing with Cetavlon 0.5% solution in 70% alcohol.

Skin diseases: A 1% aqueous solution of Cetavlon may be used to clean the skin of scabs, crusts, etc. and remove ointments. Cetavlon may also be used to prevent infection in skin conditions such as impetigo, eczema, napkin rash, etc.

Dandruff: In the treatment of seborrhoea of the scalp. Cetavlon is used at strengths of 1–3% in water, the solution being applied to the wet hair to form a lather which is finally removed by rinsing with clean water.

Sterile storage of instruments: Sterile surgical instru-

ments may be stored completely immersed in a 0.1% aqueous solution of Cetavlon. Plastic materials can be cleansed and virtually disinfected by immersion in a 0.5–1.0% aqueous solution for $\frac{1}{2}$ –1 hour.

Napkin rash in infants: After laundering, napkins are finally dipped in 0.05% aqueous Cetavlon solution and then dried. The presence of Cetavlon in the napkin inhibits bacterial decomposition of the urine and so helps to prevent napkin rash.

Cleansing of Hospital vessels, apparatus and instruments: These may be cleansed by rinsing with a 0.5–1.0% aqueous solution of Cetavlon.

Soiled linen: This can be disinfected efficiently before laundering by means of a preliminary soak in a 0.1% aqueous solution of Cetavlon.

Contra-indications, warnings, etc Cetavlon preparations are for topical use only. They must be kept away from the eyes, and must not be used on the brain, meninges and middle ear or used as an enema.

Instruments containing cemented glass components must not be immersed in Cetavlon solutions.

Syringes and needles which have been immersed in Cetavlon solutions must be thoroughly rinsed in sterile water before use. This is particularly important in the case of syringes and needles which are to be used for giving spinal injections.

Overdosage: Accidental oral or rectal administration: Fatal poisoning may arise even when the only pathological signs are visceral congestion, cloudy swelling, mild pulmonary oedema or varying degrees of gastro-intestinal irritation. Severe CNS depression, sometimes preceded by excitement and convulsions, can cause death from respiratory paralysis.

Intra-uterine administration: Introduction into the uterus can lead to haemolysis and pulmonary embolism.

Accidental intravenous transfusion: Massive haemolysis.

Specific antidotes: Soap, anionic surfactants.

General measures: Do not give alcohol in any form. If Cetrimide has been swallowed, give large quantities of, or wash out stomach with milk, egg whites, gelatin or mild soap. Central paralysis cannot be countered by curare antagonists or CNS stimulants but sympathomimetic drugs have been given.

Mechanically assisted ventilation with oxygen may be necessary. Persistent convulsions may be controlled with cautious doses of a short-acting barbiturate.

Side-effects: True sensitivity to Cetavlon preparations is very rare. The clinical appearance of the skin conforms to that of any chemical sensitisation reaction. Should a reaction occur, then Cetavlon should not be applied again.

Pharmaceutical precautions Cork may protect certain Gram-negative organisms from the action of many antiseptics. Cetavlon solutions should therefore always be stored in glass – or rubber-stoppered bottles. Add sodium nitrite 0.4% (4×1 g tablets in 1 litre) to instrument storage solutions to prevent corrosion, and change the solutions at weekly intervals.

Cetavlon Solution 40% must be stored in the manufacturer's original container, or in glass or plastic containers which comply with British Standard No. 1679.

Legal category GSL.

Package quantities Cetavlon Solution 40% – bottles of 1 litre and 5 litres.

Further information Nil.

Product licence number 0029/5054.

CORSODYL* DENTAL GEL

Presentation A clear red gel containing 5% v/w Chlorhexidine Gluconate Solution BP equivalent to 1% w/w chlorhexidine gluconate.

Uses Inhibits the formation of dental plaque, a major aetiological factor in gingivitis. It is indicated as an aid in the treatment and prevention of gingivitis.

Dosage and administration Brush the teeth with 1 inch of gel on a moistened toothbrush, once or twice daily for about one month. When the toothpaste is applied before using the gel, the brush should be rinsed between applications.

Contra-indications, warnings, etc There are no contra-indications to the use of Corsodyl Dental Gel.

Side-effects: A superficial discolouration may occur on the teeth and on silicate or composite restorations. This can usually be prevented by brushing with toothpaste daily before using the gel or at a different time of day (e.g. Corsodyl Dental Gel in the morning and toothpaste at night).

Overdosage: This has not been reported.

Pharmaceutical precautions When toothpaste is applied immediately prior to gel, rinse the brush between applications. Replace cap after use. Store away from heat.

Legal category P.

Package quantities Tubes of 50 g.

Further information Corsodyl Dental Gel has an antiplaque action. The effect on gingivitis is maximal after removal of subgingival deposits by scaling.

Product licence number 0029/0080.

CORSODYL* MOUTHWASH

Presentation A clear pink solution containing 1% v/v Chlorhexidine Gluconate Solution BP, equivalent to 0.2% w/v chlorhexidine gluconate.

Uses Corsodyl Mouthwash is an antibacterial solution which inhibits the formation of dental plaque. It is indicated as an aid in the treatment and prevention of gingivitis, and in the maintenance of oral hygiene, particularly in situations where toothbrushing cannot be adequately employed (e.g. following oral surgery or in mentally or physically-handicapped patients). It may also be used in a post-periodontal surgery regime to promote gingival healing. It is of value in the management of aphthous ulceration and oral candidal infections, e.g. denture stomatitis and thrush.

Dosage and administration Thoroughly rinse the mouth for about one minute with 10 ml (approximately one dessertspoonful) twice daily until the condition is resolved. If toothbrushing with a conventional toothpaste is carried out in addition to the use of Corsodyl this should be done immediately prior to mouthrinsing or at a different time of the day. For the treatment of gingivitis, a course of about a month is advisable although some variation in response is to be expected in the case of aphthous ulceration and oral candida

infections, treatment should be continued 48 hours after clinical resolution. For the treatment of denture stomatitis the dentures should be cleansed and soaked in the solution for 15 minutes twice daily.

Contra-indications, warnings, etc *Discolouration:*

A superficial discolouration of the dorsum of the tongue, of teeth and on silicate or composite restorations may occur. The former disappears after treatment is discontinued, the latter can largely be prevented by brushing with conventional toothpaste daily before using the mouthwash, or in the case of dentures, cleaning with a proprietary denture cleanser. Where this is not possible, as for example with intermaxillary fixation, or with extensive orthodontic appliances, a dental prophylaxis may be required once the underlying conditions has resolved.

Taste: Transient disturbances of taste sensation and a burning sensation of the tongue may occur on initial use of the mouthwash. These effects usually diminish with continued use.

Oral desquamation: In cases where oral desquamation occurs dilution of the mouthwash (5 ml mouthwash with 5 ml tap water freshly mixed) and instructions to rinse less vigorously will often allow continued use of the mouthwash.

Parotid gland swelling: Very occasionally, swelling of the parotid glands during use of chlorhexidine mouth-rinses has been reported. In all cases spontaneous resolution has occurred on discontinuing treatment.

Overdosage: Overdosage has not been reported. Gastric lavage is probably advisable but systemic effects are unlikely even if large volumes are swallowed.

Pharmaceutical precautions Replace cap after use. Protect from heat.

Legal category P.

Package quantities 250 ml bottle.

Further information Nil.

Product licence number 0029/0124.

DISULPHINE* BLUE

Presentation Disulphine Blue is a 6.2% w/v solution of the dye sulphan blue in water. It is supplied in 10 ml ampoules.

Uses Disulphine Blue is a dye used as a visual test of the state of the circulation in normal and damaged tissue. It is of particular value in the accurate diagnosis and the surgical management of burns and soft tissue trauma, especially severe crush and torsion-avulsion injuries. The dye injection technique can be applied to other branches of surgery.

Dosage and administration 0.25–0.5 ml/kg body weight is given by slow intravenous injection. These doses apply to both adults and children. Injection is made slowly into a suitable vein or indirectly into the tubing of an intravenous infusion. The injection can be given to the fully conscious, basally sedated or fully anaesthetised patient. Changes in the colour of the skin are first seen within 60–90 seconds in those areas with the most active blood supply, e.g. lips, face and ears. Complete body staining is established in three to five minutes. Delay in appearance of the skin staining may be seen in patients with poor peripheral circulation.

Contra-indications, warnings, etc Disulphine Blue staining should not be used until surgical shock has been fully treated, or in patients in whom operative shock is likely to occur. Suitable gloves should be worn during administration of Disulphine Blue as spillage will stain the fingers.

Because of the dramatic discolouration of the patient's skin it is advisable to warn and reassure the patient and his relatives of the harmless and transient nature of this discoloration.

Overdosage: No cases of overdosage have been reported, but in any such occurrence, and in cases of ingestion, symptomatic treatment should be administered.

Side-effects: With Disulphine Blue side-effects are rare enough to be considered as the idiosyncratic reactions of certain individuals. Asthmatic attacks have been precipitated in three patients, and occasional cases of nausea have been reported. Although twice-weekly subcutaneous injection for a year produced sarcomata in rats, it is unlikely that this has any relevance to a single injection of Disulphine Blue in man.

Pharmaceutical precautions As a safeguard against the presence of particulate matter it is recommended that the injection should be filtered into the syringe prior to use. A Millex or Swinnex adaptor and Millipore filter (maximum pore size 5 microns, and preferably 0.22 micron) may be used.

Disulphine Blue must be used undiluted.

Legal category POM.

Package quantities Boxes of 10 × 10 ml ampoules.

Further information *Excretion:* Disulphine Blue is excreted mainly by the kidneys. It may also be found in saliva, gastric secretion, bile, faeces, tracheobronchial secretions and in synovial fluid. It is not found in cerebrospinal fluid since nerve tissue has the power of decolourising the dye rapidly by enzyme action.

Excretion is usually complete within 48 hours.

Product licence number 0029/5007.

EPODYL*

Presentation Epodyl, a tumour inhibitor of the bis-epoxide group, is a clear, colourless, slightly viscous liquid presented in ampoules of 1 ml (containing 1.13 gramme ethoglucid). It is miscible in all proportions with water, giving neutral solutions.

Uses

1. For intracavitary instillation in multiple papillomatosis of the bladder – diluted to a 1 or 2% solution.

2. Epodyl may also be used for intra-arterial infusion or perfusion – diluted to a 10–20% solution – for all types of tumour when they are anatomically accessible. It may be given, similarly diluted, by intravenous injection in selected cases of secondary neoplasia and in the treatment of reticulosos resistant to other chemotherapeutic agents; it may also be given by injection into malignant effusions.

Dosage and administration *Note:* (i) Epodyl must be diluted before administration and only fresh, aseptically prepared solutions should be used.

(ii) Glass syringes should be used with Epodyl because some plastic materials interact with ethoglucid even in aqueous dilution.

1. *Intracavitary instillation in the treatment of bladder tumours:* A freshly prepared 1–2% v/v solution of Epodyl in sterile water or physiological saline should be instilled into the bladder and retained there for as long as possible.

Treatment may be repeated daily for two weeks and then at less frequent intervals.

2. (a) *Intra arterial* dosage ranges from about 2.5 ml ethoglucid (approx. 3 grammes) for tumours of the head and neck, up to 10 ml (approx. 12 grammes) for larger areas and is related to the volume of the tumour-bearing area supplied by the artery into which the injection is made.

(b) *Intravenous* dosage should be closely related to lean body mass and the general condition of the patient. The largest single intravenous dose should not exceed 200 mg/kg for an obese or frail patient, and 250 mg/kg for a lean or robust patient. This total dose can be repeated at intervals of three to five weeks and may be given as a single dose or divided into fractions of 50–100 mg/kg, according to the haematological profile of the patient.

Contra-indications, warnings, etc Epodyl must not be administered undiluted. The recognised contra-indications – severely impaired hepatic function, severe leucopenia, thrombocytopenia and anaemia – seem particularly relevant to administration by the intra-arterial or intravenous routes.

Pregnancy: This product should not normally be administered to patients who are pregnant, or to mothers who are breast-feeding.

Side-effects: Intracavitary administration into the bladder has produced no severe haematological changes although a fall in leucocyte count has been noted in a few patients. Local side-effects from bladder administration are dysuria and frequency. Chemical cystitis and mucosal changes have also been observed.

Overdosage: There is no specific antidote and treatment is symptomatic.

Pharmaceutical precautions The ampoule should be opened and the dilution prepared under aseptic conditions immediately before use. Water for Injection PhEur and Sodium Chloride Injection BP are suitable diluents.

Plastic disposable syringes may not be suitable for use with Epodyl and only glass syringes are recommended to be used.

The ampoules should be protected from heat.

Legal category POM.

Package quantities 1 ml ampoules in boxes of five.

Further information Following repeated intracavity use in multiple papillomatosis of the bladder, a partial or complete response may be expected in over 80% of patients without the risk of systemic side-effects (*British Journal of Urology* (1971), **43**, 133–6).

Product licence number 0029/5010.

ERALDIN[®] INJECTION

Presentation Eraldin is presented as an injectable solution in 5 ml ampoules which each contain 10 mg of Practolol BP in 5 ml of a buffered aqueous solution.

Uses Eraldin is an adrenergic beta-receptor antagonist which is cardioselective. However, treatment with prac-

tolol is now known to produce serious adverse effects (the practolol oculomucocutaneous syndrome) in some patients and oral dosage forms have been withdrawn from use. Eraldin Injection remains available for emergency use and should only be used for the control of cardiac dysrhythmias caused or maintained by excessive sympathetic activity in association with organic disease, particularly post-infarction dysrhythmias, and during anaesthesia, where clinical benefit cannot be obtained with alternative forms of treatment. A most careful assessment of the necessity for treatment with Eraldin should be made before treatment is undertaken.

This preparation is available solely for emergency use in life threatening situations and Eraldin Injection should not be considered for other use. Fuller information on the serious adverse effects associated with practolol may be obtained from the manufacturers.

Dosage and administration *Cardiac dysrhythmias:* *Intravenous:* 5 mg (2.5 ml, i.e. half an ampoule) is given slowly, and if no response occurs may be repeated. Doses of more than 20 mg (10 ml are not normally required).

Contra-indications, warnings, etc Eraldin should not be used with verapamil and neither drug should be administered within several days of discontinuing the other. Apart from the severe practolol oculomucocutaneous syndrome, there have been occasional reports of nausea, sleep disturbance, paraesthesia and also of constipation.

Eraldin need not necessarily be withheld from patients with signs of heart failure. For such patients however, the failure must be controlled before treatment with Eraldin begins. Caution is also advised with the administration of Eraldin in the presence of heart block.

Anaesthesia: Eraldin is compatible with light anaesthesia using Fluothane[®] (halothane). Ether, chloroform, cyclopropane and possibly trichloroethylene depend for their safety on increased circulating levels of endogenous catecholamines and it is probable that they are therapeutically incompatible with beta-receptor antagonists. If Eraldin is not withdrawn, or if it is used during the course of anaesthesia, atropine should be given as premedication to prevent the risk of vagal over-activity. As with all beta-receptor antagonists, Eraldin is contra-indicated in the presence of metabolic acidosis.

Pregnancy: No adverse effects have been seen in teratogenicity studies in animals, but elective drug therapy should always be considered inadvisable in pregnancy.

Overdosage: In the rare event of profound cardiovascular effects such as excessive bradycardia or hypotension, atropine 1 mg intravenously should be given immediately. This should be followed, if necessary, by specific measures to reverse beta-receptor antagonism. For this purpose, isoprenaline may be given by slow intravenous injection (5 mcg per minute) with constant monitoring until a response occurs. Alternatively orciprenaline (up to 0.5 mg) may be used.

Pharmaceutical precautions Protect from light.

Legal category POM.

Sale and supply restricted to hospitals, clinics and nursing homes.

Package quantities The ampoules (10 mg in 5 ml) are packed in boxes of 10.

Further information The physical compatibility of

Eraldin injection with the following intravenous infusion solutions has been investigated over a period of 48 hours immediately following addition of the drug solution to the respective infusion bag, in each case 6 mg Eraldin was added to 100 ml infusion fluid.

0.9% sodium chloride and 5% dextrose

0.3% potassium chloride and 0.9% sodium chloride

0.3% potassium chloride and 5% dextrose

No signs of incompatibility were seen. As these tests were done over 48 hours and long-term stability has not been investigated, it is recommended that mixtures of Eraldin with intravenous fluids should be used within 24 hours of preparation.

Product licence number 0029/5056.

FLUOTHANE*

Presentation Fluothane is a colourless, volatile liquid, non-explosive and non-flammable in the concentrations usually used. Chemically it is 2-bromo-2-chloro-1,1,1-trifluoroethane stabilised with thymol 0.01% w/w (Halothane PhEur).

Uses Fluothane is a volatile anaesthetic which is suitable for the induction and maintenance of anaesthesia for all types of surgery and in patients of all ages.

Dosage and administration A number of anaesthetic vaporisers specially designed for use with Fluothane are available. Open, semi-open, semi-closed and closed circuit systems have all been used with good results.

For induction of anaesthesia in the adult patient a concentration of 2–4% Fluothane in oxygen or oxygen/nitrous oxide may be used. In children a concentration of 1.5–2% Fluothane in oxygen or oxygen/nitrous oxide is used. A concentration of 0.5–2% is usually adequate for maintenance of anaesthesia in both adults and children.

Contra-indications, warnings, etc As Fluothane causes relaxation of the uterine muscle it is advisable that anaesthesia should be maintained in the lightest plane possible during obstetric operations.

The use of moderate hyperventilation during neurosurgery is recommended to counteract the rise in cerebrospinal fluid pressure which may occur with Fluothane.

Caution should be exercised during the administration of adrenaline to patients anaesthetised with Fluothane as dysrhythmias may be precipitated. For this reason the dose of adrenaline should be restricted and beta-receptor antagonists administered if necessary.

The role of Fluothane in the liver damage occasionally observed after anaesthesia has not been definitely established. However, as such cases appear more frequently after repeated anaesthetic administration, the appearance of unexplained jaundice following exposure to Fluothane should be regarded as a contra-indication to its later use. It has been suggested that repeated exposure to any anaesthetic within a period of four weeks should be avoided where possible, and as with all anaesthetics, consideration should be given to the frequency of usage.

Malignant hyperpyrexia has been reported in some patients receiving Fluothane. This syndrome occurs with other anaesthetic agents, and may respond to intravenous dantrolene sodium.

It is advisable to ensure adequate room ventilation when Fluothane is being used.

During the induction of Fluothane anaesthesia a moderate fall in blood pressure commonly occurs. The pressure tends to rise when the vapour concentration is reduced to maintenance levels, but it usually remains steady below the pre-operative level. This hypotensive effect is useful in providing a clear operating field and a reduction in haemorrhage. However, if necessary, intravenous doses of methoxamine (5 mg are usually adequate) can be given to counteract the fall in blood pressure.

Fluothane augments the action of non-depolarising muscle relaxants.

Pregnancy: Although the data from experimental investigations in animals cannot be directly related to man, it would be prudent to avoid general anaesthesia with inhalation agents during early pregnancy, except where such use is essential.

Accidental ingestion: Cases of internal ingestion must be treated symptomatically.

Pharmaceutical precautions Bottles of Fluothane must be securely closed and protected from heat and light. Fluothane must be kept in the original container until immediately prior to its use.

Whilst in the liquid phase, Fluothane must not be diluted or contaminated; however, in the vapour phase it may be administered together with oxygen/nitrous oxide or both.

Legal category P.

Package quantities Fluothane is supplied in bottles of 250 ml.

Further information Nil.

Product licence number 0029/5058.

FULCIN* 500 TABLETS FULCIN* 125 TABLETS FULCIN* ORAL SUSPENSION

Presentation Fulcin is griseofulvin in a fine-particle form designed to give optimal absorption when taken orally.

Fulcin 500 is presented as white, film-coated, bi-convex tablets, one side plain, the obverse marked with the ICI roundel. Each contains 500 mg Griseofulvin PhEur. Fulcin 125 Tablets are white, bi-convex, one side bisected, the obverse marked with the ICI roundel. Each contains 125 mg Griseofulvin PhEur.

Fulcin Oral Suspension is a brown aqueous suspension which contains 2.5% w/v Griseofulvin PhEur.

Uses Fulcin is an antifungal agent which when taken orally is active against the following organisms: *M. audouini*, *M. canis*, *M. fulvum*, *M. ferugineum*, *M. distortum*, *M. rivalieri*, *M. floccosum*, *T. gypsum*, *T. schoenleini*, *T. mentagrophytes*, *T. sulphureum*, *T. rubrum*, *T. crateriforme*, *T. verrocosum*, *T. equinum*, *T. violaceum*, *T. tonsurans*, *T. soudanense*.

Fulcin is indicated in fungal invasions of the skin, hair and nails. These may be known as: Tinea capitis, Tinea corporis, Tinea cruris, Tinea pedis, Tinea unguium, Tinea imbricata, Tinea barbae, Favus.

Dosage and administration The adult dosage is normally 500 mg daily, but in severe conditions up to twice this amount may be given, reducing to the lower level when a clinical response has occurred. The normal dosage may be given as one 125 mg tablet or 5 ml of

suspension four times a day, or as one 500 mg tablet once daily.

For children the most suitable form is the pleasantly flavoured Fulcin Oral Suspension. The daily dosage is 10 mg griseofulvin per kg body weight daily, i.e. 5 ml of suspension for every 12.5 kg in single or divided doses. If dilution is required Syrup BP is suitable.

The duration of treatment depends on the type of infection and the time required for normal replacement of infected tissues.

For complete eradication of the infection, Fulcin treatment should be combined with general measures of care and hygiene. Reservoirs of infection may include clothing, footwear and bedding as well as the patient's hair.

Contra-indications, warnings, etc Fulcin should not be administered in patients who have established porphyria or hepatocellular failure.

Pregnancy: Very high doses of griseofulvin in pregnant animals have been shown to cause foetal abnormalities. The significance in man is not yet known. Accordingly, the administration of Fulcin during pregnancy is not recommended.

Precaution: In those rare cases when individuals are affected by drowsiness whilst taking Fulcin, they should not drive a vehicle, nor operate machinery and should also avoid alcoholic drink.

Overdosage: Treatment of overdosage should be symptomatic.

Side-effects: Fulcin is generally well tolerated, although a few cases of urticarial reactions and erythematous rashes have been noted. These have regressed during treatment in most cases and in others reduction of dosage or termination of treatment has resulted in the disappearance of all undesirable effects. Photosensitivity associated with griseofulvin therapy has been recorded. Fulcin may decrease the response to anticoagulants administered concomitantly, and both barbiturates and anticoagulants may reduce the effectiveness of Fulcin therapy.

Pharmaceutical precautions Protect from heat and light.

Legal category POM.

Package quantities *Fulcin 500 tablets:* Containers of 25, 100 and 250 tablets.

Fulcin 125 Tablets: Containers of 100 and 1,000 tablets.

Fulcin Oral Suspension: Bottles of 100 ml.

Further information A suitable diluent for Fulcin Oral Suspension is Syrup BP.

Product licence numbers

Fulcin 500 Tablets 0029/5061

Fulcin 125 Tablets 0029/5060

Fulcin Oral Suspension 0029/5059

HIBIDIL*

Presentation A pink aqueous solution sterilised by autoclaving which contains Chlorhexidine Gluconate Solution BP 0.25% v/v (equivalent to 0.05% w/v chlorhexidine gluconate) in sachets of 25 ml, 100 ml or bottles of 500 ml and 1,000 ml. Equivalent to a dilution of 1 in 100 of Hibitane Concentrate 5%.

Uses A potent antibacterial agent for general antiseptic

purposes. It is bactericidal to a wide range of organisms and remains bacteriostatic at high dilutions. Hibidil is recommended for swabbing wounds and burns and in obstetrics.

Administration: Use without further dilution for topical application only.

Contra-indications, warnings, etc for external use only. Not for injection. Hibidil should not come into contact with the brain, meninges or middle ear. When used in aseptic procedures disinfect the outside of the sachet before opening. Discard any surplus immediately after use.

Hypochlorite bleaches may cause brown stains to develop in fabrics which have previously been in contact with Hibitane Solutions. Detailed literature is available on request.

Side-effects: Idiosyncratic skin reactions can occur, but are extremely rare.

Accidental ingestion: Carry out a gastric lavage with milk, egg white, gelatine or mild soap.

Pharmaceutical precautions Store away from heat.

Legal category P.

Package quantities Packs of 250 × 25 ml and 60 × 100 ml individual sachets. Bottles of 500 ml and 1,000 ml.

Further information The British Pharmaceutical Codex (1973) recommends that antiseptics applied to broken skin should be sterile. The use of Hibidil complies with this recommendation.

Product licence number 0029/0143.

HIBISCUB*

Presentation An antiseptic skin cleansing solution containing Chlorhexidine Gluconate Solution BP 20% v/v (equivalent to chlorhexidine gluconate 4% w/v) as the active ingredient presented as a perfumed red aqueous solution.

Uses

1. Pre-operative surgical hand preparation.
2. Antiseptic handwash.
3. Pre-operative skin preparation for patients undergoing elective surgery.

Administration: *Pre-operative surgical hand preparation:*

1. Wet the hands and forearms.
2. Apply about 5 ml undiluted Hibiscrub and wash for one minute.
3. Clean the fingernails with brush or scraper.
4. Rinse.
5. Repeat the wash for two minutes.
6. Rinse thoroughly.
7. Dry thoroughly.

Antiseptic handwash:

1. Wet hands and forearms.
2. Apply about 5 ml undiluted Hibiscrub and wash for one minute.
3. Rinse thoroughly.
4. Dry thoroughly.

Pre-operative skin preparation for patients undergoing elective surgery: This involves two stages:

First phase (e.g. on ward): The patient may prepare

himself by undertaking whole-body bathing with Hibiscrub.

On at least two occasions, usually the day before and the day of the operation, the patient, unless bedridden, should wash his whole body with Hibiscrub in the bath or shower. Hibiscrub should be used undiluted. Beginning with the face, and working down the body, particular attention should be paid to the areas around the nose, armpits, umbilicus, groin and perineum. After washing these important sites, the whole body should be rinsed and washed again, starting with the hair and working downwards. Finally, the whole body should be rinsed, and using a freshly laundered towel the entire body surface should be dried thoroughly.

Bedridden patients can be washed with Hibiscrub using the standard bed-bath technique.

Alternatively, undiluted Hibiscrub can be rubbed over the intended operation site and surrounding skin for 2 minutes using sterile gauze swab(s). Sufficient water, preferably sterile, is added to work up a lather.

Finally, the area is wiped clean and dried thoroughly with sterile swabs.

Three applications are made at suitable intervals throughout the day before operation.

Second stage (e.g. in theatre): The following procedure is recommended. With sterile gauze swabs wetted with 0.5% alcoholic Hibitane solution, rub the operation site and surrounding skin thoroughly for two minutes and allow to dry.

Contra-indications, warnings, etc Hibiscrub should not come into contact with the eyes, brain, meninges or middle ear. In patients with head or spinal injuries or perforated ear drum, the benefit of use in pre-operative preparation should be evaluated against the risk of contact.

As with all soaps avoid the eyes.

Side-effects: Idiosyncratic skin reactions can occur, but are extremely rare.

Precautions: Hypochlorite bleaches may cause brown stains to develop in fabrics which have previously been in contact with Hibitane preparations. Detailed literature is available on request.

Treatment of overdose: If swallowed, gastric lavage and symptomatic treatment.

Pharmaceutical precautions Protect from heat and light.

Legal category GSL.

Package quantities Containers of 250 ml, 500 ml., 5 litres. Elbow and foot operated dispensers are available.

Further information Nil.

Product licence number 0029/0127.

HIBISOL*

Presentation A blue, rapid acting, wide spectrum, potent antibacterial preparation containing 2.5% v/v Chlorhexidine Gluconate Solution BP (equivalent to 0.5% w/v chlorhexidine gluconate) in 70% w/w Isopropyl Alcohol BP and emollients to ensure cosmetic acceptability.

Uses *Routine disinfection of clean intact skin.*

1. Disinfection of clean hands prior to surgery.

2. Disinfection of clean hands prior to aseptic procedures or after handling contaminated material.

3. Disinfection of patient's skin.

Dosage and administration Use undiluted for topical application only. To disinfect physically clean hands.

Prior to surgery:

1. Dispense a suitable amount of Hibisol (e.g. 5 ml) into the palm of one hand, spread thoroughly over both hands, wrists and forearms, rub vigorously so that all parts are effectively treated.

2. When dry, repeat the procedure. Glove hands.

N.B. Before the first operation of the list, or subsequent operations if the hands are soiled with blood or other substances, cleanse and disinfect the hands and forearms with an effective antiseptic-detergent preparation.

In other procedures:

Dispense a suitable amount of Hibisol (e.g. 3 ml) into the palm of one hand, spread thoroughly over both hands and wrists, rub vigorously until dry so that all parts are effectively treated.

N.B. If the hands are soiled, cleanse and dry the hands before Hibisol treatment or alternatively use an effective antiseptic-detergent preparation to cleanse and disinfect the hands.

Disinfection of patient's skin:

1. Using sterile swabs, rub Hibisol vigorously on to the operation site and surrounding area. Continue for two minutes or until dry, whichever is the longer.

2. Cover with sterile drapes as necessary.

N.B. Hibisol can also be used for patient skin disinfection during routine nursing procedures (e.g. prior to injection, venepuncture, etc.).

Contra-indications, warnings, etc Hibisol should not come into contact with the eyes, brain, meninges or middle ear.

Side-effects: Idiosyncratic skin reactions can occur, but are extremely rare.

Precautions: Hypochlorite bleaches may cause brown stains to develop in fabrics which have previously been in contact with Hibitane preparations. (See detailed literature for further guidance.)

Treatment of overdose: If swallowed, gastric aspiration and lavage avoiding pulmonary aspiration. Do not use apomorphine. Assist respiration if necessary and keep patient warm. Intravenous laevulose can accelerate alcohol metabolism. In severe cases, haemodialysis or peritoneal dialysis.

Pharmaceutical precautions Protect from heat. Flammable.

Legal category GSL.

Package quantities Containers of 500 ml and 5L.

Further information A suitable antiseptic-detergent preparation which is compatible with Hibisol is Hibiscrub.

Product licence number 0029/0134.

HIBITANE* GLUCONATE 20% SOLUTION (Chlorhexidine Gluconate Solution BP)

Presentation Chlorhexidine Gluconate Solution BP is an aqueous solution containing 20%w/v chlorhexidine gluconate.

Uses Hibitane Gluconate is a potent antibacterial agent

for general antiseptic purposes. It is bactericidal to a wide range of organisms and remains bacteriostatic at high dilutions. This presentation in pure aqueous form allows Hibitane to be used on body tissues where other antiseptics would prove too irritant. It also enables delicate instruments such as cystoscopes to be chemically disinfected.

Dosage and administration As shown in table below.

Contra-indications, warnings, etc Dilute before use. Not for injection. Do not use on the eyes, brain, meninges or middle ear.

Syringes and needles which have been immersed in Hibitane solutions should be thoroughly rinsed in sterile water or saline before use for spinal injections.

Solutions introduced into body cavities, eyes, or on to broken skin must be sterilised in accordance with BPC recommendations.

After immersion in alcoholic solutions rinse instruments with sterile water or aqueous 0.02% Hibitane before use.

Hypochlorite bleaches may cause brown stains to develop in fabrics which have previously been in contact with Hibitane solutions. Detailed literature is available on request.

Side-effects: Idiosyncratic skin reactions have been reported, but are extremely rare.

<i>Mode of preparation</i>	<i>Concentration of active ingredient required (chlorhexidine gluconate)</i>	<i>Use</i>
1.0 ml made up to 1 litre with water (1 in 1,000)	1 in 5,000 (0.02%) Aqueous	Bladder irrigation* Pleural or peritoneal irrigation* Cystoscopy medium*
2.5 ml made up to 1 litre with water (1 in 400)	1 in 2,000 (0.05%) Aqueous	Instruments – clean instrument disinfection including endoscopes (30 minutes' immersion) Patient use – eye irrigation* dip bowls*
2.5 ml of sterile solution made up to 1 litre with sterile glycerine and mixed aseptically (1 in 400)	1 in 2,000 (0.05%) in glycerine	Urethral disinfection and catheter lubrication
25 ml with 225 ml water made up to 1 litre with 95% alcohol (1 in 40)	1 in 200 (0.5%) in 70% Alcohol	Emergency disinfection of clean instruments including endoscopes (2 minutes' immersion)

Sterilise the dilution by autoclaving at 115°–116°C for 30 minutes or 121–123°C for 15 minutes.

Accidental ingestion: Very poorly absorbed by oral route. Carry out gastric lavage and symptomatic treatment.

Accidental intravenous transfusion: Blood transfusion may be necessary to counteract haemolysis.

Pharmaceutical precautions Aqueous dilutions of Hibitane Gluconate 20% Solution should be prepared using freshly distilled water.

Hibitane Gluconate 20% Solution must be protected from heat. As cork may protect certain Gram-negative organisms from the action of antiseptics, Hibitane solutions must be stored in glass – or rubber – stoppered bottles. Water, Industrial Methylated Spirits and glycerol are suitable diluents, as described above.

Sodium nitrite (1 × 1 g tablet in 1 litre) may be added to instrument storage solutions to prevent corrosion.

These solutions should be freshly made up every seven days.

As a precaution against bacterial contamination, stock aqueous solutions should contain at least 4% v/v of isopropyl alcohol or 7% v/v of ethyl alcohol, which may be denatured (for example, Industrial Methylated Spirits) in the final dilution. Protect from heat.

Legal category GSL.

Package quantities Containers of 500 ml and 5 litres are available. Dispensers to fit 5L are available.

Further information Nil.

Product licence number 0029/5031.

HIBITANE* 5% CONCENTRATE

Presentation A perfumed, red, aqueous solution containing 25% v/v Chlorhexidine Gluconate Solution BP equivalent to 5% w/v chlorhexidine gluconate. A surface-active agent is present to inhibit precipitation when dilutions are made with hard water.

Uses Hibitane Concentrate 5% is a potent antibacterial agent for general antiseptic purposes. It is bactericidal to a wide range of organisms and remains bacteriostatic at high dilutions.

Dosage and administration Animate and inanimate disinfection are covered by two major dilutions as shown in table below.

Contra-indications, warnings, etc For external use only. Not for injection. Do not use in body cavities. Dilute before use. Do not use on the eyes, brain, meninges or middle ear.

Syringes and needles which have been immersed in Hibitane solutions should be thoroughly rinsed in sterile water or saline before use for spinal injections.

Instruments containing cemented glass components should not be disinfected in these solutions.

Hypochlorite bleaches may cause brown stains to develop in fabrics which have previously been in contact with Hibitane solutions. Detailed literature is available on request.

Dilutions: Dilutions can be made with tap water when bacteriologically approved.

Solutions applied to wounds, burns and broken skin must be sterilised in accordance with BPC recommendations.

Side-effects; Idiosyncratic skin reactions have been reported, but are extremely rare.

<i>Mode of preparation</i>	<i>Concentration of active ingredients required (chlorhexidine gluconate)</i>	<i>Use</i>
10 ml made up to 1 litre with water (1 in 100)	1 in 2,000 (0.05%) Aqueous	Instruments – storage of sterile instruments Patient use – swabbing in obstetric wounds and burns*
10 ml with 15 ml water made up to 100 ml with 95% alcohol (1 in 10)	1 in 200 (0.5%) in 70% Alcohol	Instruments – emergency instrument disinfection (2 minutes' immersion), [excluding endoscopes containing cemented glass components] Patient use – pre-operative skin disinfection

*Sterilise the dilution by autoclaving at 115–116°C for 30 minutes or 121–123°C for 15 minutes.

Accidental ingestion: Carry out gastric lavage and symptomatic treatment.

Accidental bladder washout: Haematuria may occur.

Pharmaceutical precautions Hibitane Concentrate 5% must be stored away from heat. As cork may protect certain Gram-negative organisms from the action of antiseptics, Hibitane solutions must always be stored in glass- or rubber-stoppered bottles. Water and Industrial Methylated Spirits may be used for dilution. Sodium nitrite (1 × 1 g tablet in 1 litre) may be added to instrument storage solutions to prevent corrosion. These solutions should be freshly made up every seven days.

As a precaution against bacterial contamination, stock aqueous solutions should contain at least 4% v/v of isopropyl alcohol or 7% v/v of ethyl alcohol, which may be denatured (for example, Industrial Methylated Spirits) in the final dilution.

Protect from heat.

Legal category GSL.

Package quantities Containers of 500 ml and 5 litres are available, as are 10 ml sachets in packets of 50. Dispensers to fit 5L are available.

Further information Nil.

Product licence number 0029/5032.

HIBITANE* (Chlorhexidine Acetate BP)

Presentation Hibitane (Chlorhexidine Acetate BP) is a white, microcrystalline powder. It is soluble in water (up to 1.9%), alcohol (up to 5%), glycerol, polyethylene glycols and propylene glycol.

Uses Hibitane (Chlorhexidine) is a potent antibacterial agent for general antiseptics. It is bactericidal to a wide range of organisms and remains bacteriostatic at high dilutions. This presentation allows Hibitane to be used on body tissues where other antiseptics would prove too irritant. It also enables delicate instruments such as cystoscopes to be chemically disinfected.

Dosage and administration The product should be diluted as follows:

<i>Concentration of active constituent</i>	<i>Use</i>
1 in 5,000 aqueous solution	Cystoscopy medium, bladder and body cavity irrigation, clean instrument disinfection, sterile instrument storage (including endoscopes)
1 in 2,000 in glycerin	Urethral disinfection Catheter lubrication
0.5% in 70% alcohol	Emergency disinfection of instruments Pre-operative skin preparation

Aqueous dilutions of Hibitane Chlorhexidine Acetate BP, should be prepared using freshly distilled water.

These dilutions apply to use with both adults and children.

Contra-indications, warnings, etc Do not use on the brain, meninges or middle ear. Solutions introduced into body cavities or used on broken skin or in eyes must be sterilised by heating in an autoclave at 115°C for 30 minutes. The solutions should not be alkaline or contain other ingredients that affect the stability of chlorhexidine. If glass containers are used they should be of neutral glass.

Accidental ingestion: Very poorly absorbed by oral route. Carry out gastric lavage and symptomatic treatment.

Side-effects: Idiosyncratic reactions to Chlorhexidine Acetate BP can occur.

Pharmaceutical precautions Hibitane (Chlorhexidine Acetate BP) should be stored in airtight containers protected from heat. Prepared solutions must be stored in glass- or rubber-stoppered bottles as cork may protect certain Gram-negative organisms from the action of antiseptics. Water, industrial methylated spirits and glycerin are suitable diluents, as described above. Sodium nitrite (1 × 1 g tablet in 1 litre) may be added to instrument storage solutions to prevent corrosion. These solutions should be freshly made up every seven days.

Hibitane (Chlorhexidine Acetate BP) must be stored in the manufacturer's original containers or in glass or metal containers. In the case of metal containers, the metal must be protected by enamel or lacquer.

Syringes and needles which have been immersed in Hibitane solutions must be thoroughly rinsed in sterile water before use for spinal injections.

Rinse instruments containing cemented glass components with sterile water before use.

Hypochlorite bleaches may cause brown stains to develop in fabrics which have previously been in contact with Hibitane solutions. Detailed literature is available on request.

As a precaution against bacterial contamination, stock solutions should contain at least 7% v/v of ethyl alcohol or 4% of isopropyl alcohol.

Legal category GSL.

Package quantities Hibitane (Chlorhexidine Acetate BP) is available in containers of 100 and 500 g.

Further information Nil.

Product licence number 0029/5029.

HIBITANE* (Chlorhexidine Hydrochloride BP)

Presentation Hibitane (Chlorhexidine Hydrochloride BP) is a white, odourless crystalline powder.

Uses Hibitane (Chlorhexidine Hydrochloride BP) is a potent antibacterial agent which is bactericidal to a wide range of Gram-positive and Gram-negative organisms. It is designed for incorporation into topical preparations where prolonged antibacterial activity is required, such as antiseptic, dusting powders, lozenges, ointments, creams and surgical dressings. It may be used for general antiseptics.

Dosage and administration The following are suitable concentrations of Hibitane (Chlorhexidine Hydrochloride BP).

Antiseptic creams: Up to 1% Hibitane (Chlorhexidine Hydrochloride BP).

Burn cream, nasal creams: 0.2% Hibitane (Chlorhexidine Hydrochloride BP).

Dusting powder: 1% Hibitane (Chlorhexidine Hydrochloride BP).

General antiseptic for wounds, burns and obstetrics: 0.05% in freshly distilled water.

These preparations may be applied topically, or by the intra-urethral or intra-uterine route, as appropriate to the formulation. Formulations made up as above are suitable for both adults and children.

Contra-indications, warnings, etc Hibitane (Chlorhexidine Hydrochloride BP) preparations must be administered by topical, intra-urethral or intra-uterine routes only.

No side-effects have been reported.

Accidental ingestion: Hibitane (Chlorhexidine Hydrochloride BP) is not absorbed by the oral route. Gastric lavage should be carried out in cases of ingestion.

Pharmaceutical precautions Hibitane (Chlorhexidine Hydrochloride BP) should be protected from heat. Hibitane (Chlorhexidine Hydrochloride BP) must be stored in the manufacturer's original containers, or in containers made from metal or glass. In the case of metal containers the metal should be protected by enamel or lacquer.

Hibitane (Chlorhexidine Hydrochloride BP) is compatible with most antibiotics, including penicillin, and the sulphonamides. The dispersing agents used for making Hibitane creams and ointments should be cationic or non-ionic in nature. Non-ionic emulsifying wax (Cetomacrogol Emulsifying Wax BP, paraffins, lanolin (Hydrous Wool Fat BP), glycerin and methylcellulose may all be used. However, sodium alginate, soaps, ethyl methylcellulose and sodium carboxymethylcellulose are unsuitable for incorporation into Hibitane preparations. Lactose and calcium phosphate are suitable diluents for preparing wound-dusting powders. Where non-absorbable powders are required, talc or starch may be used.

Hypochlorite bleaches may cause brown stains to develop in fabrics which have previously been in contact with Hibitane preparations. Detailed literature is available on request.

As a precaution against bacterial contamination stock solutions should contain at least 7%v/v of ethyl alcohol or 4%v/v of isopropyl alcohol.

Legal category GSL.

Package quantities Containers of 100 g.

Further information Nil.

Product licence number 0029/5030.

**HIBITANE* ANTISEPTIC CREAM
HIBITANE* OBSTETRIC CREAM**

Presentation Hibitane Antiseptic Cream is an off-white, water-miscible, smooth cream, which has a pleasant odour. It contains 5% v/w Chlorhexidine Gluconate Solution BP equivalent to 1% w/w chlorhexidine gluconate.

Hibitane Obstetric Cream is a pourable, water-miscible, smooth cream. It contains 5% v/w Chlorhexidine Gluconate Solution BP equivalent to 1% w/w chlorhexidine gluconate.

Uses Hibitane Obstetric and Antiseptic Creams have a powerful antibacterial action. They are pleasant to use and are non-irritating to the skin and vaginal epithelium.

Hibitane Antiseptic Cream is designed for application to broken skin surfaces. It may also be applied to the hands of nurses, surgeons and other hospital staff as a barrier against bacterial infection.

Hibitane Obstetric Cream is designed for use as a lubricant for vaginal examinations and for application to the skin on and around the vulva and perineum during labour.

Dosage and administration Hibitane Antiseptic Cream is applied liberally to the wound and surrounding skin, or to the hands.

Hibitane Obstetric Cream is applied liberally to the skin around the vulva and perineum of the patient, and to the hands of the midwife. It may also be smeared over gloved hands to facilitate vaginal examination.

Contra-indications, warnings, etc Hibitane Creams are for topical use only. They must not be applied to the eyes. The creams are not intended to replace sterile rubber gloves where these are required. Idiosyncratic skin reactions to chlorhexidine gluconate preparations may occasionally occur. It is very unlikely that excessive topical application will cause any adverse effects. Gastric lavage may be necessary if ingestion occurs.

Pharmaceutical precautions Protect from heat and use undiluted.

Legal category GSL.

Package quantities *Hibitane Antiseptic Cream:* Tubes of 50 g. Jars of 500 g.

Hibitane Obstetric Cream: Polythene Dispenser Pack 210 ml. Containers of 100 ml and 2 litres.

Further information Nil.

Product licence numbers

Hibitane Antiseptic Cream 0029/5020

Hibitane Obstetric Cream 0029/5019

HIBITANE* ANTISEPTIC LOZENGES

Presentation Hibitane Antiseptic Lozenges are circular, flat, white lozenges with a bevelled edge. Each contains 5 mg Chlorhexidine Hydrochloride BP and 2 mg Benzocaine PhEur in a pleasantly flavoured lozenge base.

Uses Hibitane Antiseptic Lozenges provide an antiseptic effect as an adjuvant to therapy in severe throat and

mouth infections. They are also recommended for use after tonsillectomy and dental extraction to help prevent secondary infection.

Dosage and administration One lozenge should be sucked every two hours. For prophylaxis 4 or 5 lozenges a day should prove adequate. These dosages are applicable both to adults and to children.

Contra-indications, warnings, etc Hibitane Antiseptic Lozenges are contra-indicated in patients with known allergies to the preparation. As chlorhexidine hydrochloride is not absorbed by the oral route no adverse reactions are likely to follow over-dosage. No side-effects have been reported following the use of Hibitane Antiseptic Lozenges.

Pharmaceutical precautions Protect from heat.

Legal category P.

Package quantities Tubes containing 20 lozenges. Containers of 250 lozenges.

Further information Nil.

Product licence number 0029/5021.

IMPERACIN* TABLETS

Presentation Yellow, biconvex, film-coated tablets marked with IMPERACIN on one side. Each tablet contains 250 mg of Oxytetracycline Dihydrate PhEur.

Uses A bacteriostatic broad-spectrum antibiotic active by the oral route against a variety of Gram-positive and Gram-negative organisms, spirochaetes, rickettsiae and some of the larger viruses. It is indicated in the following conditions:

Chronic bronchitis, including the prophylaxis of acute exacerbations.

Most types of pneumonia, notably broncho-pneumonia.

Venereal diseases, including penicillin-resistant gonorrhoea, non-gonococcal urethritis and lymphogranuloma venereum.

Brucellosis, typhus, amoebic dysentery and psittacosis.

Dosage and administration *Adults:* 1,000–2,000 mg (4–8 tablets) daily.

Children: Under 2 years 62.5–250 mg daily.

2–4 years: 250–500 mg daily.

4–12 years: 500–1000 mg daily.

The daily dosage should be divided and is best taken after food.

Contra-indications, warnings, etc Imperacin is contra-indicated in cases of chronic renal failure or where there is a history of tetracycline sensitivity.

Pregnancy: Care must be exercised in the treatment of pregnant women since prolonged administration of tetracyclines during pregnancy may cause staining of the teeth in the developing child. For the same reason avoid prolonged administration in children. Imperacin must be administered with caution in the presence of hepatic dysfunction.

Side-effects are uncommon at the recommended dosage. Nausea, diarrhoea and morbilliform skin reactions have been reported.

Overgrowth with resistant organisms, e.g. Candida, may occur and cause glossitis, rectal and vaginal

irritation. Similarly, resistant staphylococci may cause enterocolitis.

Overdosage: In cases of overdosage, allergic reactions such as drug fever, anaphylactic shock and rashes may occur. For treatment of anaphylaxis immediate administration of adrenaline, oxygen and artificial respiration is necessary.

Adrenaline is given subcutaneously as Adrenaline Injection BP (equivalent to 0.1% adrenaline) at a rate of 0.05 ml/minute. For dyspnoea, aminophylline, calcium and antihistamines must be given. General measures such as administration of plasma, blood, vasopressor drugs or hydrocortisone (100 mg i.v.) may be necessary.

Pharmaceutical precautions Protect the Imperacin Tablets from heat, light and moisture.

Legal category POM.

Package quantities *Tablets:* Containers of 100 and 1,000.

Further information Nil

Product licence number

Imperacin Tablets 0029/5087

INDERAL* TABLETS AND INJECTION

Presentation

1. Tablets each containing 10 mg Propranolol Hydrochloride BP. Pink, round, bi-convex, film coated tablets, impressed with the legend 'INDERAL' 10 on one face and ICI on the obverse. The impressions are highlighted in white.

2. Tablets each containing 40 mg Propranolol Hydrochloride BP. Pink, round, bi-convex, film coated tablets, impressed with the legend 'INDERAL' 40 on one face and ICI on the obverse. The impressions are highlighted in white.

3. Tablets each containing 80 mg Propranolol Hydrochloride BP. Pink, round, bi-convex, film coated tablets, impressed with the legend 'INDERAL' 80 on one face and ICI on the obverse. The impressions are highlighted in white.

4. Tablets each containing 160 mg Propranolol Hydrochloride BP. Pink, bi-convex, film coated tablets, impressed with the legend 'INDERAL' 160 mg on one face and ICI on the obverse. The impressions are highlighted in white.

5. Injection – a solution containing Propranolol Hydrochloride BP. 1 mg per 1 ml in printed glass ampoules of 1 ml.

Uses Inderal, a beta-adrenoceptor blocking drug, is indicated in:

- (a) the control of essential and renal hypertension
- (b) the management of angina pectoris
- (c) the long term prophylaxis after recovery from acute myocardial infarction
- (d) the control of most forms of cardiac dysrhythmia
- (e) the prophylaxis of migraine
- (f) management of essential tremor
- (g) the control of anxiety and anxiety tachycardia
- (h) the adjunctive management of thyrotoxicosis and thyrotoxic crisis
- (i) management of hypertrophic obstructive cardiomyopathy
- (j) management of phaeochromocytoma (with an alpha blocker)

Dosage and administration *Adults: Oral: Hypertension:* A starting dose of 80 mg twice a day may be

increased at weekly intervals according to response. The usual dose range is 160–320 mg per day. With concurrent diuretic or other antihypertensive drugs a further reduction of blood pressure is obtained.

Angina, anxiety, migraine and essential tremor: A starting dose of 40 mg two or three times daily may be increased by the same amount at weekly intervals according to patient response. An adequate response in anxiety, migraine and essential tremor is usually seen in the range 80–160 mg/day and in angina in the range 120–240 mg/day.

Dysrhythmias, anxiety tachycardia, hypertrophic obstructive cardiomyopathy and thyrotoxicosis: A dosage range of 10–40 mg three or four times a day usually achieves the required response.

Post myocardial infarction: Treatment should start between days 5 and 21 after myocardial infarction, with an initial dose of 40 mg four times a day for 2 or 3 days. In order to improve compliance the total daily dosage may thereafter be given as 80 mg twice a day.

Phaeochromocytoma: (Used only with an alpha-receptor blocking drug). Pre-operative: 60 mg daily for three days is recommended. Non-operable malignant cases: 30 mg daily.

Intravenous: Before injecting Inderal, atropine 1–2 mg should be given intravenously. The initial dose of Inderal is 1 mg (1 ml) injected over one minute. This may be repeated at two-minute intervals until a response is observed or to a maximum dose of 10 mg in conscious patients or 5 mg in patients under anaesthesia.

Children: *Dysrhythmias, phaeochromocytoma, thyrotoxicosis:* The dose of Inderal should be determined according to the cardiac status of the patient and the circumstances necessitating treatment. These doses are only a guide: *Oral:* 0.25–0.5 mg/kg three or four times daily as required. *Intravenous:* 0.025–0.05 mg/kg injected slowly under ECG control and repeated three or four times daily as required.

Migraine: *Oral:* Under the age of 12: 20 mg two or three times daily.

Over the age of 12: the adult dose.

Fallot's Tetralogy: The value of Inderal in this condition is confined mainly to the relief of right-ventricular outflow tract shut-down. It is also useful for treatment of associated dysrhythmias and angina. Dosage should be individually determined according to circumstances and the following is only a guide: *Oral:* Up to 1 mg/kg repeated three or four times daily as required. *Intravenous:* Up to 0.1 mg/kg injected slowly under ECG control, repeated three or four times daily as required.

Contra-indications, warnings, etc

Contra-indications: Inderal should not be used:

1. in the presence of second and third degree heart block.
2. If there is a history of bronchospasm.
3. After prolonged fasting.
4. In metabolic acidosis (e.g. in some diabetics).
5. With verapamil, and neither drug should be administered within several days of discontinuing the other.

Warning: The intravenous injection is intended for the emergency treatment of cardiac dysrhythmias and thyrotoxic crisis only.

Precautions: If the standing heart rate falls below 50–55 beats/minute the dose should not be increased further.

Special care should be taken with patients whose

cardiac reserve is poor. Heart failure due to thyrotoxicosis often responds to Inderal alone, but if other adverse factors co-exist myocardial contractility must be maintained and signs of failure controlled with digitalis and diuretics.

In patients with ischaemic heart disease, it is important that treatment with a beta-blocking agent is not discontinued abruptly. Either the equivalent dosage of another beta-blocker may be substituted or the withdrawal of Inderal should be gradual.

If Inderal and clonidine are given concurrently the clonidine should not be discontinued until several days after the withdrawal of the beta-blocker (see prescribing information on clonidine).

Anaesthesia: As with all other beta-receptor blocking drugs it may be decided to withdraw Inderal before surgery. In this case 24 hours should be allowed to elapse between the last dose and anaesthesia. If treatment is continued care should be taken when using anaesthetic agents such as ether, cyclopropane and trichloroethylene. Vagal dominance, if it occurs, may be corrected with atropine (1–2 mg i.v.).

Pregnancy: As with all other drugs, Inderal should not be given in pregnancy unless its use is essential. There is no evidence of teratogenicity with Inderal.

Adverse reactions: Inderal is usually well tolerated. Minor side-effects such as cold extremities, nausea, insomnia, lassitude and diarrhoea are usually transient, resolving on withdrawal of the drug. Isolated cases of paraesthesia of the hands have been reported.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuance of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-adrenergic blocker should be gradual. In the rare event of intolerance to Inderal manifested as bradycardia and hypotension, the drug should be withdrawn and if necessary the treatment for overdosage instituted.

Overdosage: Excessive bradycardia can be countered with atropine 1–2 mg intravenously, followed, if necessary by a beta-receptor stimulant such as isoprenaline 25 micrograms intravenously or orciprenaline 0.5 mg intravenously. Glucagon has also been reported to be useful.

Pharmaceutical precautions All Inderal preparations should be protected from light.

Note: Dilutions of Inderal Injection in Dextrose Intravenous Infusion BP, Sodium Chloride Intravenous Infusion BP or Sodium Chloride and Dextrose Intravenous Infusion BP may be used. Other admixtures may considerably reduce the stability of Inderal Injection and any combination should therefore be used immediately after preparation.

Details of a suitable formula for the extemporaneous preparation of a paediatric oral suspension of Inderal are available on request to the manufacturer.

Legal category POM.

Package quantities *Tablets 10 mg:* Containers of 100 and 1,000.

Tablets 40 mg: Containers of 100 and 1,000.

Tablets 80 mg: Containers of 60 and 500.

Tablets 160 mg: Containers of 60 and 250.

Injection: 1 ml ampoules in boxes of 10.

Further information Nil.

Product licence numbers

Inderal Tablets 10 mg	0029/5063
Inderal Tablets 40 mg	0029/5064
Inderal Tablets 80 mg	0029/5065
Inderal Tablets 160 mg	0029/0103
Inderal Injection	0029/5062

INDERAL[®] LA

Presentation Spheroids of propranolol hydrochloride having a sustained release coating to provide long action and contained in a lavender and pink, gelatin capsule marked Inderal LA and bearing the ICI roundel. Each capsule contains 160 mg of Propranolol Hydrochloride IP.

Uses Inderal LA, a beta-adrenergic receptor blocking drug, is indicated in the control of hypertension and the management of angina.

Dosage and administration Oral, once daily.

Adults: Hypertension: The starting dose is one capsule daily, taken either morning or evening. An adequate response is seen in most patients at this dosage. If necessary, it can be increased to two capsules, and a further reduction in BP can be attained if a diuretic or other antihypertensive agent is given in addition to Inderal LA.

Angina: An adequate response is usually obtained with one capsule daily, either morning or evening, depending on patient convenience.

Children: Inderal LA is not intended for use in children.

Contra-indications, warnings, etc Inderal LA should not be used:

1. In the presence of second and third degree heart block.
2. If there is a history of bronchospasm.
3. After prolonged fasting.
4. In metabolic acidosis (e.g. in some diabetics).
5. With verapamil, and neither drug should be administered within several days of discontinuing the other.

Precautions: Special care should be taken with patients whose cardiac reserve is poor. Myocardial contractility must be maintained and signs of failure controlled with digitalis and diuretics. One of the pharmacological actions of Inderal is to reduce the heart rate. Bradycardia usually less than 50–55 beats/minute indicates that dosage should not be further increased.

In patients with ischaemic heart disease it is important that treatment with a beta-blocking agent is not discontinued abruptly. Either the equivalent dosage of another beta-blocker may be substituted or the withdrawal of Inderal should be gradual. This can be achieved by first substituting the Inderal LA by the equivalent in 40 mg tablets of Inderal spread throughout the day and then gradually reducing the dose.

If Inderal LA and clonidine are given concurrently the clonidine should not be discontinued until several days after the withdrawal of the beta-blocker (see also prescribing information on clonidine).

Anaesthesia: As with all beta-receptor blocking drugs it may be decided to withdraw Inderal before surgery. In this case 24 hours should be allowed to elapse between the last dose and anaesthesia. If treatment is continued are should be taken when using anaesthetic agents such as ether, cyclopropane and trichloroethylene. Vagal

dominance, if it occurs, may be corrected with atropine (1–2 mg i.v.).

Pregnancy: As with all other drugs, Inderal LA should not be given in pregnancy unless its use is essential. There is no evidence of teratogenicity with Inderal LA.

Adverse reactions: Inderal LA is usually well tolerated. Minor side-effects, such as cold extremities, nausea, insomnia, lassitude and diarrhoea are usually transient, resolving on withdrawal of the drug. Isolated cases of paraesthesia of the hands have been reported. There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuance of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-adrenergic blocker should be gradual. In the rare event of intolerance to Inderal LA manifested as bradycardia and hypotension, the drug should be withdrawn, and if necessary, treatment for overdosage instituted.

Overdosage: Excessive bradycardia can be countered with atropine 1–2 mg intravenously, followed, if necessary, by a beta-receptor stimulant such as isoprenaline 25 micrograms intravenously, or orciprenaline 0.5 mg intravenously. Glucagon has also been reported to be useful.

Pharmaceutical precautions Protect from heat, light and moisture.

Legal category POM.

Package quantities Patient Calendar Pack of 28 capsules.

Further information Inderal LA provides controlled release such that adequate blood levels of propranolol are maintained for over 24 hours following a single oral dose and unlike therapy with conventional tablets irregular peaks and troughs of blood level are avoided.

Product licence number 0029/0128.

INDERETIC[®]

Presentation White, opaque capsules, printed with Inderetic and the ICI Roundel. Each capsule contains 80 mg Propranolol Hydrochloride BP and 2.5 mg Bendrofluazide BP.

Uses The management of hypertension. Inderal, propranolol hydrochloride, is a beta-adrenergic blocking drug, and bendrofluazide is a thiazide diuretic. Inderetic presents both these components in a single preparation for the treatment of mild to moderate hypertension.

Dosage and administration **Adults:** One capsule twice daily should prove effective in most cases.

For new patients a maximum response is achieved usually within two weeks. If a greater antihypertensive effect is desired, Inderetic is compatible with most other antihypertensives which may be added (see *Precautions* below).

In those patients being transferred from a combination of treatments, which includes a beta-blocker, this treatment should be withdrawn gradually as Inderetic is introduced.

Children: There is no specific experience with Inderetic and for this reason it is not recommended for children.

Contra-indications, warnings, etc Inderetic should not be used:

1. In the presence of second or third degree heart block.
2. If there is a history of bronchospasm.
3. In patients with anuria, renal failure, or with a history of sensitivity to thiazides.
4. After prolonged fasting.
5. In patients with metabolic acidosis (e.g. in some diabetics).
6. With verapamil, and neither drug should be administered within several days of discontinuing the other.

Precautions: One of the pharmacological effects of beta-blockade is a reduction in heart rate; if it falls much below 55 beats/minute, this indicates that dosage is excessive.

Special care should be taken with patients whose cardiac reserve is poor, although the concurrent diuretic therapy is likely to be beneficial in such cases.

Normally, cardiac failure is considered a contra-indication to beta-blockade, unless or until signs of failure are controlled with digitalis or diuretics.

In patients with ischaemic heart disease, it is important that treatment with a beta-blocking agent is not discontinued abruptly. Either the equivalent dosage of another beta-blocker may be substituted or the withdrawal of Inderetic should be gradual.

Thiazide derivatives sometimes lower carbohydrate tolerance and the insulin dosage of the diabetic patient may require adjustment. Care is necessary when Inderetic is administered to those with a known predisposition to diabetes.

Potassium depletion is a danger to digitalised patients or those with hepatic cirrhosis with ascites.

If Inderetic and clonidine are given concurrently the clonidine should not be discontinued until several days after the withdrawal of the Inderetic (see prescribing information on clonidine).

Anaesthesia: As with all beta-receptor blocking drugs, it may be decided to withdraw Inderetic before surgery. In this case 24 hours should be allowed to elapse between the last dose and anaesthesia. If treatment is continued care should be taken when using anaesthetic agents such as ether, cyclopropane and trichloroethylene. Vagal dominance, if it occurs, may be corrected with atropine (1–2 mg i.v.).

Pregnancy: Although there is no evidence of teratogenicity, both constituents cross the placental barrier and Inderetic is, therefore, considered to be unsuitable for pregnant patients.

Adverse reactions; Propranolol hydrochloride is usually well tolerated. Minor side-effects, such as cold extremities, nausea, insomnia, lassitude and diarrhoea are usually transient. Isolated cases of paraesthesia of the hands have been reported. There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuance of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-adrenergic blocker should be gradual. In the rare event of intolerance to the propranolol hydrochloride in Inderetic, manifested as bradycardia and hypotension, the drug should be withdrawn and, if necessary, treatment for overdosage instituted.

Adverse effects of bendrofluazide are very uncommon

in the small dose contain usually manifest as muscle in patients already depleted hepatic insufficiency. Pot in patients receiving digitalis in hepatic cirrhosis. Hypotension but an attack of gout increase blood urea, in patients with renal disease nitrogen. Reports of other are rare. They include photosensitivity, necrotic skin, blood dyscrasias and myopia.

Overdosage: Excessive treatment with atropine 1–2 mg intravenously, by a beta-receptor antagonist 25 mcg intravenously, or glucagon has been used. Excessive diuresis should be treated by measures to restore blood pressure and correct electrolyte imbalance.

Pharmaceutical precautions and moisture.

Legal category POM.

Package quantities C

Further information I compliance by providing the standard β -adrenocorticoid propranolol hydrochloride azide for the treatment of hypertension. Concurrent use of propranolol gives a more pronounced response than when used alone.

Product licence number

INDEREX*

Presentation Capsules: opaque grey bodies print the ICI Roundel. Each capsule contains 10 mg propranolol Hydrochloride and 5 mg Bendrofluazide.

Uses The management of hypertension. Inderex, propranolol, a non-selective adrenergic blocking drug, and Bendrofluazide, a diuretic. Inderex present in single preparation.

Dosage and administration daily should prove effective.

For new patients a maximum dosage within one week effect is desired, Inderex antihypertensives which (below). In those patients combination of treatment with Bendrofluazide, these treatments as Inderex is introduced.

Children: There is no paediatric use and for this reason it is not recommended.

Contra-indications, warnings, etc not be used:

1. In the presence of heart block.

chospasm.
renal failure, or with a
s.

ic acidosis (e.g. in some

er drug should be admin-
iscontinuing the other.

icological effects of beta-
rt rate; if this falls much
he dose should not be

en with patients whose
h the concurrent diuretic
l in such cases.

onsidered a contra-indi-
s or until signs of failure
diuretics.

art disease, it is important
king agent is not discon-
valent dosage of another
ed or the withdrawal of
s can be achieved by first
he equivalent in 40 mg
fluazide tablets spread
dually reducing the dose

nes lower carbohydrate
je of the diabetic patient
necessary when Inderex
a known disposition to
is a danger to digitalised
cirrhosis with ascites

given concurrently the
tinued until several days
nderex (see prescribing

ceptor blocking drugs, it
nderex before surgery. In
owed to elapse between
lf treatment is continued
sing anaesthetic agents
l trichloroethylene. Vagal
corrected with atropine

o evidence of teratogen-
he placental barrier and
ed to be unsuitable for

l hydrochloride is usually
ts, such as cold extremi-
and diarrhoea are usually
raesthesia of the hands
ve been reports of skin
ed with the use of beta-
reported incidence is
symptoms have cleared
1. Discontinuance of the
ny such reaction is not
of therapy with a beta-
radial. In the rare event
inolol hydrochloride in
dia and hypotension, the
, if necessary, treatment

zide are very uncommon
c. Hypokalaemia, usually
is most severe in patients

already depleted of potassium, as in renal or hepatic
insufficiency. Potassium depletion is dangerous in pa-
tients receiving digitalis. Coma may be precipitated in
hepatic cirrhosis. Hyperuricaemia sometimes occurs, but
an attack of gout is rare. The thiazide diuretics increase
blood urea, which is most pronounced in patients with
renal disease and pre-existing retention of nitrogen.
Reports of other adverse reactions to thiazides are rare.
They include skin rashes with associated photosensitiv-
ity, necrotising vasculitis, acute pancreatitis, blood
dyscrasias and aggravation of pre-existing myopia.

*Overdosage: Excessive bradycardia can be countered
with atropine 1–2 mg intravenously, followed, if neces-
sary, by a beta-receptor stimulant, such as isoprenaline
25 µg intravenously, or orciprenaline 0.5 mg intra-
venously. Excessive diuresis should be countered by
general measures to restore blood volume, maintain
blood pressure and correct electrolyte imbalance. Glu-
cagon has also been reported to be useful.*

Pharmaceutical precautions Protect from heat, light
and moisture.

Legal category POM.

Package quantities Patient calendar pack of 28
capsules.

Further information Inderex is designed to aid drug
compliance by providing a convenient presentation of a
sustained release formulation of propranolol hydrochlo-
ride with the diuretic bendrofluazide for the treatment of
mild to moderate hypertension. Concurrent use of
propranolol and bendrofluazide produces a more pro-
nounced and consistent antihypertensive response than
when either component is used alone.

Product licence number 0029/0157.

LOREXANE* CREAM 1%

Presentation Lorexane Cream 1% contains 1%
Gamma Benzene Hexachloride in a white vanishing
cream base.

Uses Lorexane is a powerful parasiticide with a rapid
action against the majority of external parasites, es-
pecially the burrowing mite *Sarcoptes scabiei* var. *hominis*.

Lorexane Cream 1% is for the eradication of scabies,
and pediculosis of the scalp, body and pubes.

Dosage and administration The following recom-
mendations are applicable to both children and adults.

Scabies: Before treatment, the body should be washed
liberally with soap and water and thoroughly dried.
Lorexane Cream is then rubbed into the skin over the
entire body surface, with the exception of the face and
scalp until completely absorbed. The contents of one
tube are adequate for the treatment of an adult and
usually, half this quantity will be found sufficient for a
single application, with proportionately reduced amounts
for children. Special attention should be given to areas
between the fingers and toes, also wrists, armpits,
genitals and buttocks. Subjective relief from irritation
appears within a few hours. A bath should be taken after
a period of 24 hours and all patients should be examined
after four days to determine if a further application is
necessary. Underclothes and bed linen should be
washed, but it is generally unnecessary to send blankets,
bedding and clothes to be disinfested.

Pediculosis: The affected area should be thoroughly
washed with soap and water and dried. Lorexane Cream

is then well rubbed into the involved skin and hair, and also adjacent areas. The hair may be combed with a dust comb after 24 hours to remove dead lice but, to ensure that any larvae which may subsequently develop from the nits are destroyed, the patient should be discouraged from washing the hair for a period of 7–10 days. As in scabies a single application usually suffices.

Contra-indications, warnings, etc For external use only.

Warning: Lorexane Cream 1% should be used with caution, especially on infants, children and pregnant women. Gamma benzene hexachloride penetrates human skin and has the potential for CNS toxicity. Studies indicate that potential toxic effects of topically applied gamma benzene hexachloride are greater in the young. Seizures have been reported after the use of gamma benzene hexachloride, but a cause and effect relationship has not been established. Simultaneous application of creams, ointments or oils may enhance the percutaneous absorption of gamma benzene hexachloride.

Overdosage: Accidental ingestion: CNS excitation, hyper-irritability, ataxia, clonic and tonic convulsions can occur. Subsequent CNS depression results in respiratory failure and pulmonary oedema. There is damage to the liver and kidneys. Carry out gastric lavage and administer saline cathartics. (Avoid oil laxatives, adrenaline, morphine, pethidine, atropine, aminophylline and tranquillisers). Give sedatives and 10% calcium gluconate (10 ml intravenously) if convulsions are present.

Give 250 000 i.u. penicillin six-hourly as a prophylactic measure.

The diet should be a low-fat, high-protein and high-carbohydrate diet. No milk or glucose should be given.

Artificial respiration may be indicated to counteract pulmonary failure.

Side-effects: Isolated incidents of mild skin reaction have been reported.

Pharmaceutical precautions Use undiluted.

Legal category P.

Package quantities 50 g tubes.

Further information Since *Pediculosis capitis* can spread rapidly, it is important that the entire family be treated when any one member is infested.

Product licence number 0029/5068.

LOREXANE* No. 3

Presentation Lorexane No. 3 is an off-white pearly cream containing 2% Gamma Benzene Hexachloride in a detergent base.

Uses Lorexane is a powerful parasiticide with a rapid action against the majority of external parasites, especially *Pediculus humanus var. capitis*.

Lorexane No. 3 is for the eradication of head lice.

Dosage and administration The following recommendations are applicable to both children and adults.

Pediculosis: After thoroughly wetting the hair, rub in about 2 inches of Lorexane No. 3 and work well into the scalp. No lather will be produced at this stage. Rinse well with warm water, apply more Lorexane No. 3 and work up to a lather. Rinse thoroughly with warm water and then comb to remove any nits remaining. Dry the hair. repeat the treatment one week later.

Contra-indications, warnings, etc For external use only.

Lorexane No. 3 should be used on the scalp only.

Lorexane No. 3 must be used with water.

Warning: Lorexane Cream 1% should be used with caution, especially on infants, children and pregnant women. Gamma benzene hexachloride penetrates human skin and has the potential for CNS toxicity. Studies indicate that potential toxic effects of topically applied gamma benzene hexachloride are greater in the young. Seizures have been reported after the use of gamma benzene hexachloride, but a cause and effect relationship has not been established. Simultaneous application of creams, ointments or oils may enhance the percutaneous absorption of gamma benzene hexachloride.

Overdosage: Accidental ingestion: CNS excitation, hyper-irritability, ataxia, clonic and tonic convulsions can occur. Subsequent CNS depression results in respiratory failure and pulmonary oedema. There is damage to the liver and kidneys. Carry out gastric lavage and administer saline cathartics (Avoid oil laxatives, adrenaline, morphine, pethidine, atropine, aminophylline and tranquillisers). Give sedatives and 10% calcium gluconate (10 ml intravenously) if convulsions are present.

Give 250 000 i.u. penicillin six-hourly as a prophylactic measure.

The diet should be a low-fat, high-protein and high-carbohydrate diet. No milk or glucose should be given.

Artificial respiration may be indicated to counteract pulmonary failure.

Side-effects: Isolated incidents of mild skin reaction have been reported.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities 50 g tubes.

Further information Since *Pediculosis capitis* can spread rapidly, it is important that the entire family be treated when any one member is infested.

Lorexane No. 3 has been formulated to leave the hair in a clean condition, and is therefore more likely to be accepted by family contacts.

Product licence number 0029/5069.

MYSOLINE* TABLETS MYSOLINE* ORAL SUSPENSION

Presentation Mysoline tablets are round, white, bi-convex, marked with a parallel line on each side of the bisecting line on one face and the ICI roundel on the obverse, and contain 250 mg Primidone BP.

Mysoline Oral Suspension is a white, pleasantly flavoured aqueous suspension which contains 250 mg Primidone BP per 5 ml.

Uses Mysoline is an anticonvulsant of high activity and low toxicity which is outstandingly effective in grand mal and psychomotor (temporal lobe) epilepsy, of considerable value against focal or Jacksonian seizure and frequently of help to petit mal and in the control of myoclonic jerks and akinetic attacks.

Dosage and administration Mysoline is given by mouth. Treatment must always be planned on an individual basis. In many patients it will be possible to use Mysoline alone, but in some, Mysoline will need to

be combined with other anticonvulsants or with supporting therapy.

Begin with $\frac{1}{2}$ tablet once daily late in the evening. Every three days increase the daily dosage by $\frac{1}{2}$ tablet until the patient is receiving 2 tablets daily. Thereafter, every three days increase the daily dosage by 1 tablet in adults or $\frac{1}{2}$ tablet in children under 9 years – until controls obtained or the maximum tolerated dosage is being given. This may be as much as 6 tablets a day in adults; 4 tablets a day in children.

Average daily maintenance doses:

	Tablets (or 5 ml measures of suspension)	Milligrams
Adults and children over 9 years	3–6	750–1,500
Children 6–9 years	3–4	750–1,000
Children 2–5 years	2–3	500–750
Children up to 2 years	1–2	250–500

The total daily dose is usually best divided and given in two equal amounts, one in the morning and the other in the evening. In certain patients, it may be considered advisable to give a larger dose when the seizures are more frequent. For instance: 1) if the attacks are nocturnal then all or most of the day's dose may be given in the evening; 2) if the attacks are associated with some particular event such as menstruation, a slight increase in the appropriate dose is often beneficial.

When it is necessary to give 125 mg of Mysoline suspension to a small child, it is advisable to dilute the suspension and administer a 5 ml dose.

A suitable diluent is:

Sodium carboxymethyl cellulose (50 cp)	1% w/v
Sucrose	20%
Methylhydroxybenzoate	0.15%
Propylhydroxybenzoate	0.015%
Water	to 100%

Contra-indications, warnings, etc *Pregnancy:* There is some evidence of a higher than average incidence of congenital abnormalities in infants born of epileptic mothers. The precise factors influencing this are unknown, but the possibility that anticonvulsant therapy may be involved and the very slight risk of an abnormal foetus must be weighed against the risks of withholding treatment during pregnancy. Long-term anticonvulsant therapy can be associated with decreased serum folate levels. As folic acid requirements are also increased during pregnancy, regular screening of patients at risk is advised, and treatment with folic acid and vitamin B₁₂, although controversial, should be considered.

Anticonvulsant therapy in pregnancy has occasionally been associated with coagulation disorders in the neonates. For this reason pregnant patients should be given vitamin K, through the last month of pregnancy up to the time of delivery. In the absence of such pre-treatment then 10 mg vitamin K₁ may be given to the mother at the time of delivery, and 1 mg should be given immediately to the neonate at risk.

As with most other anticonvulsants, patients who drive vehicles or operate machinery should be aware of the possibility of impaired reaction time.

Overdosage: Treatment of overdosage should include

aspiration of stomach contents and the usual supportive measures.

Side-effects: If side-effects do appear they are generally confined to the very early stages of treatment. Patients may feel drowsy, and listless and experience other minor neurotoxic symptoms such as giddiness, difficulty in accommodation, mild nausea and very occasionally, vomiting. A morbilliform rash has been observed in a few cases. These symptoms, even when prominent, are not usually serious and generally disappear completely within a few days, even though treatment is continued. In cases of idiosyncrasy, however, neurotic symptoms may occur in an acute and distressingly severe form and very occasionally a patient may prove unsuitable for Mysoline therapy on this account.

Other rare side-effects include oedema of the legs, thirst and polyuria and impairment of sexual potency. Exceptionally, as with phenytoin and phenobarbitone, megaloblastic anaemia may develop. This can be rectified by the simultaneous administration of folic acid or vitamin B₁₂. In some instances better results have been obtained when folic acid and vitamin B₁₂ have been used together. (See also 'Pregnancy' on previous column.)

Pharmaceutical precautions A suitable diluent for the Oral Suspension is given under Dosage and administration.

Legal category POM.

Package quantities *Tablets 250 mg:* Containers of 100 and 1,000.

Suspension (250 mg/5 ml): Bottles of 150 ml and 2 litres.

Further information Nil.

Mysoline Tablets	0029/5074
Mysoline Oral Suspension	0029/5072

NASEPTIN*

Presentation Naseptin is a non-greasy, white, water-miscible cream containing 1.0% w/w Chlorhexidine Hydrochloride BP and 0.5% w/w Neomycin Sulphate PhEur.

Uses Naseptin is an antiseptic cream, intended for application to the nares, which is active against staphylococci and other organisms.

It can be used: (i) for treating staphylococcal infections in general practice, e.g. it removes the source of the infections which causes recurrent boils, styes, etc; (ii) for prophylaxis against nasal carriage of staphylococci by hospital staff, patients and newborn infants.

Dosage and administration The following recommendations apply both to adults and children. A small amount of Naseptin, about the size of a match-head, is placed on the little finger and applied to the inside of each nostril, by squeezing the nares the cream is then spread forward into the vestibule. A smooth glass rod or swab may be used for application to infants or patients who are very ill.

For prophylaxis: Naseptin is applied as above, twice daily, to prevent patients from becoming carriers and to inhibit the dispersion of staphylococci.

For eradication of infection: Naseptin is applied four times daily for 10 days to eliminate organisms from the nares.

Contra-indications, warnings, etc Naseptin is intended for nasal application only, and it must be kept away from the eyes or ears. It is contra-indicated in patients with known sensitivity to neomycin.

Hypochlorite bleaches may cause brown stains to develop in fabrics which have previously been in contact with chlorhexidine preparations. An oxidising bleach such as sodium perborate should be used when laundering these fabrics.

Overdosage: Accidental ingestion of the contents of a Naseptin tube is not likely to have any adverse effect on the patient; neomycin is routinely taken orally, and chlorhexidine hydrochloride is not absorbed by this route.

Side-effects: Neomycin may cause skin reactions in some sensitive patients. If this occurs, use of Naseptin must be discontinued and, if necessary, symptomatic treatment given.

Pharmaceutical precautions Protect from heat, and use undiluted.

Legal category POM.

Package quantities Tubes of 5 g.

Further information Nil.

Product licence number 0029/5009.

NOLVADEX*

Presentation Nolvadex contains tamoxifen, which is the trans isomer of 1-[4-(2-dimethylaminoethoxy)-phenyl], 1,2-diphenyl 1-butene. It is presented as white, round, bi-convex tablets, marked with Nolvadex 10 on one face and ICI on the reverse. Each tablet contains 10 mg tamoxifen in the form of tamoxifen citrate (15.2 mg).

Uses At the recommended dosage Nolvadex has anti-oestrogenic properties, probably because it competes with oestrogen for binding sites in target organs. It does not have androgenic properties.

Nolvadex is indicated for:

1. The treatment of breast cancer. The proportion of patients with breast cancer who respond to Nolvadex is similar to that seen with oestrogens or androgens. However, because Nolvadex produces fewer serious side-effects it is more acceptable to the patient.
2. The treatment of anovulatory infertility.

Dosage and administration

1. **Breast cancer:** The recommended initial dose of Nolvadex is 10 mg (1 tablet) twice daily. If no response is seen within one month, dosage should be increased to 20 mg (2 tablets) twice daily.

2. **Infertility:** Before commencing any course of treatment, whether initial or subsequent, the possibility of pregnancy must be excluded. In women who are menstruating regularly, but with anovular cycles the initial course of treatment consists of twice-daily doses of 10 mg (1 tablet) of Nolvadex given on the second, third, fourth and fifth days of the menstrual cycle. If unsatisfactory basal temperature records or poor pre-ovulatory cervical mucus indicate that this initial course of treatment has been unsuccessful, further courses may be given during subsequent menstrual periods, increasing the dosage to 20 mg and then to 40 mg twice daily.

In women who are not menstruating regularly the initial course may begin on any day. If no signs of

ovulation are demonstrated then a subsequent course of treatment may start 45 days later with dosage increased as above. If a patient responds with menstruation then the next course of treatment is commenced on the second day of the cycle.

Contra-indications, warnings, etc *Pregnancy:* Nolvadex must not be given during pregnancy. Pre-menopausal patients must be carefully examined before treatment for breast cancer or infertility to exclude the possibility of pregnancy.

Menstruation is suppressed in a proportion of pre-menopausal women receiving Nolvadex for the treatment of breast cancer. Reversible cystic ovarian swelling has very occasionally been observed when such women have been treated with 40 mg Nolvadex twice daily for short periods.

A small number of patients with bony metastases have developed hypercalcaemia on initiation of therapy.

During long-term treatment side-effects are not as numerous or as serious with Nolvadex as with the androgens and oestrogens which are also used to treat breast cancer. Those that have been reported can be classified as either due to the anti-oestrogenic action of the drug, e.g. hot flushes, vaginal bleeding, and pruritis vulvae, or as more general effects, e.g. gastro-intestinal intolerance, tumour pain, light-headedness and, occasionally, fluid retention.

When side-effects are severe it is sometimes possible to control them by a simple reduction of dosage without loss of control of the disease. If side-effects do not respond to this measure, it may be necessary to stop the treatment.

Transient falls in platelet count, usually only to 80 000–90 000 but occasionally lower, have been reported in patients taking Nolvadex for breast cancer. No haemorrhagic tendency has been reported and the platelet counts have recovered even though treatment with Nolvadex has continued.

Overdosage: On theoretical grounds an overdosage would be expected to cause enhancement of the anti-oestrogenic side-effects mentioned above. Observations in animals show that extreme overdosage (100–200 × recommended daily dose) may produce oestrogenic effects.

Corneal and macular changes resulting in blurred vision have been described in a small number of cases treated continuously with 12–16 times the recommended starting dose for periods in excess of 17 months.

There is no specific antidote to overdosage, and treatment must be symptomatic.

Pharmaceutical precautions Protect from heat, and light.

Legal category POM.

Package quantities Nolvadex is packed in containers of 30 and 250 tablets.

Further information Nil.

Product licence number 0029/0064.

NOLVADEX*-D

Presentation Nolvadex-D contains tamoxifen, which is the trans isomer of 1-[4-(2-dimethylaminoethoxy)phenyl], 1,2-diphenyl 1-butene, formulated for once daily dosing. It is presented as white, octagonal bi-convex tablets, marked with 'Nolvadex D' on one face.

and ICI on the other. Each tablet contains 20 mg tamoxifen in the form of tamoxifen citrate (30.4 mg).

Uses At the recommended dosage Nolvadex-D has anti-oestrogenic properties, probably because it competes with oestrogen for binding sites in target organs. It does not have androgenic properties.

Nolvadex-D is indicated for:

1. The treatment of breast cancer. The proportion of patients with breast cancer who respond to Nolvadex-D is similar to that seen with oestrogens or androgens. However, because Nolvadex-D produces fewer serious side-effects it is more acceptable to the patient.

2. The treatment of anovulatory infertility.

Dosage and administration

1. **Breast Cancer:** The recommended initial dose of Nolvadex-D is 20 mg (1 tablet) once daily. If no response is seen within one month dosage should be increased to 40 mg (2 tablets) once daily.

2. **Infertility:** Before commencing any course of treatment, whether initial or subsequent, the possibility of pregnancy must be excluded. In women who are menstruating regularly but with anovular cycles the initial course of treatment consists of once daily doses of 20 mg (1 tablet) of Nolvadex-D given on the second, third, fourth and fifth days of the menstrual cycle. If unsatisfactory basal temperature records or poor pre-ovulatory cervical mucus indicate that this initial course of treatment has been unsuccessful, further courses may be given during subsequent menstrual periods, increasing the dosage to 40 mg (two tablets) and then to 80 mg (four tablets) daily.

In women who are not menstruating regularly the initial course may begin on any day. If no signs of ovulation are demonstrable then a subsequent course of treatment may start 45 days later with dosage increased as above. If a patient responds with menstruation then the next course of treatment is commenced on the second day of the cycle.

Contra-indications, warnings, etc Nolvadex-D must not be given during pregnancy. Pre-menopausal patients must be carefully examined before treatment for breast cancer or infertility to exclude the possibility of pregnancy.

Menstruation is suppressed in a proportion of pre-menopausal women receiving Nolvadex-D for the treatment of breast cancer. Reversible cystic ovarian swellings have very occasionally been observed when such women have been treated with 40 mg twice daily for short periods.

A small number of patients with bony metastases have developed hypercalcaemia on initiation of therapy.

During long-term treatment side effects are not as numerous or as serious with Nolvadex-D as with the androgens and oestrogens which are also used to treat breast cancer. Those that have been reported can be classified as either due to the anti-oestrogenic action of the drug, e.g. hot flushes, vaginal bleeding, and pruritus vulvae, or as more general effects, e.g. gastro-intestinal intolerance, tumour pain, light-headedness and, occasionally, fluid retention.

When side-effects are severe it is sometimes possible to control them by a simple reduction of dosage without loss of control of the disease. If side-effects do not respond to this measure, it may be necessary to stop the treatment.

Transient falls in platelet count, usually only to 80,000–10,000 but occasionally lower, have been reported in

patients taking tamoxifen for breast cancer. No haemorrhagic tendency has been reported and the platelet counts have recovered even though treatment with the drug has continued.

Overdosage: On theoretical grounds an overdosage would be expected to cause enhancement of the anti-oestrogenic side-effects mentioned above. Observations in animals show that extreme overdosage (100–200 × recommended daily dose) may produce oestrogenic effects.

Corneal and macular changes resulting in blurred vision have been described in a small number of cases treated continuously with 12–16 times the recommended starting dose for periods in excess of 17 months.

There is no specific antidote to overdosage, and treatment must be symptomatic.

Pharmaceutical precautions Protect from heat and light.

Legal category POM.

Package quantities Nolvadex-D is packed in containers of 30 tablets.

Further information Nil.

Product licence number 0029/0155.

PALUDRINE* TABLETS 100 mg

Presentation White, bi-convex tablets marked with the ICI roundel on one side and bisected on the other side with a letter P in each segment. Each tablet contains 100 mg of Proguanil Hydrochloride BP.

Uses Paludrine is an effective antimalarial agent. It is recommended for the prevention and suppression of malaria.

Dosage and administration *Adults:* The standard dosage is 1 tablet of 100 mg daily. In highly endemic areas this dose may be safely increased to 2 tablets daily. The daily dose is best taken with water after food. Non-immune subjects entering a malarious region are advised to begin treatment with Paludrine 24 hours before arrival. A daily dose of Paludrine should be continued for six weeks after leaving the area.

Children: Under 1 year: $\frac{1}{2}$ tablet (25 mg) daily.

1–4 years: $\frac{1}{2}$ tablet (50 mg) daily.

5–8 years: $\frac{3}{4}$ tablet (75 mg) daily.

9–12 years: 1 tablet (100 mg) daily.

Over 12 years: Adult dose daily.

Provided the tablet fragment gives the minimum amount specified precise accuracy in children's dosage is not essential, since the drug possesses a wide safety margin. For a young child, the dose may be administered crushed and mixed with milk, honey or jam.

Contra-indications, warnings, etc none.

Overdosage: The following effects have been reported in cases of overdosage: haematuria, renal irritation, epigastric discomfort and vomiting.

There is no specific antidote, and symptoms should be treated as they arise.

Side-effects: At normal dosage levels the side-effect most commonly encountered is mild gastric intolerance. This usually subsides as treatment is continued.

Pregnancy: It is generally accepted that all drug treat-

ment should be avoided if possible during the first trimester of pregnancy and medical advice sought. Paludrine has been widely used for over 30 years and a causal connection between its use and any adverse effect on mother or foetus has never been established.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Containers of 100 and 1,000.

Further information In any locality where drug-resistant malaria is known or suspected, it is essential to take local medical advice on what prophylactic regimen is appropriate. There have been reports on the administration of dapsone or sulphonamides concurrently with proguanil to enhance the prophylaxis.

References: Black, R. H. (1973) *Medical Journal of Australia* 1, 1265-70; Peters, W. (1970) *Chemotherapy and Drug Resistance in Malaria*. Academic Press, London and New York.

Product licence number 0029/5079.

PEPTAVLON®

Presentation Peptavlon (Pentagastrin Injection BP) is a clear, colourless, sterile, isotonic solution containing 250 mcg/ml of Pentagastrin BP. It is packed in neutral, clear glass ampoules which each contain 500 mcg of Pentagastrin BP in 2 ml of solution.

Uses Peptavlon is an analogue of the C-terminal tetrapeptide sequence of the hormone gastrin which stimulates gastric secretion. It exhibits all the physiological effects of the natural hormone. Peptavlon is used for the diagnostic testing of gastric secretion.

Dosage and administration The following procedure is adopted for testing gastric secretion with Peptavlon.

The patient receives no medication (e.g. antacids, etc.) that might affect the results of the tests for 24 hours and no food for 12 hours before the test. On the morning of the test a radio-opaque tube (Leven No. 7 or Ryle's 12-16Fr) is passed into the patient's stomach by way of the nose. Radiological observation is used to ensure that the tube is correctly positioned in the lower part of the body of the stomach.

The tube is securely fastened to the patient's nose and forehead with adhesive tape to ensure that it is not displaced. The patient lies on his left side.

The gastric juices are then collected by applying continuous suction (at 30-50 mm Hg below atmospheric pressure) to this tube, supplemented by manual suction. The patient takes occasional deep breaths to improve collection. The basal secretion is obtained by collecting samples at 15 minute intervals over an hour.

Peptavlon is then given, either at a dose of (a) 6 mcg/kg body weight subcutaneously, or (b) 0.6 mcg/kg/hour as a continuous intravenous infusion. A Tuberculin syringe is used to give a dose correct to 0.01 ml.

Specimens of the gastric juice are again collected, over periods of 10 or 15 minutes. The volume of the sample is measured and it is immediately filtered through gauze into a bottle. The acidity of each sample is determined by titration. The same doses and method may be used in both adults and children. If dilution is required normal saline may be used.

Contra-indications, warnings, etc When the pa-

tient has previously shown a severe idiosyncratic response to the drug. Peptavlon should not be administered.

Pregnancy: Peptavlon should not be administered during pregnancy.

Overdosage: The form of presentation makes it unlikely that overdosage will occur, and no such occurrence has been reported. As maximal secretory response is produced by the normal dosage, increased dosage would be expected to have no sequel other than an accentuation of the known side-effects.

Side-effects: At the recommended dosage the incidence of side-effects is extremely small, although very occasionally an individual may respond with hypotension and associated faintness. Other unwanted effects reported are sinking abdominal sensations, nausea, vomiting, flushing, sweating, headaches, drowsiness or exhaustion, heaviness or weakness of the legs. These effects disappear once administration of Peptavlon has ceased.

Pharmaceutical precautions Peptavlon ampoules must be kept below 4°C but above freezing point and protected from light. If dilution is required Sodium Chloride Injection BP may be used. This solution should be prepared immediately before it is required for use.

Legal category POM.

Package quantities Ampoules containing 2 ml Peptavlon, supplied in boxes of 5.

Further information Nil.

Product licence number 0029/5013.

PRIMAQUINE PHOSPHATE TABLETS

Presentation Primaquine phosphate is presented as a brown, bi-convex, sugar-coated tablets, which each contain 13.2 mg of Primaquine Phosphate BP (equivalent to 7.5 mg of base).

Uses Primaquine phosphate is an antimalarial drug belonging to the 8-aminoquinoline group. It is indicated for the radical cure of vivax and quartan malaria.

Dosage and administration **Adults:** A daily dose of 2 tablets is given for 10-14 days.

Children: The following dosage scheme has been found satisfactory:

up to 15 lb body weight: 1 mg daily for 14 days.

16-60 lb body weight: 2-4 mg daily for 14 days.

61-90 lb body weight: 5-7.5 mg daily for 14 days.

Over 90 lb body weight: As for adult dosage.

Contra-indications, warnings, etc To terminate overt attacks of malaria a schizonticidal drug such as Avlocor (trade mark) chloroquine phosphate should be given.

Caution is necessary when giving primaquine to non-Caucasian patients since from 5% to 10% of these have a genetic deficiency which makes them liable to develop blood dyscrasias on taking the drug. Initially only low doses of primaquine should be given to non-Caucasian patients. Further increments are then made to reach the therapeutic dose. During this period frequent blood examinations should be made to detect the possible occurrence of haemolytic anaemia or methaemoglobinaemia.

Pregnancy: If vivax malaria occurs during pregnancy a curative course of chloroquine should be given and radical cure with primaquine delayed until after delivery.

Overdosage: The symptoms of overdosage include anorexia, nausea, epigastric distress, abdominal cramps, occasional vomiting, weakness, cyanosis, haemolytic anaemia and jaundice, bone marrow depression and methaemoglobinemia.

There is no specific antidote and treatment must therefore be symptomatic.

Side-effects: It patients show the blood dyscrasias haemolytic anaemia and methaemoglobinemia) mentioned above, treatment must be stopped.

Pharmaceutical precautions Protect from light.

Legal category P.

Package quantities Containers of 1,000 tablets.

Further information Nil.

Product licence number 0029/5081.

RAZOXIN* ▼

Presentation Razoxin Tablets, each containing 25 mg razoxane as free base, are white to pale cream, and marked on one side with the ICI roundel and a division line on the other.

Uses In contrast to most anti-cancer agents Razoxin interferes with cell division at the G₂/M phase of the cycle.

Razoxin in combination with radiotherapy may be used for all forms of soft-tissue, chondro- and osteosarcomas. In comparison with radiotherapy alone, this combination may increase the response rate and reduce recurrence. Razoxin can produce remissions in previous radio-resistant lesions.

Razoxin may be useful alone or in combination with other antimitotic agents in the treatment of malignant lymphomas, including mycosis fungoides, acute leukaemias, especially the acute blast cell-crisis of chronic myeloid leukaemia, and Kaposi's sarcoma. Experience to date has been in open studies which indicated that the product is of value in patients in whom previous therapies have been unsuccessful.

Dosage and administration *Adults and children:* Razoxin is administered orally. The following guidelines are based on the regimes with which responses have been obtained. In all regimes, if unacceptable degrees of leucopenia thrombocytopenia or gastrointestinal disturbance occur, the dosage of Razoxin should be reduced or temporarily withdrawn to allow recovery.

Soft-tissue, Osteo- and Chondro-sarcomata: 125 mg (1 tablet) twice daily 3 days before the start of radiotherapy, continued throughout that therapy. On days when radiation is given, 1 tablet of Razoxin should be taken 1-4 hours before radiotherapy; the other tablet in the evening. The dosage of radiation should be selected and administered using normal criteria.

When a remission is obtained, 1 tablet of Razoxin twice daily should be continued after completion of the course of radiotherapy 5 days each week on a regular basis until there is evidence of tumour regrowth.

If unacceptable degrees of leucopenia or thrombocytopenia occur, the drug may be interrupted more frequently (e.g. alternate day dosing).

Malignant lymphomas (including mycosis fungoides): 1.5 to 1.5g/m²/week should be administered orally as

long as a remission is maintained. For example the dosage can be given as:

- 125 mg (1 tablet) twice daily on 3-5 days/week or
- three doses of 375 mg (3 tablets) given eight hours apart and repeated weekly

If an inadequate response is obtained the dosage may be increased, provided that the white cell count permits.

Leukaemias: 150-500 mg/m²/day for 3-5 days. Treatment should be repeated at 14-28 day intervals, depending on the blood count. Allopurinol may also be given to prevent uric acid deposition.

Kaposi's sarcoma: 333 mg/m² three times daily for 3 days every 3 weeks, and adjusted as necessary according to peripheral blood count.

Contra-indications, warnings, etc Razoxin is contra-indicated in pregnancy because of its action on cell division. Animal studies have revealed abnormalities of foetal development. It should not normally be administered to mothers who are breast feeding.

The use of Razoxin in non-malignant conditions, such as psoriasis, is not recommended.

The peripheral blood count should be monitored throughout Razoxin therapy. Unacceptable degrees of leucopenia or thrombocytopenia are quickly reversed on cessation of treatment. Unacceptable degrees of myelosuppression are more likely to occur in patients who have received extensive chemotherapy previously.

Female mice and rats developed tumours following long term intraperitoneal administration of Razoxin. The relevance of this finding to man is uncertain.

Razoxin is normally well tolerated; principal reported side-effects include leucopenia, thrombocytopenia, nausea, vomiting, diarrhoea, skin reactions and alopecia. Early skin reactions in patients receiving Razoxin plus radiotherapy may be more marked than those expected from radiotherapy alone. Severe late subcutaneous fibrosis has been reported in some patients receiving the combined therapy. There appears to be an increased likelihood of oesophagitis and pneumonitis in patients who require radiotherapy for thoracic lesions.

In cases of overdosage, signs and symptoms are likely to be qualitatively similar to side-effects; there is no specific antidote and treatment must be symptomatic.

Pharmaceutical precautions The tablets should be protected from heat, light and moisture.

Legal category POM.

Package quantities Aluminium tubes of 30 tablets.

Further information Activity as a component of multiple-drug chemotherapy regimes, in combination with radiotherapy and in maintaining responses initiated by other forms of therapy is under investigation in a variety of tumours. Because of its cell-cycle specific action it is logical to combine it with drugs which act at other stages in the cell cycle.

Product licence number 0029/0065.

SAVLOCLENS*

Presentation An amber yellow aqueous solution sterilised by autoclaving which contains Chlorhexidine Gluconate Solution BP 0.25% v/v (equivalent to 0.05% w/v chlorhexidine gluconate) and Cetrimide PhEur 0.5% w/v in sachets of 100 ml. Equivalent to a dilution of 1 in 30 of Savlon Hospital Concentrate.

Uses A broad-spectrum antiseptic with added detergent properties. Savlocens is used for cleansing and disinfecting physically contaminated wounds and burns.

Dosage and administration Use without further dilution for topical application only.

Contra-indications, warnings, etc For external use only. Not for injection. Savlocens should not come into contact with the brain, meninges or middle ear. When used in aseptic procedures disinfect the outside of the sachet before opening. Discard any surplus immediately after use.

Hypochlorite bleaches may cause brown stains to develop in fabrics which have previously been in contact with Hibitane Solutions. Detailed literature is available on request.

Side-effects: Idiosyncratic skin reactions can occur but are extremely rare

Accidental ingestion: carry out a gastric lavage with milk, egg white, gelatine or mild soap.

Pharmaceutical precautions Store away from heat.

Legal category P.

Package quantities Pack of 60 individual sachets.

Further information The British Pharmaceutical Codex (1973) recommends that antiseptics applied to broken skin should be sterile. The use of Savlocens complies with this recommendation.

Product licence number 0029/0142.

SAVLODIL*

Presentation A clear yellow aqueous solution sterilised by autoclaving and containing 0.075% v/v Chlorhexidine Gluconate Solution BP equivalent to chlorhexidine gluconate 0.015% w/v and Cetrimide PhEur 0.15% w/v in sachets of 25 ml and 100 ml.

Uses A broad-spectrum antiseptic with detergent properties for swabbing in obstetrics and during dressing changes. For disinfecting and cleansing traumatic and surgical wounds and burns.

Dosage and administration Use without further dilution for topical application only.

Contra-indications, warnings, etc For external use only. Not for injection. Savlodil should not come into contact with the eyes, brain, meninges or middle ear. When used in aseptic procedures disinfect the outside of the sachet before opening. Discard any surplus immediately after use.

Hypochlorite bleaches may cause brown stains to develop in fabrics which have previously been in contact with Hibitane Solutions. Detailed literature is available on request.

Side-effects: Idiosyncratic skin reactions can occur but are extremely rare.

Accidental ingestion: Carry out a stomach lavage with milk, egg white, gelatin or mild soap.

Pharmaceutical precautions Store away from heat.

Legal category P.

Package quantities Packs of 250 × 25 ml and 60 × 100 ml individual sachets. Bottles of 500 ml and 1,000 ml.

Further information The British Pharmaceutical Codex (1973) recommends that antiseptic applied to broken skin should be sterile. The use of Savlodil complies with this recommendation.

Product licence number 0029/0114.

SAVLON* HOSPITAL CONCENTRATE

Presentation A clear, deep orange, pleasantly perfumed aqueous solution containing 7.5% v/v Chlorhexidine Gluconate Solution BP equivalent to chlorhexidine gluconate 1.5% w/v and Cetrimide PhEur 15% w/v.

Uses An antiseptic for general use combining antibacterial activity against a wide range of organisms with useful cleansing properties.

<i>Mode of preparation</i>	<i>Dilution rate</i>	<i>Use</i>
10 ml made up to 1 litre with water	1 in 100 (1%) Aqueous	<i>Patients</i> Cleansing/disinfection of post-operative and casualty wounds. Antiseptic treatment of burns. Swabbing in obstetrics, gynaecology and urology. <i>Inanimates</i> Cleansing/disinfectant soak for used metal instruments. Clean instrument disinfection (30 minutes immersion). Cleansing/disinfection of equipment, furniture and fittings in the vicinity of the patient. Storage of clinical thermometers and sterile instruments.
35 ml made up to 1 litre with water	1 in 30 (approx.) Aqueous	<i>Patients</i> Cleansing/disinfection of post-operative wounds and casualty wounds where extra detergency/antimicrobial effects are indicated. Antiseptic treatment of burns where this higher strength is indicated. <i>Inanimates</i> Cleansing/disinfectant soak for used items which are normally contaminated with adherent substances, e.g. catheters, rubber appliances, etc.
35 ml with 200 ml water made up to 1 litre with 95% alcohol	1 in 30 (approx.) in 70% Alcohol	<i>Patients</i> Skin disinfection before pre-operative and other invasive procedures. <i>Inanimates</i> Disinfection of clean instruments and equipment (two minutes immersion). Disinfection of clinical thermometers.

Dosage and administration *Dilutions:* Dilutions are with tap water when bacteriologically approved. Pour diluent in slowly to prevent excessive foaming. Solutions applied to broken skin, wounds and burns should be sterilised by autoclaving at 115–116°C for 30 minutes or at 121–123°C for 15 minutes.

Contra-indications, warnings, etc For external use only. Dilute before use. Savlon should not come into contact with the eyes, brain, meninges or middle ear.

Prolonged immersion of rubber appliances in solutions prepared from Savlon Hospital Concentrate is undesirable. Syringes and needles intended for use in spinal injections should be rinsed very carefully with sterile water or saline after immersion in antiseptic solutions.

Hypochlorite bleaches may cause brown stains to develop in fabrics which have previously been in contact with Hibitane Solutions. Detailed literature is available on request.

Side-effects: Idiosyncratic skin reactions can occur but are extremely rare.

Accidental ingestion: Carry out a stomach lavage with milk, egg white, gelatin or mild soap.

Central paralysis cannot be countered by curare antagonists or CNS stimulants. Mechanically assisted ventilation with oxygen may be necessary. Control persistent convulsions with minimum doses of a short-acting barbiturate.

Pharmaceutical precautions Savlon Hospital Concentrate must be protected from heat and light.

Cork may protect certain Gram-negative organisms from the action of many antiseptics. Savlon Hospital Concentration Solutions should therefore always be stored in the manufacturer's original container.

Water and Industrial Methylated Spirits are suitable diluents, as described above. Where it is required to leave instruments stored in Savlon Solutions for more than eight hours, sodium nitrite 0.4% w/v should be added to prevent metal corrosion. For this purpose tablets containing 1 g sodium nitrite are available free of charge and four of these should be dissolved in each litre of the final dilute solution. The solution should be changed every seven days.

As a precaution against bacterial contamination, stock aqueous solutions should contain at least 4% v/v of isopropyl alcohol or 7% v/v of ethyl alcohol, which may be denatured (for example Industrial Methylated Spirits) in the final dilution.

Legal category GSL.

Package quantities The following packings are available: Containers of 1 litre and 5 litres. Laminated foil sachets of 10 ml and 25 ml. Dispensers to fit 5L are also available.

Further information Nil.

Product licence number 0029/5012.

SIOPEL* CREAM

Presentation Siopel is a white, water-repellant barrier cream which contains 0.3% w/w Cetrimide PhEur and 10% w/w Dimethicone 1,000 BPC.

Uses Siopel Cream combines the bactericidal power of cetrimide with the water-repellant properties of the silicone dimethicone. It is useful whenever the skin

needs to be protected from water-soluble irritants. Specific indications are:

Chronic dermatoses – especially useful to doctors, nurses and veterinary surgeons whose skins are sensitive to antibiotics, local anaesthetic and other sensitising agents.

Colostomies, ileostomies, haemorrhoidectomies and other forms of surgery where skin requires protection from body fluids and discharges.

Pruritus ani due to persistent diarrhoea; napkin rash; and the effects of incontinence in geriatric patients.

Eczematous and neurodermatitic lesions, and for protecting the intact skin surrounding varicose ulcers.

Dosage and administration The skin is washed and dried. Siopel Cream is then applied sparingly and massaged well into the skin. For continuous protection Siopel is applied three to five times daily for three to four days, then used once or twice daily. These recommendations apply to both children and adults.

Contra-indications, warnings, etc Siopel Cream is for external use only. It is contra-indicated when the patient has shown a previous idiosyncratic reaction to its use. Siopel Cream must not be used on skin that is acutely inflamed or weeping, or before the skin has been cleansed of contaminating irritants.

Overdosage: Excessive external application or ingestion of Siopel Cream is not likely to have any toxic effect.

Side-effects: Skin sensitivity to the components of Siopel Cream has been reported on a few occasions. In such cases treatment with Siopel should be stopped.

Pharmaceutical precautions Use undiluted.

Legal category GSL.

Package quantities Containers of 50 g and 500 g.

Further information Nil.

Product licence number 0029/5014.

SULPHAMEZATHINE* INJECTION

Presentation A pale straw-coloured, sterile, aqueous solution containing 1 g Sulphadimidine Sodium BP in 3 ml.

Uses Sulphamezathine is a broad-spectrum bacteriostat, particularly effective in the following conditions: meningococcal meningitis, urinary tract infections, bacillary dysentery.

Dosage and administration The adult dose given represents the average of current practice. It can be modified to suit individual needs; in very severe infections, for instance, the dose for Sulphamezathine both initially and in maintenance can be increased with safety by one-third.

Initial Maintenance

Adults and children over 16 years	3 g	1–1½ g every six hours
Children 6 months	0.5 g	0.25 g six-hourly
Children ½–4 years	1.0 g	0.5 g six-hourly
Children 4–8 years	1.5 g	0.75 g six-hourly
Children 8–12 years	2.0 g	0.75–1.0 g six-hourly
Children 12–16 years	2.5 g	1.0–1.25 g six-hourly

Urinary tract infections: Adults: Initial dose 2 g: subsequent doses 0.5–1 g every six or eight hours.

Prophylaxis: 0.5–1 g daily.

Parenteral administration: In cases of emergency, Sulphamezathine is given parenterally as the sodium salt in solution, either by intravenous or intramuscular injection.

Contra-indications, warnings, etc Sulphamezathine must not be administered intrathecally.

Pregnancy: On theoretical grounds all sulphonamides, including Sulphamezathine are contra-indicated in pregnant women and premature infants.

Overdosage: Give sodium bicarbonate 10 g every hour orally, or continuous intravenous infusion of one-sixth molar sodium lactate (1.87%). Ensure a high fluid intake to produce at least 1.5 litres of urine daily.

Side-effects: Sulphamezathine is one of the best tolerated and least toxic sulphonamides. Side-effects are infrequent, but may include nausea, vomiting, cyanosis, drug fever, rashes and leucopenia. Isolated reports have been received of crystalluria, haematuria and short-lasting anuria.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Ampoules 3 ml. Boxes of 25.

Further information Nil.

Product licence number 0029/5033.

**SYNALAR* CREAM
SYNALAR* OINTMENT
SYNALAR* LOTION
SYNANDONE* CREAM
SYNANDONE* OINTMENT
SYNALAR* FORTE CREAM**

Presentation Synalar and Synandone are presented as white, water-miscible creams and greasy ointments. Synalar is also presented as an aqueous lotion. Synalar Forte is presented as a white, water-miscible cream.

Synalar, Synandone and Synalar Forte (referred to as Synalar Preparations below) are presentations of the steroid Fluocinolone Acetonide BP.

The following percentages of this corticosteroid are contained in the three preparations:

Synandone 0.01% w/w fluocinolone acetonide

Synalar 0.025% w/w fluocinolone acetonide

Synalar Forte 0.2% w/w fluocinolone acetonide

Uses Synalar preparations contain an effective topical corticosteroid, and are suitable for treating a wide variety of local inflammatory, pruritic and allergic disorders of the skin. Synalar is particularly suitable for topical application in:

Eczema and dermatitis; atopic eczema, seborrhoeic eczema, discoid eczema, pompholyx, otitis externa, contact dermatitis, neurodermatitis, intertrigo.

Non-specific ano-genital pruritis; prurigo.

Psoriasis. Lichen planus. Discoid lupus erythematosus.

Synandone is indicated for milder forms of these conditions; for maintenance therapy when control has been achieved with Synalar; for use under occlusive dressings; and for paediatric dermatology, e.g. infantile eczema.

Synalar Forte is a more concentrated preparation and is useful in intractable skin conditions, particularly: mycosis fungoides, chronic discoid lupus erythematosus and localised conditions, e.g. pretibial myxoedema, necrobiosis lipoidica diabetorum and granuloma annulare.

Dosage and administration A small quantity of the Synalar preparation is applied lightly to the affected area two or three times a day, and massaged gently and thoroughly into the skin. When an occlusive dressing is required, the affected area should first be thoroughly cleansed, the Synalar preparation is then applied and covered with a suitable plastic dressing.

In some cases the application of hot, moist compresses may be an advantage. The creams are particularly suitable for moist or weeping surfaces and for flexures of the body, the ointments are suitable for dry, scaly lesions; and the lotion is best suited for application to large areas and hairy regions of the body. The lotion should be shaken before use.

These recommendations apply to both children and adults.

Contra-indications, warnings, etc Synalar preparations are contraindicated in primary infections of the skin caused by fungi (e.g. candida, dermatophytes), viruses (e.g. herpes simplex, chicken pox), bacteria (e.g. impetigo, syphilis) and in rosacea, acne and perioral dermatitis.

Precautions: Long-term continuous topical steroid therapy can produce local atrophic skin changes. Particular care should therefore be taken if applying steroids to the face. Prolonged use of topical steroids or treatment of extensive areas, even without occlusion, can result in sufficient absorption of the steroid to produce the features of adrenal suppression, especially in infants and children. When there is a bacterial infection associated with an inflammatory skin condition, Synalar preparations should only be administered if adequate antibacterial cover is given.

Treatment should be discontinued if unfavourable reactions are seen.

Pregnancy: Topical administration of corticosteroids to pregnant animals has been shown to cause abnormalities of foetal development. Although the relevance of this finding to human application has not been established, when topical steroid treatment is considered necessary during pregnancy both the amount applied and the length of treatment should be minimised.

The amount of Synalar Forte used under occlusion should be restricted to 2 g per day.

Side-effects: With Synalar preparations, side-effects are extremely rare, but, as with all topical corticosteroids, the occasional patient may show an adverse reaction such as hypersensitivity. Extensive treatment can result in both local atrophic changes, such as striae, skin thinning and telangiectasia and systemic effects such as adrenal suppression.

The use of topical steroids on infected lesions, without the addition of appropriate anti-infective therapy, can result in the spread of opportunist infections.

The 50 g tube of Synalar contains 12.5 mg of the steroid, other tubes containing proportionately less. No toxic effects are likely to occur even if the full contents of a 50 g tube are ingested orally. Similarly the ingredients of the base are unlikely to have any toxic effect in the quantities in which they occur. Therefore no remedial action is required in the event of accidental ingestion.

Pharmaceutical precautions Protect from heat and use undiluted.

Legal category POM.

Package quantities

	<i>Cream and ointment</i>				<i>Lotion</i>	
	<i>Dispensing packs – tubes</i>				<i>Hospital pack only – jar</i>	<i>Polythene container</i>
	<i>5 g</i>	<i>15 g</i>	<i>30 g</i>	<i>50 g</i>		
Synalar	†	†	†	†	†	†
Synandone			†			
Synalar Forte	†					

Further information Nil.

Product licence numbers

Synalar Cream	0029/5037
Synalar Ointment	0029/5041
Synalar Lotion	0029/5040
Synandone Cream	0029/5047
Synandone Ointment	0029/5049
Synalar Forte	0029/5038

SYNALAR* CREAM 1 IN 4 DILUTION SYNALAR CREAM 1 IN 10 DILUTION

Presentation Synalar Cream in dilutions of 1 in 4 and 1 in 10 are presented as white, water-miscible creams which contain 0.00625% and 0.0025% w/w Fluocinolone Acetonide BP respectively.

Uses Synalar Cream dilutions contain an effective topical corticosteroid and are suitable for treating the milder forms of a wide variety of local inflammatory, pruritic and allergic disorders of the skin. Synalar Cream dilutions are particularly suitable for topical application in:

Eczema and dermatitis: atopic eczema, seborrhoeic eczema, discoid eczema, pompholyx, otitis externa, contact dermatitis, neurodermatitis, intertrigo.
Non-specific ano-genital pruritus; prurigo.
Psoriasis. Lichen planus.

Synalar Cream dilutions are indicated for milder forms of these conditions; for maintenance therapy when control has been achieved with Synalar; for use under occlusive dressings; and for paediatric dermatology, e.g.: infantile eczema.

Dosage and administration A small quantity of Synalar Cream dilution is applied lightly to the affected area two or three times a day, and massaged gently and thoroughly into the skin. When an occlusive dressing is required, the affected area should first be thoroughly cleansed; Synalar Cream dilution is then applied and covered with a suitable plastic dressing. Synalar Cream dilutions are particularly suitable for moist or weeping surfaces and for flexures of the body.

These recommendations apply to both children and adults.

Contra-indications, warnings, etc Synalar Cream dilutions are contra-indicated in primary infections of the skin caused by fungi (e.g.: candida, dermatophytes), viruses (e.g.: herpes simplex, chicken pox), bacteria (e.g.: impetigo, syphilis) and in rosacea, acne and peri-oral dermatitis.

Precautions: Long-term continuous topical steroid therapy can produce local atrophic skin changes. Particular care should therefore be taken if applying steroids to the face. Prolonged use of topical steroids or treatment of extensive areas, even without occlusion, can result in sufficient absorption of the steroid to produce the features of adrenal suppression, especially in infants and children. When there is a bacterial infection associated with an inflammatory skin condition, Synalar preparations should only be administered if adequate antibacterial cover is given.

Treatment should be discontinued if unfavourable reactions are seen.

Pregnancy: Topical administration of corticosteroids to pregnant animals has been shown to cause abnormalities of fetal development. Although the relevance of this finding to human application has not been established, when topical steroid treatment is considered necessary during pregnancy both the amount applied and the length of treatment should be minimized.

Side-effects: With Synalar Cream dilutions, side-effects are extremely rare, but, as with all topical corticosteroids, the occasional patient may show an adverse reaction such as hypersensitivity or peri-oral dermatitis. Extensive treatment can result in both local atrophic changes, such as striae, skin thinning and teleangiectasia and systemic effects such as adrenal suppression.

The use of topical steroids on infected lesions, without the addition of appropriate anti-infective therapy, can result in the spread of opportunist infections.

Pharmaceutical precautions Protect from heat and use undiluted.

Legal category POM.

Package quantities Synalar Cream dilutions 1 in 4 and 1 in 10 are supplied 50 g tubes and 500 jars.

Further information Nil.

Product licence numbers

Synalar Cream 1 in 4 dilution	0029/0151
Synalar Cream 1 in 10 dilution	0029/0152

SYNALAR* GEL

Presentation Synalar Gel consists of Fluocinolone Acetonide BP 0.025% w/w, presented as a clear, water-miscible gel.

Uses Synalar Gel is an effective topical corticosteroid formulated as a clear, non-greasy gel. It is designed for application to the scalp and other hairy regions, but can equally well be applied elsewhere on the body. Specific indications for Synalar gel are seborrhoea, seborrhoeic dermatitis and psoriasis of the scalp, but it may be administered satisfactorily to inflammatory dermatoses on other parts of the body.

Dosage and administration A small quantity of Synalar Gel is massaged into the scalp night and morning using the finger tips. For maintenance therapy, treatment should be repeated once or twice weekly. For maintenance therapy it may be advantageous to combine treatment with the weekly use of a suitable medicated cleaning preparation such as Cetavlon (trade mark) PC. Synalar Gel should be well washed out of the scalp before applying the Cetavlon PC.

These recommendations apply to both children and adults.

Contra-indications, warnings, etc Synalar Gel is contra-indicated in primary infections of the skin caused by fungi (e.g. candida, dermatophytes), viruses (e.g. herpes simplex, chicken pox), bacteria (e.g. impetigo, syphilis) and in rosacea, acne and peri-oral dermatitis.

Precautions: Long-term continuous topical steroid therapy can produce local atrophic skin changes. Particular care should therefore be taken if applying steroids to the face. Prolonged use of topical steroids or treatment of extensive areas, even without occlusion, can result in sufficient absorption of the steroid to produce the features of adrenal suppression, especially in infants and children. Where there is a bacterial infection associated with an inflammatory skin condition, Synalar preparations should only be administered if adequate anti-bacterial cover is given.

Treatment should be discontinued if unfavourable reactions are seen.

Pregnancy: Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. Although the relevance of this finding to human application has not been established, when topical steroid treatment is considered necessary during pregnancy both the amount applied and the length of treatment should be minimised.

Side effects: With Synalar preparations, side-effects are extremely rare, but, as with all topical corticosteroids, the occasional patient may show an adverse reaction such as hypersensitivity. Extensive treatment can result in both local atrophic changes, such as striae, skin thinning and telangiectasia and systemic effects such as adrenal suppression.

The use of topical steroids on infected lesions, without the addition of appropriate anti-infective therapy, can result in the spread of opportunist infections.

The 30 g tube of Synalar Gel contains 7.5 mg of the steroid. No toxic effects are likely to occur, even if the full contents of a 30 g tube are ingested orally. Similarly the ingredients of the base are unlikely to have any toxic effects in the quantities in which they occur. Therefore no remedial action is required in the event of ingestion.

Pharmaceutical precautions Protect from heat and use undiluted.

Legal category POM.

Package quantities Synalar Gel is supplied in 30 g tubes.

Further information Nil.

Product licence number 0029/5039.

SYNALAR* C CREAM AND OINTMENT

Presentation These products contain 0.025% w/w of the steroid Fluocinolone Acetonide BP and 3% w/w of Clioquinol BP (chinoxaline, iodochlorohydroxyquinoline). Synalar C is presented as an off-white, water-miscible cream and as a grey ointment.

Uses Synalar C combines the effective topical corticosteroid Synalar with the effective antibacterial and antifungal agent Clioquinol BP.

It is indicated for inflammatory dermatoses – including eczema, dermatitis, seborrhoea, psoriasis, sycosis barbae, intertrigo and ano-genital pruritus – where bacterial and/or fungal infection is present or is likely to occur.

Dosage and administration A small quantity of the Synalar C preparation is applied lightly to the affected area two or three times a day, and massaged gently and thoroughly into the skin. If an occlusive dressing is indicated, the affected area is first thoroughly cleansed, the Synalar C preparation is then applied and covered with a suitable plastic dressing. Synalar C Cream is particularly suitable for very inflamed or weeping surfaces and for flexures of the body; whilst Synalar C Ointment is more suitable for dry scaly lesions. These recommendations apply to both children and adults.

Contra-indications, warnings, etc Synalar C preparations are contra-indicated in primary infections of the skin caused by fungi (e.g. candida, dermatophytes), viruses (e.g. herpes simplex, chicken pox), bacteria (e.g. impetigo, syphilis) and in rosacea, acne and peri-oral dermatitis.

Precautions: Long-term continuous topical steroid therapy can produce local atrophic skin changes. Particular care should therefore be taken if applying steroids to the face. Prolonged use of topical steroids or treatment of extensive areas, even without occlusion, can result in sufficient absorption of the steroid to produce the features of adrenal suppression, especially in infants and children.

Treatment should be discontinued if unfavourable reactions are seen.

Pregnancy: Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. Although the relevance of this finding to human application has not been established, when topical steroid treatment is considered necessary during pregnancy, both the amount applied and the length of treatment should be minimised.

Side effects: With Synalar preparations, side-effects are extremely rare, but, as with all topical corticosteroids, the occasional patient may show an adverse reaction such as hypersensitivity. Extensive treatment can result in both local atrophic changes, such as striae, skin thinning and telangiectasia and systemic effects such as adrenal suppression.

Local application of clioquinol in creams or ointments may occasionally cause severe irritation, which may be less marked because of the fluocinolone acetonide. Treatment should be discontinued if unfavourable reactions occur.

Staining may occur due to breakdown of the clioquinol. A protective covering may be placed over the application to prevent staining of clothing or linen.

The 15 g tube of Synalar C contains 3.75 mg of steroid and 0.45 g of Clioquinol BP. No toxic effects are likely to occur, even if the full contents of a tube are ingested orally. Similarly the ingredients of the base are unlikely to have any toxic effects in the quantities in which they occur. Therefore no remedial action is required in the event of ingestion.

Pharmaceutical precautions Protect from heat, and use undiluted.

Legal category POM.

Package quantities Synalar C Cream and Ointment are available in tubes of 15 g.

Further information Nil.

Product licence numbers

Synalar C Ointment 0029/5043

Synalar C Cream 0029/5042

SYNALAR* N CREAM, OINTMENT AND LOTION

Presentation These products contain 0.025% w/w of the steroid Fluocinolone Acetonide BP and 0.5% w/w of Neomycin Sulphate PhEur. Synalar N is presented as a white, water-miscible cream, a greasy ointment and an aqueous lotion.

Uses Synalar N combines the effective topical corticosteroid Synalar with an effective antibacterial agent, Neomycin Sulphate PhEur.

It is indicated for inflammatory dermatoses – including eczema, dermatitis, seborrhoea, psoriasis, intertrigo and ano-genital pruritus – where bacterial infection is present or is likely to occur.

Dosage and administration A small quantity of the Synalar N preparation is applied lightly to the affected area two or three times a day, and massaged gently and thoroughly into the skin. If an occlusive dressing is indicated, the affected area is first thoroughly cleansed, the Synalar N preparation is then applied and covered with a suitable plastic dressing. Synalar N Cream is particularly suitable for very inflamed or weeping surfaces and for flexures of the body, whilst Synalar N Ointment is more suitable for dry, scaly lesions. These recommendations apply to both children and adults.

Contra-indications, warnings, etc Synalar N preparations are contra-indicated in primary infections of the skin caused by fungi (e.g. candida, dermatophytes), viruses (e.g. herpes simplex, chicken pox), bacteria (e.g. impetigo, syphilis) and in rosacea, acne and peri-oral dermatitis. Synalar N is contra-indicated in those patients with a history of hypersensitivity to neomycin. Topical neomycin preparations should not be applied to the external auditory canal of patients with perforated eardrums.

Precautions: Long-term continuous topical steroid therapy can produce local atrophic skin changes. Particular care should therefore be taken if applying steroids to the face. Prolonged use of topical steroids or treatment of extensive areas, even without occlusion, can result in sufficient absorption of the steroid to produce the features of adrenal suppression, especially in infants and children.

Because of the potential hazard of nephrotoxicity and ototoxicity associated with neomycin, prolonged use or use of large amounts of the product should be avoided in conditions where absorption of neomycin is possible.

These preparations are not for ophthalmic use.

Treatment should be discontinued if unfavourable reactions are seen.

Pregnancy: Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. Although the relevance of this finding to human application has not been established, when topical steroid treatment is considered necessary during pregnancy, both the amount applied and the length of treatment should be minimised.

Side effects: With Synalar preparations, side-effects are extremely rare, but, as with all topical corticosteroids, the occasional patient may show an adverse reaction such as hypersensitivity. Extensive treatment can result in both local atrophic changes, such as striae, skin thinning and telangiectasia and systemic effects such as adrenal suppression.

The 30 g tube of Synalar N contains 7.5 mg of steroid and 150 mg of neomycin. No toxic effects are likely to

occur, even if the full contents of a 30 g tube are ingested orally. Similarly the ingredients of the base are not likely to have any toxic effects in the quantities in which they occur. Therefore no remedial action is required in the event of ingestion.

Pharmaceutical precautions Protect from heat and use undiluted.

Legal category POM.

Package quantities Synalar N Cream and Ointment are available in tubes of 5 g, 15 g and 30 g. Synalar N Lotion is available in 20 ml plastic containers. Synalar N Ointment is also available in 500 g jars.

Further information Nil.

Product licence numbers

Synalar N Cream	0029/5044
Synalar N Ointment	0029/5046
Synalar N Lotion	0029/5045

TETMOSOL* SOLUTION

Presentation Tetmosol Solution is a clear, brown liquid, forming a fine suspension when diluted with water. It contains Monosulfiram BP (Sulfiram INN) as a 25% w/w solution in industrial methylated spirit.

Uses Tetmosol Solution is a parasiticide active against the burrowing mite *Sarcoptes scabiei*. It is indicated for the treatment and prophylaxis of scabies.

Dosage and administration Before application Tetmosol Solution should be diluted with two to three parts of water. The patient's body should be liberally washed with soap and water and thoroughly dried. Apart from the face and scalp, the entire body should be painted with the dilute solution, which is rubbed well in and left to dry. About ten minutes is allowed for the skin to dry naturally and the patient then dresses. Application is suitable for use in clinics dealing with children. In difficult cases this routine may be repeated successively for two or three days. These instructions are applicable to adults and children.

Contra-indications, warnings, etc Tetmosol Solution is contra-indicated when the patient has previously shown an idiosyncratic response to its application. The solution should not be applied near a naked flame. Because of the close chemical relationship between monosulfiram and disulfiram, it is considered advisable to abstain from alcohol before and for at least 48 hours after the application of Tetmosol.

Overdosage: The solution contains alcohol and monosulfiram, and if ingested this combination will produce a severe reaction, with flushing, dyspnoea, headache, dizziness, nausea, vomiting, drowsiness or sleep. Tachycardia and hypotension may also occur and the resultant myocardial ischaemia may be fatal.

Symptomatic measures are required – oxygen, if dyspnoea is excessive, and control of the blood pressure. Other treatment which has been found useful includes cardiac stimulants, intravenous iron, ascorbic and nicotinamide, adenine and intravenous sodium thiosulphate.

Side-effects: Very few side-effects occur with Tetmosol Solution, even in cases of undiluted application. A few cases of erythematous rash have been reported, but these are rare enough to be considered as idiosyncratic responses of the patients concerned.

Pharmaceutical precautions Tetmosol Solution should not be stored in a cold place as this causes deposition of crystals. These can be redissolved by immersing the bottle in warm water. The solution is flammable and should not be kept near a naked flame. Water is a suitable diluent for Tetmosol.

Legal category P.

Package quantities Bottles of 100 ml and 2 litres.

Further information Nil.

Product licence number 0029/5011.

TRILENE*

Presentation Trilene is Trichloroethylene PhEur. It is a clear blue, volatile liquid, non-explosive and non-flammable in the concentration usually used. It resembles chloroform in odour but is distinguished by the inclusion of an inert blue dye.

Trilene consists of trichloroethylene stabilised with thymol 0.01% w/w.

Uses Trilene is a volatile anaesthetic, which is suitable for the induction and maintenance of anaesthesia for all types of surgery and in patients of all ages. Trilene can be used for the production of analgesia without loss of consciousness.

Dosage and administration A number of special Trilene vaporisers are available for administration.

The vapour concentration should be minimal at all times (0.5–2% by volume) and it is never necessary to bubble the carrier gas through the liquid. Trilene may be used alone with air or oxygen, but it is more commonly used as an adjunct to nitrous oxide/oxygen anaesthesia.

For the production of analgesia without loss of consciousness, Trilene should be administered in low concentrations (0.35–0.5%), from draw-over units using room air as carrier gas. Several vaporisers capable of delivering Trilene in analgesic concentrations are available.

The above dosages are suitable for both adults and children.

Contra-indications, warnings, etc Trilene must never be used in closed circuit systems with soda lime.

Profound muscular relaxation cannot be achieved with unsupplemented Trilene anaesthesia, and if tachypnoea and cardiac arrhythmias are to be avoided, no attempt should be made to deepen anaesthesia by using Trilene concentrations in excess of 2.5%.

The concurrent administration of adrenaline and Trilene is inadvisable. Trilene should be withdrawn before the completion of surgery to facilitate recovery. Trichloroethylene anaesthesia in the presence of high grade beta-blockade may result in dangerous reductions of cardiac output.

Overdosage: Ingestion cases should be treated by gastric emptying and supportive treatment.

Side-effects: Post-operative nausea, vomiting and headache occur rarely. Cardiac arrhythmias may occur if attempts to deepen anaesthesia are made.

Pharmaceutical precautions Trilene and its vapour are not flammable, but they must not come into contact with hot surfaces as toxic decomposition products are thereby produced. Trilene must be stored in closed containers and protected from light and air.

Trilene should be kept in its original container until immediately prior to use.

It is not advisable to retain Trilene in an inhaler or anaesthetic machine for any length of time after use, and to avoid possible oxidation it is recommended that a fresh supply is placed in the vaporiser every few days.

Whilst in the liquid phase Trilene must not be diluted or contaminated; however, in the vapour phase it may be administered with air, oxygen or nitrous oxide/oxygen.

Legal category P.

Package quantities Bottles of 500 ml.

Further information Trilene allows a smooth, simple induction of anaesthesia without the patient coughing or struggling. Absence of capillary oozing is particularly appreciated with Trilene, and the nonflammable nature of the vapour avoids the risk of fire, or explosion from lights, cauteries, etc. In addition Trilene provides a marked degree of post-operative analgesia, which contributes greatly to the comfort of the patient.

Product licence number 0029/5083.

VIVALAN*

Presentation Vivalan Tablets, each containing viloxazine hydrochloride equivalent to 50 mg of viloxazine, are round, bi-convex, yellow, film-coated and marked with the name Vivalan.

Indications: Symptoms of depressive illness, especially where sedation is not required.

Dosage and administration *Adults:* Most patients respond to 150–300 mg/day in divided doses and the total daily dose should not exceed 400 mg. The last dose of the day should be taken not later than 6 p.m.

Elderly: 100mg/day initially. The initial dose should be increased with caution under close supervision. Half the normal maintenance dose may be sufficient to produce a satisfactory clinical response.

Children: Vivalan is not recommended in children under 14 years of age.

Contra-indications, warnings, etc Mania, severe liver disease, history of peptic ulcer, recent myocardial infarction, during breast feeding.

Use in pregnancy: There is no evidence as to the drug's safety in human pregnancy; do not use during pregnancy, especially during the first and third trimesters, unless there are compelling reasons.

Precautions: Vivalan should be used with caution in patients with ischaemic heart disease and congestive cardiac failure, or any degree of heart block.

Caution is advised when administering Vivalan to patients with epilepsy, especially those receiving phenytoin (see below).

Patients posing a high suicidal risk require close initial supervision.

If surgery is necessary during therapy, the anaesthetist should be informed that the patient has received Vivalan.

Drug interactions: Vivalan should not be given concurrently with, or within two weeks of cessation of therapy with monamine oxidase inhibitors.

Vivalan may decrease the antihypertensive effect of guanethidine, debrisoquine, bethanidine, and possibly clonidine.

Caution is advised when administering Vivalan to patients taking phenytoin. The dose of phenytoin may need reducing to prevent toxic blood levels occurring.

On theoretical grounds, caution is advised when patients receiving L-DOPA are treated with Vivalan.

Most antidepressants have been shown to potentiate the central nervous depressant action of alcohol, and, therefore, patients should be advised of the risks involved in drinking alcohol whilst on antidepressant medication.

Warnings and adverse effects: Nausea is frequently observed, but may be transient. Headache and vomiting may also occur.

As improvement may not occur during the first two weeks of treatment, patients should be closely monitored during this period.

Vivalan initially may impair alertness, and patients should be advised of the possible hazard when driving or operating machinery.

Anticholinergic side-effects, such as dry mouth, disturbance of accommodation, tachycardia, constipation and hesitancy of micturition have been reported less frequently with viloxazine than with tricyclic antidepressants.

Cardiac arrhythmias and severe hypotension are less likely to occur with viloxazine than with tricyclic antidepressants in high dosage or in deliberate overdose.

Adverse effects which have been reported rarely with viloxazine include exacerbation of anxiety and agitation, drowsiness, confusion, ataxia, dizziness, insomnia, tremor, paraesthesia, sweating, musculo-skeletal pain, mild hypertension and skin rashes.

Psychotic manifestations, including hypomania and aggressive behaviour may be exacerbated.

Two serious adverse effects possibly associated with Vivalan have been reported:

- (a) jaundice with elevated transaminases
- (b) convulsions

Withdrawal symptoms are rare, but may include malaise, headache and vomiting.

Overdosage: Vivalan is rapidly absorbed and gastric lavage should be carried out with minimum delay. Overdosage should be treated on general principles with careful monitoring of vital functions, together with intensive supportive therapy where necessary. As the drug is almost exclusively excreted in urine, forced diuresis may be performed to reduce blood levels. There is no specific antidote.

Further information Vivalan is an oxazine and is chemically distinct from the tri- and tetracyclic antidepressants, while retaining the biogenic amine reuptake inhibitory properties in the central nervous system. Pharmacologically, it differs from these drugs in its decreased sedative and anticholinergic properties, and its lesser effect on the cardiovascular system.

Legal category POM.

Product licence number 0029/0074

**Trade Mark*

International Laboratories Limited

Charwell House

Wilsom Road

Alton, Hampshire GU34 2TJ

MIGRALEVE*

Presentation *Pink Migraleve*: Blister-packed, pink, capsule-shaped, film-coated tablets, engraved 'MGE' on one face, each containing:

Bucizine dihydrochloride	6.25 mg
Paracetamol BP	500 mg
Codeine Phosphate BP	8 mg
Diocetyl Sodium Sulphosuccinate BPC	10 mg

Yellow Migraleve: Blister-packed, yellow, capsule-shaped, film-coated tablets, engraved 'MGE' on one face, each containing:

Paracetamol BP	500 mg
Codeine Phosphate BP	8 mg
Diocetyl Sodium Sulphosuccinate BPC	20 mg

Uses Symptomatic and prophylactic treatment of classical and non-classical migraine and variants, including migrainous neuralgia (cluster headache), facial and ophthalmoplegic migraine and 'sick' headache. Paracetamol and codeine phosphate are analgesics. Bucizine dihydrochloride is an antihistamine which is included for its antinauseant properties. These three in combination appear to act synergistically in preventing and/or aborting migraine attacks. The surface active agent diocetyl sodium sulphosuccinate prevents codeine constipation.

Dosage and administration *Adult: Treatment*: 2 Pink Migraleve immediately or prior to the attack if warning symptoms are apparent. If symptoms persist, 2 Yellow Migraleve every three or four hours. Maximum 8 tablets (2 Pink and 6 Yellow) in 24 hours.

Prophylaxis: 2 Pink tablets at night during periods of impending attacks.

Children: Normally 1 tablet of the appropriate colour where 2 are indicated for adults.

Contra-indications, warnings, etc *Side-effects*: Drowsiness is an occasional feature of migraine attacks. It may, theoretically, also be caused by the small

antihistamine content of Pink Migraleve, but this has never been apparent from clinical observations.

Precautions: Migrainous patients suffering from high blood pressure should first be treated for this condition independently. Individuals with a history of renal disease should be treated cautiously as with any long-term analgesic therapy. Because of the possibility of drowsiness, consideration should be given to patients involved in hazardous occupations.

Treatment of overdosage: If more than 10 tablets have been taken, stomach washout. Correct electrolyte imbalance. Early alkaline diuresis may be valuable. Seek advice from specialised treatment centre

Pharmaceutical precautions Nil.

Legal category P.

Package quantities 24 (16 Pink and 8 Yellow) and 12 (8 Pink and 4 Yellow). Also continuation packs of 24 and 12 Pink and of 24 and 12 Yellow tablets.

Further information *Treatment*: Migraleve does not contain ergotamine, making it particularly suitable for those patients in whom ergotamine induces nausea and vomiting or potentiates any nausea and/or vomiting already present as symptoms. Clinical trials have shown an appreciable reduction in nausea and vomiting with Migraleve.

Migraleve does not compromise the peripheral circulation and no significant side-effects have been reported.

Prophylaxis: Migraleve is particularly valuable for prophylactic treatment, its use not being restricted to attacks of any single aetiology. Again, no significant side-effects have been reported with prophylactic treatment and it can be used for those patients in whom depression is present.

Product licence number 0232/5008.

***Trade Mark**

Ernest Jackson and Company Limited

Crediton

Devon EX17 3AP



Est. 1817

GASTRILS*

Presentation Acacia gum pastille base: each containing 500 mg co-dried gel of aluminium hydroxide and magnesium carbonate. The pastilles are round and sugar-coated, coloured yellow (fruit-flavoured) and green (peppermint-flavoured); and supplied as a random mixture.

Uses Slow-release antacid, indicated in: Hyperacidity, peptic ulcer, dyspepsia, oesophagitis, gastritis, hiatus hernia, heartburn of pregnancy.

Gastrils maintain the acidity at an optimum physiological pH (3–5), with a prolonged plateau in the centre of this range where most peptic activity will cease to be stimulated.

Dosage and administration *Adults:* One or two pastilles to be sucked when necessary. For the continuous relief of ulcer symptoms and gastric acidity, Gastrils should be sucked at regular intervals, from one to four hours, according to clinical requirements.

Children: One pastille, three times daily.

Contra-indications, warnings, etc No side-effects have been reported with Gastrils, and there are no known

contra-indications to their use in the recommended dosage. When prescribing for diabetics it should be noted that Gastrils have a carbohydrate content of 1.75 g per pastille. As with all therapeutic agents, caution should be exercised in the first trimester of pregnancy.

Pharmaceutical precautions No special precautions.

Legal category GSL.

Package quantities Gastrils are supplied in dispensing packs of 900 g (containing approximately 220 pastilles) and in 90 g packs (containing approx. 22 pastilles) as a mixture of fruit and peppermint-flavoured pastilles. Gastrils may be prescribed in multiples of 90 g (approx. 22 pastilles).

Further information Gastrils are pleasant tasting and have a soothing demulcent action with minimal effects on bowel movements.

Gastrils are available through registered pharmacies only.

Product licence number 0094/5901.

* *Trade Mark*

Janssen Pharmaceutical Limited
Janssen House
Chapel Street
Marlow, Bucks SL7 1ET



ANQUIL*

Presentation White, uncoated tablets marked 'JANSSEN' on one side and 'A' above '0.25' on the reverse. Each tablet contains 0.25 mg benperidol.

Uses Anquil is a neuroleptic for the control of deviant and anti-social sexual behaviour, e.g. exhibitionism, compulsive masturbation, paedophilia.

Dosage and administration Anquil is intended for oral administration to adults only. The recommended daily dose is 0.25–1.5 mg in divided doses.

Contra-indications, warnings, etc

Contra-indications: Anquil is contra-indicated in patients with pyramidal or extra-pyramidal symptoms.

Teratological effects have not been reported but, as with other drugs, it is not advisable to administer Anquil during the first three months of pregnancy.

Warnings: Anquil may potentiate the action of other CNS depressants and care is required during the concomitant administration of opiates, barbiturates and other neuroleptics.

Precautions: Where prolonged treatment with Anquil is envisaged, it would be a reasonable precaution to carry out regular blood counts and tests of liver function.

Overdosage: There is no specific antidote other than the use of anti-Parkinson medication and gastric lavage.

Side-effects: In common with other neuroleptic agents Anquil may induce extra-pyramidal reactions, but these are readily controllable with anti-Parkinson drugs. Drowsiness has been reported in some patients and insomnia in others, but these effects tend to regress after a few days' treatment. Rarely hypotension and allergic skin reactions have been reported. In general side-effects can be minimised by starting with a low dose increasing at intervals of a few days.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Anquil Tablets, each containing 0.25 mg benperidol, are supplied in packs of 100.

Further information Nil.

Product licence number 0242/0014.

CLINIUM*

Presentation White, flat, uncoated tablets marked 'Janssen' on one side and 'C/120' on the reverse. Each tablet contains lidoflazine 120 mg.

Uses Clinium is indicated in ambulant patients with ischaemic heart disease for the long term management of angina pectoris. Clinium increases exercise tolerance and allows greater cardiac work to be done without altering the maximal heart rate achieved and with the

resting heart rate virtually unchanged. As a result the amount of external work possible before the onset of anginal pain is increased.

Clinium has no β adrenergic blocking activity, no significant effect on blood pressure and no autonomic activity. It has no negative inotropic effects on the heart.

The response to Clinium therapy develops gradually and is usually apparent after 6–8 weeks of treatment. In some cases up to six months will be needed for maximum clinical benefit.

Dosage and administration Clinium is for oral administration and should be taken with or after meals.

The usual daily dose is 360 mg (120 mg three times daily).

Side effects are minimised by gradual achievement of this dose and the following schedule is recommended:

Week 1 (initial)	120 mg once daily
Week 2	120 mg twice daily
Week 3 and subsequently	120 mg three times daily

Contra-indications, warnings, etc

Contra-indications: Clinium should not be given to women unless pregnancy has been excluded.

Warnings: Clinium may cause prolongation of the QT interval of the ECG in some patients. In common with other drugs which affect repolarisation Clinium may precipitate ventricular tachycardia in some patients already susceptible to this arrhythmia. Patients with severe ischaemia, with conduction defects or with clinically significant arrhythmia have potential for developing ventricular tachycardia which may, in a small proportion of cases, be aggravated by Clinium.

Overdosage: In the event of accidental overdosage supportive measures including gastric lavage should be employed. Continuous ECG monitoring is recommended. Forced diuresis may be of benefit since 33% of Clinium excretion is renal.

Side effects: Gastric upset or transient dizziness, tinnitus and headaches have all been observed occasionally. More rarely disturbing dreams or hallucinations have been reported. These usually occur in the initial phase of treatment and may normally be avoided by the gradual dosage increment regime recommended.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Clinium is supplied in packs of 100 tablets.

Product licence number 0242/0002

DAKTACORT*

Presentation A white, non-staining, water-miscible cream containing miconazole nitrate 2% w/w and hydrocortisone 1% w/w.

Uses Daktacort is indicated for the topical treatment of skin conditions where inflammation and infection by susceptible organisms co-exist, e.g. infected eczema.

Miconazole nitrate is a potent, broad spectrum antifungal and antibacterial agent with marked activity against dermatophytes, pathogenic yeasts (e.g. *Candida* spp.) and many Gram-positive bacteria including most strains of streptococcus and staphylococcus.

Hydrocortisone is a widely used topical anti-inflammatory of value in the treatment of inflammatory skin conditions including atopic and infantile eczema, contact sensitivity reactions and intertrigo.

Dosage and administration Daktacort should be applied topically two or three times daily, rubbing gently into the affected area. Occlusive dressing is necessary only in the case of nail lesions.

Contra-indications, warnings, etc True hypersensitivity to any of the ingredients.

Care, as with any topical corticosteroid, is advised with infants and children where the preparation is to be applied to extensive surface areas or under occlusive dressing. However, continuous prolonged treatment should not be necessary.

Topical administration of corticosteroids to pregnant animals can cause foetal abnormalities. The relevance of this finding to humans has not been established. However, topical corticosteroids should not be used extensively in pregnancy.

Side-effects: Rarely, local sensitivity may occur requiring discontinuation of treatment.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Daktacort is supplied in 15 g and 30 g tubes.

Further information Nil.

Product licence number 0242/0042.

DAKTARIN* CREAM AND TWIN PACK

Presentation Cream: White, non-staining, water-miscible cream containing miconazole nitrate 2% w/w.

Twin pack: White, non-staining, water-miscible cream containing miconazole nitrate 2% w/w plus white, non-staining powder containing miconazole nitrate 2% w/w.

Uses Daktarin exhibits potent antifungal activity and antibacterial activity against Gram-positive organisms. It is used for the topical treatment of fungal infections of the skin and nails and super-infection due to Gram-positive bacteria.

Dosage and administration Both Daktarin cream and powder are applied topically.

Skin infections: Daktarin cream should be applied to the lesions in the mornings and in the evenings. Daktarin powder should be applied to the lesions simultaneously and dusted inside articles of clothing in contact with the affected areas. To prevent relapse treatment should be continued for ten days after all lesions have disappeared.

Nail infections: Daktarin cream should be applied thinly to the infected nail once daily and the nail should be covered with an occlusive dressing. Treatment should continue uninterrupted until the growth of the new nail is established.

Contra-indications, warnings, etc

Contra-indications: None known.

Side-effects: Occasionally, irritation has been reported. Rarely, local sensitisation may occur, requiring discontinuation of treatment.

Overdosage: Not applicable.

Pharmaceutical precautions Store away from direct heat.

Legal category P.

Package quantities Cream: Daktarin cream, 30 g tube.

Twin Pack: Daktarin cream 30 g tube plus Daktarin powder 30 g 'puffer' pack.

Further information Daktarin twin pack is particularly indicated for those infections involving moist areas of the body especially Athlete's Foot.

A leaflet outlining to the patient the hygiene routines to be observed and the correct method of application of Daktarin is included in each pack of cream and in the twin pack.

Product licence numbers

Daktarin Cream 0242/0016

Daktarin Twin Pack 0242/0016

0242/0017

DAKTARIN* ORAL GEL

Presentation Sugar-free orange flavoured oral gel containing miconazole base 2% w/w (25 mg/ml).

Uses Miconazole is a synthetic imidazole anti-fungal substance with a broad spectrum of activity against pathogenic fungi (including yeast and dermatophytes) and Gram-positive bacteria (staph. and strep. spp.).

Miconazole is incompletely absorbed from the gastrointestinal tract. Blood levels of up to 1 mcg/ml can be achieved following ingestion of 1 gram per day of miconazole base.

Daktarin oral gel is indicated for the treatment of fungal infection of the oropharynx and gastrointestinal tract. This includes oral candidosis in adults and children; also for the eradication of fungi from gut reservoirs when necessary (such as an adjunct to local treatment of vulvo-vaginitis).

Dosage and administration Daktarin oral gel should be taken after meals (one 5 ml spoonful contains 125 mg miconazole).

Adults: One to two spoonfuls (5–10 ml) of gel four times daily.

Children Aged over 6: One spoonful (5 ml) of gel four times daily.

Aged 2–6: One spoonful (5 ml) of gel twice daily.

Infants under 2 years of age: Half spoonful (2.5 ml) of gel twice daily.

Treatment should be continued for two days after symptoms have cleared.

For best results in the treatment of oral lesions, miconazole should be kept in contact with the affected area as long as possible. This can be achieved by retaining the gel in the mouth for the maximum time possible.

Contra-indications, warnings, etc

Contra-indications: There are no known contra-indications to the use of miconazole.

Warnings: Although teratogenic effects have not been observed in animals, the safety of oral miconazole in pregnancy has not been definitely established; its use during pregnancy is therefore not recommended.

Side effects: No major side effects have been recorded from the use of Daktarin oral gel. Mild gastrointestinal disturbances have occasionally been reported.

Overdosage: No cases of overdosage have been reported.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Daktarin oral gel is supplied in 40 g and 80 g tubes, each provided with a 5 ml plastic spoon, marked with a 2.5 ml graduation.

Further information Oral miconazole is also available as Daktarin oral tablets, supplied in blister packs of 20 tablets each containing miconazole base 250 mg. For details of dosage and administration refer to separate data sheet.

Product licence number
Daktarin Oral Gel 0242/0048

DAKTARIN* ORAL TABLETS

Presentation White, cross-scored tablets containing miconazole base 250 mg.

Uses Miconazole is a synthetic imidazole anti-fungal substance with a broad spectrum of activity against pathogenic fungi (including yeasts and dermatophytes) and Gram-positive bacteria (staph. and strep. spp.).

Miconazole is incompletely absorbed from the gastrointestinal tract. Blood levels of up to 1 mcg/ml can be achieved following ingestion of 1 gram per day of miconazole base.

Daktarin oral tablets may be used prophylactically in the management of patients at high risk from opportunistic fungal infection. Patients likely to benefit from this treatment include those who are immuno-suppressed such as transplant patients, cancer patients (particularly those undergoing cytoreductive therapy) and patients suffering from congenital immunological abnormalities. Daktarin oral tablets may also be used for the eradication of fungi from gut reservoirs when necessary (such as prior to relevant surgery).

Dosage and administration Daktarin oral tablets should be taken after meals.

Adults: one tablet (250 mg) four times daily.

Treatment should be continued for two days after symptoms have cleared.

Contra-indications, warnings, etc

Contra-indications: There are no known contra-indications to the use of miconazole.

Warnings: Although teratogenic effects have not been observed in animals, the safety of oral miconazole in pregnancy has not been definitely established; its use during pregnancy is therefore not recommended.

Side effects: No major side effects have been recorded from the use of Daktarin oral tablets. Mild gastrointestinal disturbances have occasionally been reported.

Overdosage: No cases of overdosage have been reported.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Daktarin oral tablets are supplied in blister packs of 20.

Further information Oral miconazole is also available as a sugar-free orange flavoured gel containing miconazole base 2% w/w (25 mg/ml). Daktarin Oral Gel is supplied in 40 g and 80 g tubes, each provided with a 5 ml plastic spoon. For details of dosage and administration refer to separate data sheet.

Product licence number

Daktarin Oral Tablets 0242/0047

DAKTARIN* INTRAVENOUS SOLUTION ▼

Presentation Clear glass ampoules (20 ml) each containing a sterile solution of miconazole (base) 200 mg. (10% of Cremophor EL is included as solvent.)

Uses **Indications:** Daktarin intravenous solution is indicated for the treatment of systemic mycoses such as systemic candidosis, aspergillosis, coccidioidomycosis, cryptococcosis, blastomycosis.

Actions: Miconazole, a synthetic imidazole compound has a broad spectrum of *in vitro* activity against fungi, yeasts and Gram-positive bacteria, including *Candida albicans*, *Candida tropicalis*, *Candida parapsilosis*, *Aspergillus fumigatus*, *Aspergillus niger*, *Cryptococcus neoformans*, *Coccidioides immitis*, *Paracoccidioides brasiliensis*, and a range of other less commonly occurring pathogens.

Intravenous infusion of doses above 9 mg/kg produces effective peak blood levels in excess of 1 mcg/ml. The drug is rapidly metabolised. The pharmacokinetics are unaffected in patients with renal insufficiency, including those on haemodialysis. Plasma levels, however, may be somewhat elevated. Clinical use has revealed no evidence of serious renal or hepatic toxicity associated with intravenous miconazole. Effective levels of miconazole in the CSF have been achieved by intratheca administration.

Dosage and administration Daktarin intravenous solution must be diluted with either physiological saline (Sodium Chloride Injection BP) or 5% Dextrose Injector BP and administered slowly by intravenous infusion over a period of at least 30 minutes. The usual adult dose is 600 mg (3 ampoules) three times daily; as an infusion of 200–500 ml infusion fluid. The incidence of side-effects or the sensitivity of the fungal strain involved may require individual adjustment of this dose.

As a guide, clinically effective daily doses have ranged as low as 600 mg/day to, in a few patients, as high as 3,600 mg/day.

In children a daily dose of about 40 mg/kg is recommended. A dose of 15 mg/kg per infusion should not be exceeded.

Duration of treatment is dictated by the rate of response of the infection to miconazole rather than an arbitrary number of days. Treatment should be continued until mycological evidence of remission or cure is obtained. Daktarin intravenous solution has been used without major side-effects or toxicity for periods of over 20 weeks.

Local treatment with Daktarin intravenous solution may be useful as an adjunct to intravenous treatment:

Intrathecal administration: 15–20 mg once or twice daily. Injections may be alternated between lumbar, cervical and cisternal sites. Penetration may be assisted by placing the patient in the Trendelenburg position for 90 minutes following injection.

Bladder instillation: 100 mg (undiluted) twice daily. If discomfort is experienced with undiluted drug the daily dose may be given as a 12-hourly continuous irrigation in 500 ml physiological saline.

Intra-pulmonary route: 200 mg daily, divided into 2–4 administrations by intratracheal instillation or by inhalation (e.g. Wrights nebuliser or IPPB); under careful clinical supervision. Preliminary experience suggests that administration via an endobronchial catheter placed close to the lesion may be effective in aspergilloma.

Wound Infection: Local irrigation of wound area. Daktarin given solely by the intravenous route is inadequate for treatment of bladder infections or for clearance of the fungus ball in aspergilloma.

Contra-indications, warnings, etc

Contra-indications: Patients who are hypersensitive to Daktarin intravenous solution, since anaphylactic reactions have been observed in rare cases.

Warnings: Rapid injection of a bolus of undiluted drug can produce transient tachycardia and cardiac arrhythmias. These, if not spontaneously reversible, usually respond promptly to lignocaine. Daktarin intravenous solution is well tolerated (including patients with pre-existing cardiovascular disorders) if given by intravenous infusion.

The safety of Daktarin intravenous solution in pregnancy has not been established and its use in pregnant women should be avoided if possible.

Systemic miconazole may potentiate the activity of anticoagulant or hypoglycaemic drugs, the dosage of which may require adjustment. Antagonism of the *in vitro* activity of miconazole by amphotericin B has been reported.

Side effects: Haematological and biochemical controls are recommended since the infusion of Daktarin intravenous solution in large volumes of fluid may produce a decrease in haemoglobin, haematocrit and serum sodium. Hyperlipidaemia, aggregation of erythrocytes or rouleau formation on blood smears may occur as a result of administration of the triglyceride containing vehicle, Cremophor EL. These effects are reversible on discontinuation of treatment and are not usually sufficiently severe to warrant discontinuation of intravenous miconazole.

The adverse reactions reported during clinical investigations of Daktarin intravenous solution were phlebitis, pruritus, nausea and vomiting, febrile reactions, rash, drowsiness, diarrhoea, anorexia and flushes. Using a subclavian catheter or changing the sites of infusion every 48–72 hours reduces the incidence and severity of phlebitis. Nausea and vomiting can be prevented by giving an antiemetic drug before infusion, by reducing the dose, by slowing the rate of infusion or by avoiding mealtime administration.

No cases of overdosage have been reported.

Pharmaceutical precautions Storage should be at room temperature, shelf life is five years. Daktarin intravenous solution should be mixed only with the recommended diluents. Sodium Chloride Injection BP or 5% Dextrose Injection BP.

Legal category POM.

Package quantities Daktarin intravenous solution is supplied in 20 ml glass ampoules, packed in boxes of ten. Each ampoule contains miconazole (base) 200 mg.

Further information Miconazole's broad spectrum of antifungal activity and its lack of serious toxicity suggest that Daktarin intravenous solution may be considered for first line treatment in cases of life-threatening systemic fungal infection.

Product licence number 0242/0052.

DIPIDOLOR*

Presentation Clear, colourless, aqueous injection presented in 2 ml ampoules. Each ml contains 10 mg piritramide.

Uses Dipidolor is a narcotic analgesic used specifically for post-operative analgesia.

Dosage and administration Dipidolor is for intramuscular injection to adults only. A 20 mg dose is recommended initially. Depending on the severity of pain repeat doses of 2 ml may be given every six hours to a maximum of four doses.

At present there is insufficient clinical evidence to recommend piritramide for use in children.

Contra-indications, warnings, etc **Precautions:** Physical dependence to Dipidolor has not been reported, but it should be regarded as a possibility and care should be taken when repeated doses are required.

There is evidence that piritramide is metabolised in the liver and excreted in the faeces, so that the drug should be administered with caution to patients with hepatobiliary disease.

Dipidolor has not given rise to teratological effects, but, as with any medication, caution should be exercised in administering the product during the first three months of pregnancy.

Overdosage: The main pharmacological effects of Dipidolor can be reversed with naloxone 0.1–0.2 mg intravenously.

Side-effects: As with all narcotic analgesics, respiratory depression, nausea, vomiting and constipation can occur, although rarely seen. Drowsiness has been reported.

Pharmaceutical precautions Nil.

Legal category POM MDA.

Package quantities Dipidolor is supplied in 2 ml ampoules in packs of 10.

Further information Dipidolor is characterised by its potent action, which is rapid in onset and lasts for at least six hours after a single dose of 20 mg.

Product licence number 0242/0007.

DROLEPTAN*

Presentation **Injection:** Clear, colourless, aqueous injection in 2 ml ampoules. Each millilitre contains 5 mg droperidol.

Tablets: Yellow uncoated, scored tablets marked 'JANSSEN' on one side and D above 10 on the reverse. Each tablet contains 10 mg droperidol.

Liquid: Clear, colourless, odourless liquid containing 1 mg droperidol/ml for oral administration.

Uses Droleptan is a major tranquilliser with the following indications:

- 1.) In anaesthetics; (a) in conjunction with a narcotic analgesic in the technique of neuroleptanalgesia; (b) either alone or in combination with a narcotic analgesic for premedication.
- 2.) In psychiatry: for rapidly calming the manic, agitated patient.
- 3.) As an anti-emetic.

Dosage and administration Droleptan can be administered to both adults and children.

Droleptan Injection is for intravenous or intramuscular administration. Droleptan tablets and liquid are for oral administration. The following dosages are recommended.

Route	Adults	Children
Intravenous	5–15 mg	0.2–0.3 mg/kg
Intramuscular	Up to 10 mg	0.3–0.6 mg/kg
Oral	5–20 mg	0.2–0.6 mg/kg

A single dose is normally appropriate for use in anaesthetics. In psychiatry the dosage may be repeated at intervals of four to six hours (parenteral) or four to eight hours (oral).

Contra-indications, warnings, etc

Contra-indications: Droperidol is contra-indicated in the severely depressed patient.

Precautions: Since droperidol is metabolised in the liver, care should be taken in patients with severe hepatic disease.

Minor central effects can, in some instances, persist for up to 48 hours after administration of droperidol and hence where early discharge is envisaged, patients should be advised not to drive or operate machinery on the day following administration.

Overdosage: The therapeutic ratio for Droleptan is high and in the event of overdosage extrapyramidal effects can be suppressed by anti-Parkinson drugs.

Side-effects: Droperidol may give rise to extrapyramidal side-effects but these are readily controlled with anti-Parkinson drugs.

Pharmaceutical precautions Droperidol preparations should be protected from light.

If desired, Droleptan injection can be mixed with intravenous infusion solutions and with most agents commonly used in anaesthesia, but it is chemically incompatible with the induction agents thiopentone, propofol and methohexitone, because of the wide difference in pH.

Legal category POM.

Package quantities Droleptan injection is supplied in 2 ml ampoules (5 mg/ml) in packs of 10.

Droleptan tablets each containing 10 mg droperidol are supplied in packs of 50.

Droleptan liquid is supplied in amber glass bottles of 100 ml (1 mg/ml).

Product licence numbers

Droleptan injection	0242/5003
Droleptan tablets	0242/5004
Droleptan liquid	0242/0080

GYNO-DAKTARIN*

Presentation *Intravaginal Cream:* White, non-staining, water-miscible cream containing miconazole nitrate 2% w/w.

Pessary: White, non-staining pessaries each containing 100 mg miconazole nitrate.

Combi-pack: White, non-staining pessaries each containing 100 mg miconazole nitrate plus white, non-staining, water miscible topical cream containing miconazole nitrate 2% w/w.

Tampon: Tampons, each coated with 100 mg miconazole nitrate.

Uses Gyno-Daktarin exhibits potent antifungal activity and antibacterial activity against Gram-positive bacteria (Strep. and Staph. spp.). Gyno-Daktarin is used for the local treatment of vulvo-vaginal candidosis and superinfection due to Gram-positive bacteria (Strep. and Staph.). Also for prophylactic treatment of the male partner and for the treatment of mycotic balanitis.

Dosage and administration Gyno-Daktarin may be used in both adults and children. Nightly, 10 g of the intravaginal cream or two pessaries should be inserted high into the vagina. Disposable applicators are provided for insertion of the cream.

This procedure should be repeated for 7 days, even though symptomatic cure of the pruritus and leukorrhoea will have been noted within a few days of commencing therapy.

In the case of the combi-pack, the cream should be applied topically twice daily.

Gyno-Daktarin tampons: One tampon should be inserted high in the vagina, twice daily (morning and evening) for five days.

Contra-indications, warnings, etc

Contra-indications: None known.

Side-effects: Occasionally, irritation has been reported. Rarely, local sensitisation may occur requiring discontinuation of treatment.

Overdosage: Not applicable.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities *Cream:* Gyno-Daktarin intravaginal cream is supplied in 78 g tubes with disposable applicators – seven days' treatment.

Pessary: Gyno-Daktarin pessaries are supplied in packs each containing 14 pessaries – seven days' treatment.

Combi-pack: Gyno-Daktarin combi-pack consists of 14 pessaries plus 15 g topical cream.

Tampons: Gyno-Daktarin tampons are supplied in packs each containing 10 tampons.

Further information Gyno-Daktarin may be used with confidence in 'problem vaginitis' as seen in pregnant and diabetic patients and in women using oral contraceptives.

A leaflet instructing the patient on the correct use is included in each package of Gyno-Daktarin.

Product licence numbers

Gyno-Daktarin Cream	0242/0015
Gyno-Daktarin Pessaries	0242/0037
Gyno-Daktarin Combi-Pack	0242/0015
Gyno-Daktarin Cream	0242/0037
Gyno-Daktarin Tampons	0242/0056

HALDOL*

Presentation Yellow scored uncoated tablets marked Janssen on one side and H/1.5* on the reverse, containing 1.5 mg Haloperidol BP.

Pale blue scored uncoated tablets marked Janssen on one side and H/5* on the reverse, containing 5.0 mg Haloperidol BP.

Yellow scored uncoated tablets marked Janssen on one side and H/10* on the reverse, containing 10 mg Haloperidol BP.

White scored uncoated tablets marked Janssen on one side and H/20* on the reverse containing 20 mg Haloperidol BP.

Clear glass ampoules containing 5 mg Haloperidol BP in 1 ml aqueous solution for injection.

Clear glass ampoules containing 10 mg Haloperidol BP in 2 ml aqueous solution for injection.

Clear, colourless, odourless liquid containing 2 mg Haloperidol BP per ml for oral administration.

Clear, colourless, odourless liquid containing 10 mg Haloperidol BP per ml for oral administration following dilution (see Package insert).

Uses Haldol is a highly effective neuroleptic butyrophenone drug, with a wide range of actions. Haldol is recommended for the rapid control of the symptoms of hostility, aggression, hyperactivity, disruptive and violent behaviour, confusion, emotional withdrawal, hallucinations and delusions associated with acute and chronic schizophrenia, mania and hypomania, organic brain syndrome, alcohol withdrawal syndrome and delirium tremens, childhood behavioural disorders. Haldol is also indicated for the treatment of motor tics, stuttering and persistent hiccoughs, nausea and vomiting, anxiety states and as pre-anaesthetic medication.

Dosage and administration *Adults:* As with all neuroleptic drugs it is vitally important to titrate the dose of Haldol to the needs of each patient. Titration should be carried out as rapidly as practicable to achieve optimum therapeutic control. To determine the initial dose, consideration should be given to the patient's age, severity of symptoms and previous response to other neuroleptic drugs. It is important to increase dosage progressively until maximum control of symptoms has been achieved. Thereafter, dosage may be reduced gradually to the lowest effective maintenance level.

Patients who are elderly or debilitated or those with previous adverse reactions to neuroleptic drugs may require less Haldol. The optimal response in such patients is usually obtained with more gradual titration and at lower dose levels. In adolescents a lower dose may be advisable.

1. Oral administration-initial dosage: General

Moderate symptomatology 0.5–2.0 mg b.i.d. or t.i.d.

Severe symptomatology 3.0–5.0 mg b.i.d. or t.i.d.

To achieve prompt control, higher doses may be required in some cases.

Geriatric or debilitated patients 0.5–2.0 mg b.i.d. or t.i.d.

Resistant patients:

Chronic or resistant patients 3.0–5.0 mg b.i.d. or t.i.d.

Patients who remain severely disturbed or inadequately controlled may occasionally require further titration of dosage. Daily dosages up to 100 mg may be necessary to achieve an optimal response. Haldol (haloperidol) has been used in doses of 200 mg for severely resistant patients.

Maintenance dosage: Upon achieving a satisfactory therapeutic response, dosage should be gradually reduced to the lowest effective maintenance level, often as low as 5–10 mg/day. Too rapid dosage reduction should be avoided.

Anxiety states: 0.5 mg twice daily. At this dosage level no interaction with moderate amounts of alcohol nor any deleterious effect on intellectual or psychomotor (including driving) abilities has been demonstrated.

Tics, choreiform movements, stuttering: Haldol administered orally in doses of 0.5–1.5 mg t.d.s. significantly reduces the degree of stuttering in most but not all stutterers. Tics, choreiform movements and dyskinesias have all been treated with Haldol. In Gilles de la Tourette syndrome daily maintenance doses of 10 mg and higher may be required.

2. Parenteral administration: Parenteral medication administered intramuscularly in initial doses of 2–10 mg is utilised for prompt control of the acutely agitated patient with moderate symptoms. Very severely disturbed patients may require an initial dose of up to 30 mg. Depending on the response of the patient subsequent doses of 5 mg may be given as often as every hour if necessary, although 4–8 hour intervals may be satisfactory to achieve control. Oral treatment should succeed intramuscular administration as soon as practicable.

Haldol can also be parenterally administered by the intravenous route.

For pre-anaesthetic medication: a single intravenous or i.m. dose of 1–5 mg effectively reduces the incidence of postoperative nausea and vomiting, and also controls apprehension and nervousness before surgery.

Haldol administered parenterally by intramuscular injection 2–5 mg every 4–6 hours for up to 24 hours effectively controls anxiety, irritability, insomnia, anorexia and nausea in the *Alcohol withdrawal syndrome*.

Children – Oral administration

Childhood behavioural disorders: Orally administered Haldol provides useful adjunctive therapy in controlling overactivity, destructiveness, resentment and aggressiveness in disturbed and schizophrenic children, in total daily maintenance doses of 0.05 mg/kg/day, half the total dose given in the morning and the other half in the evening.

Gilles de la Tourette disease: The sudden involuntary movements and utterances of this syndrome can be controlled with oral maintenance doses of up to 10 mg per day in most cases.

Stuttering: Oral doses of 0.05 mg/kg/day have proved useful adjunct therapy in the treatment of stuttering.

Contra-indications, warnings, etc There are no absolute contra-indications to the use of Haldol but caution should be observed in patients with manifest lesions of the basal ganglia, and in patients with arteriosclerosis who may have occult lesions of the basal ganglia. Haldol may safely be given to epileptics, but normal anticonvulsant therapy should be continued. Although Haldol has minimal soporific action, it should be appreciated that the drug will potentiate the action of CNS depressants. Where extrapyramidal side effects are encountered in the form of dystonic reactions or motor restlessness (akathisia) they may be controlled by a barbiturate or antiparkinsonian drug. There have been no serious toxic effects attributable to Haldol and fatal overdosage has not been reported. Treatment of over-

dosage consists of supportive measures combined with sedative or antiparkinsonian drugs.

Pharmaceutical precautions Store in a cool dry place.

Legal category POM.

Package quantities

1.5 mg Tablet: 100 and 1,000 in canisters.

5.0 mg Tablet: 100 and 1,000 in canisters.

10.0 mg Tablet: 100 and 500 in canisters.

20.0 mg Tablet: 100 in canisters.

5 mg/ml Injectable Solution: 5 × 1 ml ampoules.

10 mg/2 ml Injectable Solution: 5 × 2 ml ampoules.

2 mg/ml Oral Liquid: 100 ml amber glass bottles, with calibrated pipette. 500 ml amber glass bottles.

10 mg per ml Oral Liquid: 100 ml amber glass bottles with leaflet insert.

Further information Extensive use of haloperidol since 1958 shows that it is an effective antipsychotic drug with a wide therapeutic safety margin. Haldol does not significantly reduce blood pressure and can therefore be safely given to the disturbed patient at an adequate dosage in an emergency. Despite its extensive use reports of toxic effects such as blood dyscrasias and liver damage are extremely rare. Haldol is well absorbed following oral administration of either the tablet or the oral liquid. Plasma levels and areas under the plasma level-time curve are essentially the same for the tablet and oral liquid, thus bioavailability of Haldol tablets is the same as that of an oral solution.

Dilution instructions Haldol Oral Liquid Concentrate 10 mg/ml should normally be diluted with purified water to meet individual patient requirements. Following dilution it is advised that the solution be used as soon as possible. If a more prolonged shelf life is required, dilution with an aqueous solution of methyl paraben (0.5 mg/ml) and propyl paraben (0.05 mg/ml) is recommended, thus maintaining the original concentration of preservatives. Further information is to be found in the package insert leaflet.

Product licence numbers

1.5 mg tablet	0242/0034
5.0 mg tablet	0242/0031
10.0 mg tablet	0242/0039
20.0 mg tablet	0242/0046
5 mg/ml injectable solution	0242/0036
10 mg/2 ml injectable solution	0242/0036
2 mg/ml oral liquid	0242/0035
10 mg/ml oral liquid	0242/0049

HALDOL* DECANOATE ▼

Presentation Straw coloured, viscous solution presented in 1 ml brown glass ampoules equivalent to 100 mg/ml haloperidol (as decanoate ester).

Uses Haldol decanoate is an ester of the potent butyrophenone neuroleptic, haloperidol. The active agent is slowly released from an intramuscular depot injection of Haldol decanoate. Haldol decanoate is indicated where long term maintenance treatment with a neuroleptic is required; for example in schizophrenia, other psychoses (especially paranoid), and other mental or behavioural problems where maintenance treatment is clearly indicated.

Dosage and administration Haldol decanoate is for use in adults only and has been formulated to provide one month's therapy for most patients following a single deep intramuscular injection in the gluteal region.

Since individual response to neuroleptic drugs is variable, dosage should be individually determined and is best initiated and titrated under close clinical supervision.

In mild symptomatology and in the elderly up to 100 mg every 4 weeks, in moderate symptomatology 100–200 mg every 4 weeks, and in severe cases 200–300 mg or more every 4 weeks.

For patients previously maintained on low doses of neuroleptics (e.g. up to 10 mg/day; oral haloperidol) the monthly dosage of Haldol decanoate may be calculated at 20 × the usual daily oral dose of haloperidol or the equivalent dose of other similar drugs.

Contra-indications, warnings, etc *Contra-indications:* Haldol is excreted in breast milk and is not recommended during lactation: if the use of Haldol is considered essential, breast feeding should be discontinued.

Use in pregnancy: The safety of haloperidol in pregnancy has not been established. There is some evidence of harmful effects in some but not all animal studies. Human experience suggests that there may be teratogenic effects, although a causal relationship has not been established.

Precautions: Caution is advised in patients with liver disease, renal failure, Parkinson's disease, pheochromocytoma, thyrotoxicosis, epilepsy and conditions predisposing to epilepsy (e.g. alcohol withdrawal and brain damage).

In common with all neuroleptics Haldol can increase the central nervous system depression produced by other CNS-depressant drugs, including alcohol, hypnotics, sedatives or strong analgesics.

Haldol may antagonise the action of adrenaline and other sympathomimetic agents and reverses the blood-pressure-lowering effects of adrenergic-blocking agents such as guanethidine.

Haldol may impair the metabolism of tricyclic antidepressants (clinical significance unknown) and the anti-Parkinson effects of levodopa. The dosage of anti-convulsants may need to be increased to take account of the lowered seizure threshold.

Antagonism of the effect of phenindione has been reported.

Enhanced CNS effect, when combined with methyl-dopa, has been reported.

Neurotoxic reactions to combined treatment with lithium and Haldol have been reported, but the mechanism for this effect is undetermined.

Warnings and adverse effects: Some degree of sedation or impairment of alertness may occur, particularly with higher doses and at the start of treatment. Patients should be advised not to drive or operate machinery during treatment, until their susceptibility is known.

In common with all neuroleptics, extra-pyramidal symptoms may occur. Acute dystonias may occur early in treatment. Parkinsonian rigidity, tremor and akathisia tend to appear less rapidly. Oculogyric crises and laryngeal dystonias have been reported.

Anti-Parkinson agents should only be given as required; they should not be prescribed routinely because of the possible risk of impairing haloperidol's therapeutic efficacy. Preliminary results suggest that withdrawal of

anti-Parkinson medication may be attempted following transfer from oral to monthly depot injections of Haldol decanoate.

Tardive dyskinesia is common among patients treated with moderate to high doses of antipsychotic drugs for prolonged periods of time and may prove irreversible, particularly in patients over 50 years.

The potential seriousness and unpredictability of tardive dyskinesia and the fact that it has occasionally been reported to occur when neuroleptic antipsychotic drugs have been prescribed for relatively short periods in low dosage means that the prescribing of such agents requires especially careful assessment of risk versus benefit. Tardive dyskinesia can be precipitated or aggravated by anti-Parkinson drugs. Short-term dyskinesias may occur after abrupt drug withdrawal.

In schizophrenia, the response to antipsychotic drug treatment may be delayed. If drugs are withdrawn, recurrence of symptoms may not become apparent for several weeks or months.

Haldol, even in low dosage in susceptible (especially non-psychotic) individuals, may cause unpleasant subjective feelings of being mentally dulled or slowed down, dizziness, headache or paradoxical effects of excitement, agitation or insomnia.

Gastro-intestinal symptoms, nausea, loss of appetite and dyspepsia have been reported.

Hormonal effects of antipsychotic neuroleptic drugs include hyper-prolactinaemia, which may cause galactorrhoea, gynaecomastia and oligo- or amenorrhoea.

Weight changes may occur.

Dose-related hypotension is uncommon, but can occur, particularly in the elderly.

Autonomic effects, such as blurring of vision and tachycardia, are uncommon.

The following effects have been reported rarely: oedema; various skin rashes and reactions, including exfoliative dermatitis and erythema multiforma; jaundice or transient abnormalities of liver function in the absence of jaundice; confusional states or epileptic fits; impairment of sexual function, including erection and ejaculation. The elderly are more susceptible to the sedative and hypotensive effects.

The following effects have been reported very rarely: blood dyscrasias, including agranulocytosis and transient leucopenia, and photosensitive skin reactions.

Overdosage: There have been no serious toxic effects attributed to Haldol decanoate and fatal overdosage has not been reported. Treatment of overdosage consists of supportive measures combined with sedative or anti-Parkinsonian drugs, as required.

Pharmaceutical precautions Haldol decanoate should be protected from light and stored at room temperature. If stored for long periods in the cold precipitation may occur which may clear on storage at room temperature, in common with other depot neuroleptics.

Further information Haloperidol is a butyrophenone. Its pharmacological profile of activity includes a low incidence of autonomic side effects, such as hypotension, and a capacity to induce extrapyramidal reactions.

Legal category POM.

Package quantities 100 mg/ml ampoules: 1 ml ampoules in packs of 5.

Product licence number 0242/0095.

HYPNOMIDATE* ▼

Presentation Clear, colourless solution containing 2 mg/ml etomidate. The aqueous vehicle contains 35% propylene glycol.

Uses Hypnomidate is an intravenous anaesthetic agent.

Dosage and administration A dose of 0.3 mg/kg at induction of anaesthesia given intravenously gives sleep lasting from 6 to 10 minutes.

Anaesthesia can be maintained by supplemental doses of 0.1 or 0.2 mg/kg Hypnomidate given when there are signs of returning consciousness.

Since Hypnomidate has no analgesic action, appropriate analgesics should be used in procedures involving painful stimuli.

Hypnomidate is pharmacologically compatible with the muscle relaxants, premedicant drugs and inhalation anaesthetics in current clinical use.

Contra-indications, warnings, etc Side-effects: The use of narcotic analgesics as premedication and during surgery will reduce the uncontrolled spontaneous muscle movement shown by some patients after Hypnomidate administration.

Pain can occur after injection into the small veins of the dorsum of the hand. Use of larger veins reduces pain on injection. Other side-effects are rare.

Precautions: Hypnomidate injections should be given slowly.

Animal experiments have shown no evidence of teratogenicity but Hypnomidate should be used with caution in pregnancy.

Pharmaceutical precautions Store at room temperature.

Legal category POM.

Package quantities Hypnomidate is supplied as ampoules of 10 ml in cartons of 10 ampoules.

Further information Hypnomidate is rapidly metabolised and eliminated and recovery of consciousness from a single dose is rapid and complete. Supplemental doses can be used without unduly prolonging recovery in short surgical procedures.

Product licence number 0242/0019.

HYPNOMIDATE* for Infusion ▼

Presentation Concentrate for infusion: clear colourless liquid presented in 1 ml ampoules. Each millilitre contains etomidate hydrochloride equivalent to 125 mg etomidate base.

Uses Hypnomidate is a short-acting intravenous hypnotic drug which may be used both for induction and maintenance of anaesthesia. Hypnomidate provides marked cardiovascular stability.

Dosage and administration The concentrate for infusion (125 mg/ml) should be diluted with a suitable volume of infusion fluid before use. Sodium Chloride or Dextrose infusion fluids B.P. are recommended diluents. The volume of infusion fluid required depends on the technique used to determine infusion dosage rates. Each ampoule should be diluted in at least 50 ml of infusion fluid.

Steady-state levels are rapidly obtained by giving a loading dose for induction by infusion (0.1 mg/kg/

minute for the first 10 minutes) and thereafter at 0.01 mg/kg/minute until 5 minutes before the end of surgery. For short operations (15–30 minutes) the duration of the loading infusion may be reduced to 5 minutes.

The infusion rate for Hypnomidate to maintain anaesthesia is dependent on anaesthetic technique and individual response.

As a guide, overall infusion rates (including loading dose) are usually 0.015–0.04 mg/kg/minute when Hypnomidate is used as part of a total intravenous anaesthetic technique.

The dose rate of Hypnomidate may be reduced to 0.005–0.01 mg/kg/minute if inhalation anaesthetics (nitrous oxide) are used simultaneously.

Since Hypnomidate has no analgesic action, appropriate analgesics should be used in procedures involving painful stimuli.

Hypnomidate is pharmacologically compatible with the muscle relaxants, premedicant drugs and inhalation anaesthetics in current clinical use.

Contra-indications, warnings, etc *Warnings:* The concentrate is for infusion and must be diluted before use.

Contra-indications: There are no absolute contra-indications to the use of Hypnomidate. Safety in human pregnancy has not been established although studies in animals have not demonstrated teratogenic effects. As with other drugs, risk should be weighed against potential benefit to the patient.

Side effects: The use of narcotic analgesics as premedication and during surgery will reduce the uncontrolled spontaneous muscle movements shown by some patients after Hypnomidate administration, in some cases such muscle movements may limit successful maintenance of anaesthesia.

Pain can occur after administration in the small veins of the dorsum of the hand. Use of larger veins reduces pain on injection; venous irritation has also been occasionally reported following Hypnomidate infusions.

Other side effects are rare.

Pharmaceutical precautions Store at room temperature. The concentrate is stable following dilution for up to one week at room temperature. Hartmann's solution is not recommended for use with Hypnomidate.

A pharmaceutical overfill of 0.1 ml is included in each 1 ml ampoule of the concentrate for infusion.

Further information Nil

Legal category POM.

Package quantities *Concentrate for infusion:* Packages of 10 ampoules.

Product licence number 0242/0082.

IMODIUM*

Presentation *Capsules:* Hard gelatin capsules with a dark green, opaque cap and a standard grey opaque body. Each capsule contains loperamide hydrochloride 2 mg.

Syrup: Red, fruity flavoured syrup containing loperamide hydrochloride 1 mg in 5 ml.

Uses Imodium acts by selectively slowing intestinal motility. It specifically inhibits peristaltic activity by a

direct effect on circular and longitudinal muscles of the intestinal wall by interaction with cholinergic as well as non-cholinergic neuronal mechanisms.

Imodium is indicated for the symptomatic control of acute and chronic diarrhoea of any aetiology.

As persistent diarrhoea can be an indicator of potentially more serious conditions, Imodium should not be used for prolonged periods until the underlying cause of the diarrhoea has been investigated.

Dosage and administration Imodium capsules and Imodium syrup are for oral administration.

Acute diarrhoea: Adults: Two capsules initially, followed by 1 capsule after every loose stool.

The usual dosage is 3 to 4 capsules a day; the maximum daily dose should not exceed 8 capsules.

Children: 4–8 years: Syrup 5 ml four times daily until diarrhoea is controlled. In children under 8 years, further investigation may be necessary if diarrhoea has not responded to three days' treatment.

9–12 years: Syrup 10 ml (or 1 capsule) four times daily until diarrhoea is controlled.

Chronic diarrhoea: Adults: Studies have shown that patients may need widely differing amounts of Imodium. The starting dosage should be between 2 and 4 capsules per day in divided doses, depending on severity. If required, this dose can be adjusted according to response.

Having established the patient's daily maintenance dose, the capsules may be administered on a twice daily regimen. Tolerance has not been observed and therefore subsequent dosage adjustment should be unnecessary.

Use of Imodium syrup: 10 ml is equivalent to 1 capsule.

Contra-indications, warnings, etc There are no specific contra-indications to Imodium. Safety in human pregnancy has not been established although studies in animals have not demonstrated any teratogenic effects. As with other drugs, it is not advisable to administer Imodium in pregnancy. In trials no side effects have been reported that can reliably be distinguished from the symptoms of the gastro-intestinal disorder being treated.

No instances of overdosage have been reported. Overdosage will result in constipation; gastric lavage or induced emesis and/or enema or laxatives may be recommended.

Pharmaceutical precautions No special storage requirements.

Legal category POM.

Package quantities Imodium is supplied in packs of 12, 60 and 250 capsules. Imodium syrup is supplied in bottles of 100 ml.

Further information Water is a satisfactory diluent for Imodium syrup; dilutions are stable for at least two weeks at 20°C.

Imodium syrup is sugar-free

No drugs are known to be incompatible with Imodium.

Product licence numbers

Capsules 0242/0028

Syrup 0242/0040

MOTILIUM* ▼

Presentation *Tablets:* Small, white, film-coated tablets marked M/10 each containing 10 mg domperidone.

Injection: Clear, colourless, aqueous solution in 2 ml ampoules containing 5 mg domperidone per millilitre for intramuscular or intravenous administration.

Uses Motilium is indicated for the symptomatic relief of acute nausea and vomiting in adults, from any cause. Motilium is not recommended for use in children unless indicated for the management of nausea and vomiting following cancer chemotherapy or irradiation. Motilium is not recommended for chronic administration or for routine use in postoperative vomiting.

Dosage and administration Dose, route and frequency of administration should be adjusted according to severity and duration of the symptoms. Where an episode of vomiting can be predicted, as with anticancer therapy, prophylactic administration may be helpful.

Adults: 1–2 tablets by mouth or 1–2 ampoules by IV or IM injection at 4–8 hourly intervals.

Children: 0.2–0.4 mg/kg by mouth or injection at 4–8 hourly intervals.

Contra-indications, warnings, etc In common with other dopamine blocking agents Motilium raises serum prolactin; however the clinical relevance of this has not been established.

Safe use in pregnant women has not been established, although studies in animals have not demonstrated teratogenic effects. As with any new drug, it is not advisable to administer Motilium in pregnancy.

Side-effects: In placebo-controlled trials, incidence of side effects has not differed from placebo.

Overdosage: No case has been reported. There is no specific antidote to Motilium but in the event of overdosage, gastric lavage may be useful.

Pharmaceutical precautions Store tablets and injection at room temperature.

Legal category POM.

Package quantities Tablets – packs of 100 tablets
Injection – 2 ml ampoules in packs of 10.

Further information Nil.

Product licence numbers Tablets 0242/0071
Injection 0242/0073.

NIZORAL* ▼

Presentation White, flat, half-scored, uncoated tablets. Each tablet is marked 'Janssen' on one side and K/200 on the reverse. Each tablet contains ketoconazole 200 mg.

Uses Nizoral is an imidazole-dioxolane antimycotic which is effective after oral administration and has a broad spectrum of activity against dermatophytes, yeasts and other pathogenic fungi.

The indications for Nizoral are:

In adults:

1. Treatment of superficial and deep mycoses:
 - Vaginal candidosis.
 - Infections of the skin, hair and nails by dermatophytes and/or yeasts (including onychomycosis, pityriasis versicolor and chronic mucocutaneous candidosis).
 - Yeast infection of the mouth and gastrointestinal tract.
 - Systemic mycoses e.g. systemic candidosis,

paracoccidioidomycosis, coccidioidomycosis, histoplasmosis.

2. Maintenance treatment to prevent recurrence in systemic mycotic infections and in chronic mucocutaneous candidosis.

3. Prophylactic treatment to prevent mycotic infection in patients with reduced immune responses for example, in cancer, during treatment with immunosuppressive medication or burns.

In Children: Systemic mycoses, severe infections of skin, hair, nails, mouth, vagina and GI tract which have not responded to topical treatment.

Dosage and administration Nizoral is for oral administration and should always be taken with meals.

In Adults:

Vaginal candidosis: One tablet (200 mg) morning and evening for 5 days.

Superficial and deep mycoses: One tablet (200 mg) once daily until at least one week after the symptoms have cleared and cultures have become negative. The dose may be increased to a maximum of 400 mg once daily if a satisfactory response is not obtained.

Prophylaxis and maintenance treatment: One tablet (200 mg) once daily.

In Children: Dosage should be reduced to 50 or 100 mg depending on bodyweight (i.e. approximately 3 mg/kg) for example:

Age 1–4 years – 50 mg

Age 5–12 years – 100 mg.

Contra-indications, warnings, etc When administered in high doses (>80 mg/kg) to pregnant rats, Nizoral has been shown to cause abnormalities of foetal development. The relevance of this finding to humans has not been established and consequently Nizoral is contra-indicated in pregnancy.

Precautions: Absorption of Nizoral is maximal when taken during a meal as it depends on stomach acidity. Concomitant treatment with agents that reduce gastric secretion (anti-cholinergic drugs, antacids, H₂ blockers) should be avoided and, if indicated, such drugs should be taken not less than two hours after Nizoral.

'Side effects: Gastric upset (nausea), rash, headache and pruritus have occasionally been observed. Alterations in liver function tests have occurred in patients on ketoconazole, these changes may be transient. Cases of hepatitis have been reported with an incidence of about 1 per 10,000 patients. Some of these may represent an idiosyncratic adverse reaction to the drug. This should be borne in mind in patients on long term therapy, e.g. for onychomycosis. If a patient develops jaundice or any symptoms suggestive of hepatitis treatment with ketoconazole should be stopped.'

Overdosage: In the event of overdosage, cases should be treated symptomatically with supportive measures or gastric lavage as necessary.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Nizoral is supplied in packs of 10 and 30 tablets.

Further information Nizoral is extensively bound to plasma proteins. No information on potential drug interactions is available.

Product licence number 0242/0083.

OPERIDINE*

Presentation Clear colourless aqueous injection presented in 2 ml ampoules. Each millilitre contains 1 mg phenoperidine hydrochloride.

Uses Operidine is a narcotic analgesic. It is used:

- (a) as an analgesic.
- (b) in conjunction with a neuroleptic in neuroleptanalgesia.
- (c) as a respiratory depressant/analgesic in patients requiring prolonged assisted ventilation in intensive care.

Dosage and administration Operidine, by the intravenous route, can be administered to both adults and children according to the following dosage regimen:

	<i>Adults</i>		<i>Children</i>
	<i>initial</i>	<i>supplemental</i>	
Spontaneous respiration	Up to 1 mg	0.5 mg	0.03–0.05 mg/kg
Assisted ventilation	2–5 mg	1.0 mg	0.1–0.15 mg/kg

Depending on the degree of pain stimulus and/or the depth of respiratory depression required, supplemental doses should be administered at intervals of 40–60 minutes.

In intensive care, Operidine may be administered by the intramuscular route at the above dosages.

Contra-indications, warnings, etc

Contra-indications: Obstructive airways disease; respiratory depression if not electively ventilating.

Concomitant administration with monoamine oxidase inhibitors or within 2 weeks of discontinuation of them.

Warnings: Significant respiratory depression will occur following administration of phenoperidine in doses in excess of 1 mg. This and the other pharmacological effects of Operidine can be reversed with naloxone 0.1–0.2 mg i.m. or i.v.

Bradycardia may occur and this may be antagonised by atropine. Muscular rigidity (morphine-like effect) may occur, in which case muscle relaxants have been found helpful.

If other narcotic or CNS depressant drugs are used concomitantly with phenoperidine, the effects of the drugs can be expected to be additive.

Precautions: It is wise to reduce the dosage in the elderly, in hypothyroidism and chronic hepatic disease.

As with other narcotic analgesics, administration in labour may cause respiratory depression in the newborn infant.

Side-effects: Tolerance and dependence may occur. Nausea and vomiting may be troublesome. A few cases of jaundice have been reported.

Use in Pregnancy: Little human usage but no adverse animal evidence.

Overdosage: Overdosage should be treated with the antidotes mentioned above.

Pharmaceutical precautions If desired Operidine can be mixed with 5% dextrose or 0.9% saline solutions for infusion and with most agents commonly used in

anaesthesia, but the product is chemically incompatible with the induction agents thiopentone, propomid, and methohexitone because of the wide difference in pH.

Legal category POM. MDA.

Package quantities Operidine is supplied in 2 ml ampoules (1 mg/ml) in packs of 10

Further information Operidine does not contain preservatives.

Product licence number 0242/5000R.

ORAP*

Presentation White, scored, uncoated tablets marked 'JANSSEN' on one side and $\frac{1}{2}$ on the other, each contains 2 mg pimozide.

Pale green, scored, uncoated tablets marked 'JANSSEN' on one side and $\frac{1}{4}$ on the other, each contains 4 mg pimozide.

White, scored uncoated tablets marked 'JANSSEN' on one side and $\frac{1}{10}$ on the other, each contains 10 mg pimozide.

Uses Orap is an antipsychotic of the diphenyl butyl piperidine series and is indicated for the treatment of acute or chronic schizophrenia. Hallucinations, delusions, thought disorders, emotional withdrawal respond well to lower doses of the drug. Higher doses may be needed for the control of acutely agitated, hyperactive or aggressive patients.

Dosage and administration Orap is intended for oral administration to both adults and children. Patients may be maintained on a once daily dosage regime.

As with all neuroleptics, it is important to determine the dose of Orap according to the individual response of each patient.

In adults: Dosage ranges between 2–20 mg daily. The usual initial dose is 4–10 mg, which may be varied according to response and tolerance to achieve an optimum maintenance dosage. In the acutely agitated patient the initial dose is 20 mg. Gradual reduction to the lowest effective maintenance dose may be attempted once control of symptoms is achieved.

In children: In children over 12 years of age dosage should normally be 1–3 mg daily. Clinical experience in young children is limited and, therefore, Orap should be used at the physician's discretion in children under 12 years of age.

Contra-indications, warnings, etc

Contra-indications: Although no teratological changes have been observed in experimental animals, the drug should not be administered to pregnant women.

Warnings: Endogenous depression, pre-existing Parkinson's disease and epilepsy may be aggravated.

Overdosage: There is no specific antidote to an overdose of pimozide. Cases should be treated symptomatically. A suicide attempt with 100 mg pimozide produced only slight tremor and another with over 200 mg showed no specific side-effects and needed no treatment.

Side-effects: Extra-pyramidal effects may occur at higher dosage levels. Occasional skin rashes have been reported. Glycosuria has been reported following Orap administration, but it has not been established whether this effect was drug related.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Orap tablets each containing 2 mg pimozone are supplied in packs of 100 and 500.

Orap tablets each containing 4 mg pimozone are supplied in a pack of 250.

Orap tablets each containing 10 mg pimozone are supplied in a pack of 100.

Further information Nil.**Product licence numbers**

Orap 2 mg 0242/5010

Orap 4 mg 0242/0038

Orap 10 mg 0242/0069

STUGERON[®] FORTE 75 mg

Presentation Hard gelatin capsules (No. 4) with an orange cap and yellow body; each capsule contains cinnarizine 75 mg.

Uses Cinnarizine protects arterial smooth muscle from the effects of vasospastic agents including angiotensin, bradykinin, serotonin and noradrenaline. Cinnarizine has been shown to reduce the viscosity of whole blood in arteriosclerotic patients.

Stugeron Forte is indicated for the long term management of peripheral arterial disease, including intermittent claudication, rest pain, muscular cramps and vasospastic disorders, e.g. Raynaud's disease.

Dosage and administration Stugeron Forte is for oral administration to adults.

The recommended starting dose is 1 capsule three times daily. Maintenance dose is 1 capsule, two or three times daily according to response.

Peripheral arterial disease is slow to improve with any form of drug treatment. *Maximum benefit with Stugeron Forte will not be seen until after several weeks of continuous treatment* although significant improvement in blood flow has frequently been demonstrated after one month.

Contra-indications, warnings, etc

Contra-indications: There are no specific contra-indications. Stugeron Forte has not been found to decrease blood pressure significantly. However, the drug should be used with reasonable caution in hypotensive patients. The safety of Stugeron Forte in human pregnancy has not been established although studies in animals have not demonstrated teratogenic effects. As with other drugs, it is not advisable to administer Stugeron Forte in pregnancy.

Warnings: Stugeron Forte may cause drowsiness; patients affected in this way should not drive or operate machinery. Avoid alcoholic drink.

Overdosage: There is no specific antidote to Stugeron Forte and, in the event of overdosage, gastric lavage is recommended.

Side-effects: Allergic skin reactions and fatigue have been reported on rare occasions.

Pharmaceutical precautions No special precautions. The product has a shelf life of five years.

Legal category P.

Package quantities Stugeron Forte is supplied in packs of 100 capsules.

Further information No drug interactions have been seen with Stugeron Forte when administered concomi-

tantly with antihypertensives, diuretics, anticoagulants or hypoglycaemics.

Animal studies have shown that cinnarizine protects the arterial wall from arteriosclerotic degeneration due to hypertension.

Product licence number 0242/0008.

STUGERON[®]

Presentation White, uncoated, scored tablets marked 'JANSSEN' on one side and S above 15 on the reverse. Each tablet contains 15 mg cinnarizine.

Uses Stugeron is used for the control of vestibular disorders such as vertigo, tinnitus, nausea and vomiting as seen in Ménière's disease. Stugeron is also effective in the control of motion sickness.

Dosage and administration Stugeron is for oral administration to both adults and children according to the following dosage regimen:

Vestibular symptoms: Adults and children over 12: 2 tablets three times a day.

Children 5–12 years: One half the adult dose.

Motion sickness: Adults and children over 12: 2 tablets 2 hours before you travel and 1 tablet every 8 hours during your journey.

Children 5–12 years: One half the adult dose.

Contra-indications, warnings, etc

Contra-indications: The safety of Stugeron in human pregnancy has not been established although studies in animals have not demonstrated teratogenic effects. As with other drugs, it is not advisable to administer Stugeron in pregnancy.

Warnings: Stugeron may cause drowsiness; patients affected in this way should not drive or operate machinery. Avoid alcoholic drink.

Overdosage: There is no specific antidote to Stugeron and, in the event of overdosage, gastric lavage is recommended.

Side-effects: Rarely, allergic skin reactions have been reported which have responded to discontinuation of therapy.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Stugeron tablets each containing 15 mg cinnarizine are supplied in packs of 250 and 1,000.

Further information Nil.

Product licence number 0242/5009.

SUBLIMAZE[®]

Presentation Clear, colourless, aqueous injection presented in 2 ml and 10 ml ampoules. Each millilitre contains 0.05 mg fentanyl.

Uses Sublimaze is a narcotic analgesic. It is used in low doses to provide analgesia during short surgical procedures. In larger doses it is used as an analgesic/respiratory depressant in patients requiring assisted ventilation. In combination with a neuroleptic, Sublimaze is used in the technique of neuroleptanalgesia.

Dosage and administration Sublimaze, by the intravenous route, can be administered to both adults and children according to the following dosage regimen table.

	<i>Initial</i>	<i>Supple- mental</i>
Adults:		
Spontaneous respiration	50–200 mcg	50 mcg
Assisted ventilation	300–3500 mcg	100–200 mcg
Children:		
Spontaneous respiration	3–5 mcg/kg	1 mcg/kg
Assisted ventilation	15 mcg/kg	1–3 mcg/kg

Doses in excess of 200 mcg are for use in anaesthesia only. As a premedicant, 0.05–0.1 mg Sublimaze may be given intramuscularly 45 minutes before induction of anaesthesia.

After intravenous administration in unpremedicated adult patients 2 ml Sublimaze may be expected to provide sufficient analgesia for 10–20 minutes in surgical procedures involving low pain intensity. 10 ml Sublimaze injected as a bolus gives analgesia lasting about one hour. The analgesia produced is sufficient for surgery involving moderately painful procedures. Giving a dose of 50 mcg/kg Sublimaze will provide profound analgesia for some four to six hours, for intensely stimulating surgery. When judging the dose it is important to assess the likely degree of surgical stimulation, the effect of premedicant drugs, and the duration of the procedure.

Contra-indications, warnings, etc Respiratory depression: Obstructive airways disease.

Concurrent administration with monoamine oxidase inhibitors, or within two weeks of discontinuation of treatment with them.

Warnings: Following intravenous administration of fentanyl, a transient fall in blood pressure may occur.

Significant respiratory depression will occur following the administration of fentanyl in doses in excess of 200 mcg. This, and the other pharmacological effects of fentanyl, can be reversed with naloxone 0.1–0.2 mg.

Bradycardia may occur and this can be antagonised by atropine. Muscular rigidity (morphine-like effect) may occur, in which case muscle relaxants have been found helpful.

If other narcotics or CNS depressant drugs are used concomitantly with fentanyl, the effects of the drugs can be expected to be additive. Tolerance and dependence may occur. Nausea and vomiting may be troublesome.

Precautions: As with all narcotic analgesics, care should be observed when administering fentanyl to patients with myasthenia gravis.

It is wise to reduce dosage in the elderly, in hypothyroidism, and chronic hepatic disease.

Administration in labour may cause respiratory depression in the new born infant.

Use in pregnancy: Safety in human pregnancy has not been established although studies in animals have not demonstrated teratogenic effects.

Overdosage: Overdosage should be treated with the antidotes mentioned above.

Pharmaceutical precautions If desired Sublimaze can be mixed with i.v. infusion solutions and with most agents commonly used in anaesthesia, but the product is chemically incompatible with the induction agents thiopentone, propanidid and methohexitone because of the wide differences in pH.

Legal category POM MDA.

Package quantities Sublimaze is supplied in 2 ml ampoules (0.05 mg/ml) in packs of 10 and in 10 ml ampoules (0.05 mg/ml) in packs of 10.

Further information Nil.

Product licence number 0242/5001 R.

THALAMONAL*

Presentation Clear, colourless, aqueous injection presented in 2 ml ampoules. Each millilitre contains 0.05 mg fentanyl and 2.5 mg droperidol.

Uses Thalamonal is a combination of a major tranquiliser and narcotic analgesic and is used primarily for pre-medication. Additionally, it can be used as an adjunct to general and regional anaesthesia in major, minor and diagnostic surgical procedures. Thalamonal can also be used in intractable labyrinthine vertigo, e.g. Ménière's disease, where immediate relief of symptoms can be expected.

Dosage and administration Thalamonal can be administered intravenously to adults or intramuscularly to both adults and children. The following dosage regimen is recommended:

Pre-medication:

Route: Intramuscular.

Adults: 1–2 ml.

Children: 0.4–1.5 ml.

15–45 minutes pre-operatively.

At induction of anaesthesia:

Route: Intravenous.

Adults: 6–8 ml.

Followed by assisted respiration.

Maintenance of anaesthesia:

Route: Intravenous.

Adults: 1–2 ml.

When signs of lightening of anaesthesia are observed.

Intractable labyrinthine vertigo:

Route: Intravenous.

Adults: 1–2 ml.

By slow injection.

Contra-indications, warnings, etc

Contra-indications: Thalamonal is contra-indicated in the severely depressed patient.

Warnings: Following intravenous administration of Thalamonal a transient fall in blood pressure may occur.

Respiratory depression (reversed with naloxone), bradycardia (antagonised by atropine), muscular rigidity, a typical morphine-like effect (relieved with muscle relaxants) and extrapyramidal effects (counteracted by anti-Parkinson drugs) are possible effects resulting from the use of Thalamonal.

Precautions: Care is required when using Thalamonal with other CNS depressants as the individual effects can be potentiated. Care is also required when administering Thalamonal to patients with severe hepatic disease or myasthenia gravis. As with all narcotic analgesics caution

should be observed when administering Thalamonal to patients receiving MAO inhibitors.

Minor central effects can in some instances persist for up to 48 hours after administration and hence where early discharge is envisaged patients should be advised not to drive or operate machinery on the day following administration.

Overdosage: Overdosage should be treated with the antidotes mentioned.

Pharmaceutical precautions Thalamonal should be protected from light. Thalamonal can be mixed with intravenous infusion solutions where slow administration is desired.

This product is chemically incompatible with thiopentone, propanidol and methohexitone because of the wide difference in pH.

Legal category POM MDA.

Package quantities Thalamonal is supplied in 2 ml ampoules in packs of 10.

Further information Nil.

Product licence number 0242/5002.

FINSET* ▼

Presentation White biconvex scored tablets marked 'JANSSEN' on one side and Ox/30 on the reverse; containing oxatamide 30 mg.

Uses Oxatamide is indicated for the symptomatic control of allergic rhinitis, conjunctivitis and urticaria and other conditions responsive to drugs with anti-histaminic properties. Food allergy.

Dosage and administration Twice daily oral administration (morning and evening after meals):

Adults and children over 14: 30 mg b.d. which may be increased to 60 mg b.d. if required (i.e. 1–2 tablets, twice daily).

Children aged 5–14: 15–30 mg b.d. ($\frac{1}{2}$ –1 tablet, twice daily).

Contra-indications, warnings, etc There are no specific contra-indications to the use of oxatamide.

Although no teratogenic effects have been observed in experimental animals, the safety of oxatamide in pregnancy has not yet been established.

Side-Effects: Oxatamide may cause drowsiness in some patients, who, if affected, should not drive or operate machinery. Avoid alcoholic drink. Increased appetite leading to weight gain has been occasionally reported in patients at higher dosage levels (above 60 mg b.d.), but is rare at the recommended dosage. This effect is reversible on discontinuation of treatment.

Overdosage: In event of accidental overdosage supportive measures and/or gastric lavage are recommended.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Packs of 25 tablets.

Further information Nil.

Product licence number 0242/0064.

VERMOX*

Presentation *Vermox tablets:* Pale pink, flat, scored, chewable tablets, approximately 10 mm in diameter, marked 'JANSSEN' on one side and Me/100 on the reverse. Each tablet contains mebendazole 100 mg.

Vermox suspension: White, banana flavoured suspension of mebendazole 2% w/v. Each 5 ml contains mebendazole 100 mg.

Uses Vermox is a broad spectrum anthelmintic indicated for the treatment of:

<i>Enterobius vermicularis</i>	}	(Threadworm/Pinworm)
<i>Oxyuris vermicularis</i>		
<i>Trichuris trichiura</i>		(Whipworm)
<i>Ascaris lumbricoides</i>		(Large Roundworm)
<i>Ancylostoma duodenale</i>		(Common Hookworm)
<i>Necator americanus</i>		(American Hookworm)

in single or mixed infestations.

Dosage and administration Vermox tablets and suspension are for oral administration. The tablets are orange flavoured and may be chewed or swallowed whole. Vermox suspension provides an alternative liquid formulation.

The same dosage applies to adults and children aged two years and above. No special procedures such as purging, use of laxatives and/or dietary changes are required.

(a) Threadworm (*Enterobius vermicularis*)

A single dose of one tablet, or 5 ml suspension.

(b) Whipworm (*Trichuris trichiura*)

Large Roundworm (*Ascaris lumbricoides*)

Common Hookworm (*Ancylostoma duodenale*)

American Hookworm (*Necator americanus*)

One tablet or 5 ml suspension twice daily (morning and evening) for three consecutive days.

Contra-indications, warnings, etc *Pregnancy:* Vermox has shown embryotoxic and teratogenic activity in rats at single oral doses. No such findings have been reported in the rabbit, dog, sheep, or horse. Since there is a risk that Vermox could produce foetal damage if administered during pregnancy, it is contra-indicated in pregnant women.

Use in infants: Vermox has not been studied extensively in children under two years of age – for this reason it is not currently recommended in the treatment of children under two years.

Side effects reported for Vermox have been minor. Transient abdominal pain and diarrhoea have been reported, only rarely, in cases of massive infestation and expulsion of worms.

No case of overdose has so far been reported for Vermox and there have been no reports of intolerance or adverse effects with doses up to 20 tablets daily for periods of 4 weeks.

Pharmaceutical precautions Vermox suspension should be shaken before use.

Legal category POM.

Package quantities

Tablets: Blister pack of 6 tablets.

Suspension: 30 ml bottle.

Further information The efficacy of Vermox in threadworm (*Enterobius vermicularis*) infestations is such that treatment failures will be rare. However, the possibility of re-infection means that some patients may require a second treatment after two or three weeks.

Product licence numbers

Tablets	0242/0011
Suspension	0242/0050

**Trade Mark*

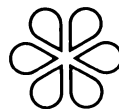
KabiVitrum Limited

KabiVitrum House

Riverside Way

Uxbridge

Middlesex UB8 2YF



ADDAMEL* ▼

Presentation Sterile straw coloured solution containing electrolytes and trace elements for addition to the Vamin amino acid solutions in the intravenous nutrition of adults. Addamel corresponds to the following formula:

Calcium chloride 2H ₂ O	73.5 mg
Magnesium chloride 6H ₂ O	30.42 mg
Ferric chloride 6H ₂ O	1.35 mg
Zinc chloride	0.27 mg
Manganese chloride 4H ₂ O	0.79 mg
Copper chloride 2H ₂ O	85 mcg
Sodium fluoride	0.21 mg
Potassium iodide	17 mcg
Sorbitol	0.3 g

Water for injection to 1 ml
pH 2.5

One ampoule (10 ml of Addamel) contains the following amounts of electrolytes and trace elements:

Ca ²⁺	5 mmol
Mg ²⁺	1.5 mmol
Fe ³⁺	50 micromol
Zn ²⁺	20 micromol
Mn ²⁺	40 micromol
Cu ²⁺	5 micromol
F ⁻	50 micromol
I ⁻	1 micromol
Cl ⁻	13.3 mmol

One ampoule of Addamel contains less than 1 mmol of both potassium and sodium.

Uses Addamel is an integral part of a complete intravenous nutritional regimen. It should be used in conjunction with a Vamin solution, Intralipid and a suitable phosphate preparation containing potassium. This will provide the patient's basal requirements for electrolytes and trace elements. As the requirements for electrolytes and trace elements may vary in different clinical conditions these substances may have to be added as appropriate in the individual patient.

Dosage and administration *Recommended dosage for adults:* 1 ampoule (10 ml) of Addamel is added to 500 ml or 1,000 ml of Vamin Glucose, or Vamin N which is infused over six to eight hours. In this way the normal daily requirements of Ca, Mg, Fe, Zn, Mn, Cu, F, I and Cl are supplied. Where higher amounts of trace elements are considered necessary, 2 ampoules of Addamel may be added to 1,000 ml of the Vamin preparation.

Recommended dosage for infants: For infants the electrolyte solution Ped-el should be used.

One ampoule of Addamel should be infused over a minimum of 2-3 hours in patients with normal renal function so as to avoid renal losses.

The requirements of potassium and sodium vary with different patient conditions, Addamel is not intended to

meet these requirements. Potassium and sodium salts should be added as appropriate to the individual patient. (20 mmol potassium and 50 mmol sodium are contained in 1 litre of Vamin solutions).

Contra-indications, warnings, etc Should not be given undiluted. Care should be taken in the administration of Addamel to patients with impaired renal function.

One ampoule of Addamel contains 3 g sorbitol which is metabolised to fructose, and should therefore be given with caution to patients with fructose intolerance.

Pharmaceutical precautions Addition of other drugs to be avoided due to the risk of precipitation.

Store at below 25°C.

The addition of Addamel should be performed aseptically immediately before the start of the infusion and should be used within 24 hours unless the mixture is refrigerated when it may be used within 48 hours of preparation.

Legal category POM.

Package quantities 10 ml ampoules packed in boxes of five.

Further information The manufacturer can be consulted for full information on balanced and complete intravenous feeding regimens.

Product licence number 0022/0034.

ALBUMIN KABI* (HUMAN, SOLUTION 20%)

Presentation Vials containing 100 ml sterile solution of human serum albumin (20%) straw to amber in colour with acetyltryptophanate and sodium caprylate as stabilisers. pH 6.8. Electrolyte content (mmol/l): Na⁺ max. 120, K⁺ 1, Ca⁺⁺ approx. 4, Cl⁻ 15.

Uses In hypoalbuminaemia, which may be associated with the indications listed below. Albumin expands plasma volume, reduces blood and plasma viscosity, and maintains osmotic pressure.

Indications: Defective synthesis: Severe malnutrition. Hepatic cirrhosis.

Abnormal losses of protein: Nephrotic syndrome. Gastric cancer. Ulcerative colitis. After abdominal treatment with ionising radiation. Hypovolaemic shock, e.g. haemorrhagic and traumatic shock, shock caused by burns and shock with pronounced intravascular aggregation.

Increased catabolism. Postoperatively and after other trauma. In burns. Severe infections.

Open cardiovascular surgery and organ perfusions. As an additive to the perfusion fluid in extracorporeal circulation.

Albumin solution is recommended as a perfusate in the preservation of kidneys for transplantation in pre-

ference to human plasma. The advantages are a standardised fluid as to protein content and electrolyte composition.

Dosage and administration *Route of administration:* By intravenous infusion.

Recommended dosage: Defective synthesis. Hypoproteinaemia, severe malnutrition. The dosage should be suited to the protein and albumin deficiency.

Albumin Kabi is administered by slow intravenous injection or infusion in a dose of 2–4 ml per kg body weight per hour.

Hepatic cirrhosis: 20–50 g albumin (100–250 ml Albumin Kabi 20%) daily for three or more days postoperatively.

Abnormal losses of protein: Nephrosis: 25–50 g albumin (125–250 ml Albumin Kabi 20%) should be given daily for one or more weeks.

Gastric cancer: The dosage usually recommended is 20 g albumin (100 ml Albumin Kabi 20%) daily for three to four days preoperatively and 5–10 g albumin (25–50 ml Albumin Kabi 20%) daily for two or more days postoperatively.

Ulcerative colitis: In acute exacerbations 20 g albumin (100 ml Albumin Kabi 20%) are given daily for one to two weeks. When surgery is planned, 20 g albumin (100 ml Albumin Kabi 20%) are given daily three to four days preoperatively and 5–10 g albumin (25–50 ml Albumin Kabi 20%) daily for three or more days postoperatively.

Other gastro-intestinal diseases: Before and during operation, 20–40 g albumin (100–200 ml Albumin Kabi 20%) are given. The dosage should be suited to the patient's condition. Postoperatively, about 20 g albumin (about 100 ml Albumin Kabi 20%) are given daily for the first two to three days. In strangulation ileus larger dosages of albumin over a longer period of time are usually needed. Preferably, Albumin Kabi 20% should be diluted to 5% with isotonic sodium chloride solution, e.g. 3 ml of infusion solution per ml Albumin Kabi 20%.

Hypovolaemic shock and shock with pronounced intravascular aggregation: The albumin dose should match the size of the blood or plasma loss and depends on the haematocrit value. In blood losses exceeding 1,000 ml, blood transfusions should be given in the first instance. Albumin Kabi 20% should be diluted to 5% for example with an isotonic sodium chloride solution, e.g. 3 ml of infusion solution per ml Albumin Kabi 20%.

Increased catabolism: Shock prophylaxis in surgery and postoperatively. Usually a dosage of 500–1,000 ml albumin solution 5% is recommended. (Albumin Kabi 20% is diluted in the same way as for hypovolaemic shock. See above.) Postoperatively the dosage should be suited to the patient's condition.

Burns: Parenteral substitution therapy should be instituted as soon as possible, based on the severity of the patient's condition and on laboratory tests. During the first 24 hours shocked patients should be given 1.5 ml of colloids (blood, plasma or albumin) and 1 ml of electrolyte solution per kg body weight multiplied by the percentage of body surface burned, together with about 2 litres of invert sugar solution. Half of this fluid volume is given during the first eight hours, the remaining half being given over the next 16 hours. Thereafter, on the second day it is suitable to give half the volume of fluid solution given during the first day, and from the second to the seventh day about 100 g albumin (about 500 ml Albumin Kabi 20%). In severe burns it may be necessary

to give albumin over a longer period of time in order to replace the losses due to the remaining increased albumin catabolism and increased albumin leakage.

Open cardiovascular surgery and local perfusion as an additive to the perfusion fluid in extracorporeal circulation: 400–1,200 ml albumin solution 5% are added to the oxygenator. Albumin Kabi 20% may be diluted with glucose solution 5%, e.g. 3 ml of glucose solution 5% per ml Albumin Kabi 20%.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Store protected from light, below 25°C. A cloudy solution must not be used.

Legal category POM.

Package quantities Bottles of 100 ml.

Further information In conditions of dehydration a 5% solution should be given.

Albumin Kabi 20% can be mixed with the following infusion solutions: Isotonic saline, Ringer's solution, Ringer-Acetate, sodium chloride-acetate, isotonic glucose or 10% invertose. The electrolyte content of these mixtures can be increased by the addition of suitable stock preparations, e.g. 2 ml per 100 ml of sodium chloride sterile stock solution 4M. Because of the viscosity of albumin solutions, thorough mixing is required. Obviously, directions for the total daily dose of stock solutions and the rate of infusion of the mixture should be followed carefully.

Product licence number 0022/5008.

CETIPRIN®

Presentation *Cetiprin Tablets 100 mg:* White, coated and slightly bulged tablets of 10 mm diameter, marked (CT) on one side. Each tablet contains 100 mg emepromonium bromide.

Uses *Main pharmacological action:* Emepromonium bromide is a quaternary ammonium anticholinergic drug which blocks peripheral cholinergic nerves and ganglionic transmission. In man, it increases bladder capacity, delays the first desire to void and decreases voiding pressure.

Indications:

1. Urinary frequency and incontinence in old people
2. Nocturnal frequency.
3. After bladder surgery, prostatectomy or bladder radiotherapy.

In order to obtain an optimal response the treatment should continue for at least three to four weeks.

Dosage and administration *Route of administration* By mouth with an adequate amount of fluid (minimum 100 ml).

Cetiprin tablets should always be taken with the patient sitting or standing and the patient should not lie down within 10–15 minutes following ingestion.

Recommended dosage:

1. Urinary frequency and incontinence in old people up to 200 mg (2 × 100 mg tablets) three times daily dependant on response.
2. Nocturnal frequency: 200–400 mg at bedtime.
3. After bladder surgery, prostatectomy or bladder radiotherapy: 200 mg (2 × 100 mg tablets) three times daily in most cases.

Contra-indications, warnings, etc Cetiprin is contra-indicated in the following:

1. In patients with symptoms or signs of oesophageal obstruction.
2. In patients with pre-existing oesophagitis.
3. In patients with prostatic enlargement associated with large amounts of residual urine and flaccid bladder.

Precautions:

1. Caution should be observed in patients with glaucoma or gastric retention.
2. No teratogenic effect has been observed but the usual precautions in early pregnancy should be observed.

Side-effects: Rarely, dryness of the mouth. Ulceration of the gums and mouth has been reported, particularly in geriatric patients who hold the tablets in their mouths for long periods. There have also been instances of oesophageal ulceration when the tablets have not been swallowed with an adequate amount of fluid. See dosage recommendations above.

Antidote: As for atropine; gastric lavage.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Cetiprin 100 mg. Bottles of 50, 250 and 500 tablets.

Further information Nil.

Product licence numbers

100 mg tablets 0022/5001

CRESCORMON*, HUMAN GROWTH HORMONE, KABI

Presentation A vial of sterile lyophilised powder of human growth hormone 4 i.u. (about 2 i.u./mg, immunologically determined), containing also aminoacetic acid and sodium phosphate q.s., and supplied with a 2 ml ampoule of physiological saline for use in reconstituting the injection.

Uses *Main pharmacological action:* Stimulating growth in hypopituitary dwarfs.

Indications: The treatment of dwarfism due to decreased or failed secretion of pituitary growth hormone. The diagnosis should be verified by investigation of pituitary function before Crescormon is administered.

Dosage and administration *Route of administration:* by intramuscular injection.

Recommended dosage: Only patients with open epiphyses should be treated.

The dosage is individual but in general a dose each week of at least 0.5 i.u. per kg body weight divided in 2 or 3 intramuscular injections is recommended.

Preparation of solution: The solution is prepared by adding 2 ml saline solution to the lyophilised substance in the vial. A made-up solution should be used immediately after preparation.

Contra-indications, warnings, etc Diabetes mellitus.

In spite of rigorous requirements for the collection and control of the pituitary glands used in the preparation of Crescormon, the risk of transmitting hepatitis cannot be excluded. However, the risk is extremely small.

Antidote: Nil.

Side-effects: Crescormon has, in clinical trials, stimulated

the formation of antibodies in low titre in a few patients but this has no effect on efficacy. Otherwise no adverse reactions have been observed.

Pharmaceutical precautions Store in a refrigerator (+5°C).

Legal category POM.

Package quantities Combined package containing 1 vial of sterile lyophilised human growth hormone 4 i.u. and one ampoule of 2 ml of saline solution to reconstitute the preparation.

Further information Crescormon (Human Growth Hormone, Kabi) is prepared from human pituitary glands according to Roos *et al.* (*Biochim. Biophys. Acta*, **74**, 525, 1963). The immunological content is determined against IRP Growth Hormone, Human for Immunoassay (WHO).

Product licence number 0022/0020.

CYKLOKAPRON*

Presentation *Cyklokapron tablets:* White, flat, uncoated tablets of 13 mm diameter engraved CY, each containing 500 mg tranexamic acid.

Cyklokapron syrup: A colourless or slightly yellow syrup containing 500 mg Tranexamic Acid in each 5 ml.

Cyklokapron solution for injection: Ampoules of 5 ml of colourless solution containing tranexamic acid 100 mg/ml.

Uses *Action:* Tranexamic acid is an antifibrinolytic agent which competitively inhibits the activation of plasminogen to plasmin.

Indications: Short-term use for haemorrhage or risk of haemorrhage in increased fibrinolysis or fibrinogenolysis.

1. Local fibrinolysis as occurs in the following conditions:

- (a) Prostatectomy and bladder surgery.
- (b) Menorrhagia.
- (c) Epistaxis.
- (d) Sub-arachnoid haemorrhage.
- (e) Conisation of the cervix.
- (f) Traumatic hyphaema.

2. Hereditary angioneurotic oedema.
3. Management of dental extraction in haemophiliacs.
4. General fibrinolysis, as in prostatic and pancreatic cancer; after thoracic and other major surgery in obstetrical complications such as abruptio placentae and post-partum haemorrhage, and in connection with thrombolytic therapy.

Dosage and administration *Local fibrinolysis:* The recommended standard dose is 5–10 ml by slow intravenous injection at a rate of 1 ml/minute or 2–3 tablets or 10–15 ml syrup, two to three times daily. For the indications listed below the following doses may be used:

1a. Prostatectomy and bladder operations: 1.0 g (2 ampoules of 5 ml) by slow intravenous injection every eight hours (the first injection being given during the operation) for the first three days after surgery; thereafter 2 tablets or 10 ml syrup, three to four times daily until macroscopic haematuria is no longer present. As a bladder washout, 1 g (2 ampoules) is added to 1,000 ml of normal saline daily, for 2–5 days after surgery. The bladder is then irrigated at a rate of 1 ml/minute.

1b. Menorrhagia: 2–3 tablets or 10–15 ml syrup three to four times daily for three to four days. Cyklokapron therapy is initiated only after heavy bleeding has started and its use should be restricted to not more than three menstrual cycles.

1c. Epistaxis: Cyklokapron solution for injection may be applied topically to the nasal mucosa of patients suffering from epistaxis. This can be done either using a spray or by soaking a gauze strip in the solution, and then packing the nasal cavity. Where recurrent bleeding is anticipated oral therapy (2 tablets or 10 ml syrup three times a day) should be administered for seven days.

1d. Sub-arachnoid haemorrhage. Therapy should be commenced as soon as possible after initial haemorrhage. 1.0 g (2 ampoules of 5 ml) by slow intravenous injection six times daily for one week, followed by 1.5 g (3 tablets or 15 ml syrup) orally four times daily for a further five weeks, or until operation.

1e. Conisation of the cervix: 1.5 g (3 tablets or 15 ml syrup or 3 ampoules) three times a day.

1f. Traumatic hyphaema: 2–3 tablets or 10–15 ml syrup three times daily. The dose is based on 25 mg/kg three times a day.

2. Hereditary angioneurotic oedema: Some patients are aware of the onset of the illness, a suitable treatment for these patients is intermittently 2–3 tablets or 10–15 ml syrup two to three times daily for some days. Other patients are treated continuously at this dosage.

3. Haemophilia. 1.0–1.5 g (2–3 tablets or 10–15 ml syrup) every eight hours in the management of dental extractions. The dose is based on 25 mg/kg.

4. General fibrinolysis: 1.0 g (2 ampoules of 5 ml) by slow intravenous injection every six to eight hours (15 mg/kg). Alternatively, 20–25 mg/kg orally, two to three times daily.

Children's dosage: This should be calculated according to body weight, at 25 mg/kg/dose orally and 10 mg/kg/dose intravenously.

Contra-indications, warnings, etc Cyklokapron is contra-indicated in patients with thromboembolic disease.

Precautions:

1. In patients with renal insufficiency, because of the risk of accumulation. The dose should be reduced according to the following table:

Serum creatinine	Dose i.v.	Dose frequency
120–250 mcmlol/l	10 mg/kg	twice daily
250–500 mcmlol/l	10 mg/kg	every 24th hour
> 500 mcmlol/l	5 mg/kg	every 24th hour

2. In massive haematuria from the upper urinary tract (especially in haemophilia) since, in a few cases, ureteric obstruction has been reported.

3. In patients with a recent history of a thromboembolic episode.

4. In the long-term treatment of patients with hereditary angioneurotic oedema regular eye examination (e.g. visual acuity, slip lamp, intra-ocular pressure, visual fields) and liver function tests should be performed.

5. Although there is no evidence from animal studies of a teratogenic effect, the usual caution with use of drugs in pregnancy should be observed.

Side-effects: Gastro-intestinal disorders (nausea, vomiting, diarrhoea) may occur but disappear when the dosage is reduced. Rare instances of giddiness have

been reported when intravenous injection is given too rapidly.

Antidote: In case of overdosage stomach lavage and maintain high fluid intake.

Pharmaceutical precautions The solution for injection may be mixed with the following solutions:

Isotonic sodium chloride

Isotonic glucose

20% fructose

10% invertose

Dextran 40

Dextran 70

Ringer's solution

Cyklokapron solution for injection may be mixed with heparin.

Cyklokapron syrup may be diluted with Syrup BP.

Cyklokapron solution for injection should NOT be added to blood for transfusion or to injections containing penicillin.

Legal category POM.

Package quantities Bottle of 50 tablets, bottle of 250 ml syrup, box of 6 ampoules, each of 5 ml.

Further information Cyklokapron passes to the mother's milk but risk to the child unlikely for therapeutic doses. Levels in breast milk are approximately one hundred times lower than the maternal serum peak concentration.

Product licence numbers

Tablets 500 mg 0022/0003

Syrup 0022/0044

Solution for injection 0022/0004

DIAZEMULS* ▼

Presentation Ampoules of a white, opaque emulsior containing 10 mg of diazepam in 2 ml.

Uses Action: Diazepam is a potent anxiolytic, anticonvulsant and central muscle relaxant mediating its effect mainly via the limbic system as well as the polysynaptic spinal reflexes. The formulation of diazepam in an oil-in-water emulsion similar to Intralipid® reduces the incidence of local pain and thrombophlebitis after injection.

Indications:

1. As a premedication before major or minor surgery or dental procedures, endoscopy, cardiac catheterization.

2. In the control of acute muscle spasms such as tetanus, status epilepticus and convulsions due to poisoning.

3. In the management of severe acute anxiety or agitation including delirium tremens.

Dosage and administration Diazemuls can be administered by intravenous injection or infusion.

1. Premedication: 0.1–0.2 mg diazepam/kg body weight by i.v. injection.

2. Status epilepticus: An initial dose of 0.15–0.25 mg/kg by i.v. injection repeated in 30 to 50 minutes if required, and followed if necessary by infusion (see below) of up to 3 mg/kg over 24 hours.

Tetanus: 0.1–0.3 mg diazepam/kg body weight by i.v. injection and repeated every 1 to 4 hours as required.

Alternatively, a continuous infusion (see below) of 3–10 mg/kg body weight every 24 hours may be used.

3. Anxiety and tension, acute muscle spasms, acute states of excitation, delirium tremens: The usual dose is 10 mg repeated at intervals of 4 hours as required.

A clinical effect is frequently seen at lower doses in elderly or debilitated patients. If a continuous infusion is required Diazemuls can be added to dextrose solution 5% or 10% up to a final concentration of diazepam of 0.4 mg/ml. A dextrose solution containing added Diazemuls should be used within 6 hours of the admixture. Diazemuls can also be mixed in the container with Intralipid 10% or 20% but not with saline solutions. It can be injected into the infusion tube during an ongoing infusion of isotonic saline or dextrose solution 5% or 10%. As with other diazepam injections, adsorption may occur to plastic infusion equipment. This adsorption occurs to a lesser degree with Diazemuls than with aqueous diazepam injection preparations when mixed with dextrose solutions.

Contra-indications, warnings, etc Concomitant use of central nervous system depressants, e.g. alcohol, general anaesthetics, narcotic analgesics, or antidepressants, including MAOI's will result in accentuation of their effects. Treatment with diazepam may cause drowsiness and increase the patient's reaction time. This should be considered in situations where alertness is required, e.g. driving a car. As with any benzodiazepine, excessive or prolonged use may result in the development of some psychological dependence with withdrawal symptoms on discontinuation. Use with caution in patients with impairment of renal or hepatic function.

This product should not be used during pregnancy unless considered essential by the physician. Clinical effects may occur in the foetus and the newborn when Diazemuls is administered during late pregnancy or delivery. Diazepam can be transmitted in breast milk and clinical effects may occur in the breast fed infant.

This formulation may rarely cause local pain or thrombophlebitis in the vein used for administration.

Overdose: CNS depression and coma. Treatment symptomatic.

Pharmaceutical precautions For full information on admixture see dosage and administration. Diazemuls should only be mixed in the same container or syringe with dextrose solution 5% or 10% or Intralipid 10% or 20%. The contents of the ampoule should not be mixed with any drugs other than the infusion solutions mentioned above. Store at room temperature. Do not freeze.

Legal category POM

Package quantities Boxes of 5 × 2 ml ampoules
50 × 2 ml ampoules

Further information Nil.

Product licence number 0022/0043.

EPSIKAPRON*

Presentation Epsikapron Effervescent Powder 50% is a white powder supplied in sachets each containing 3.0 g aminocaproic acid.

Epsikapron Syrup is an orange tasting clear, colourless syrup containing 0.3 g/ml aminocaproic acid in bottles of 250 ml.

Uses Action: Aminocaproic acid competitively inhibits the activation of plasminogen to plasmin.

Indications: Inhibition of increased fibrinolysis or fibrinogenolysis with haemorrhage or risk of haemorrhage.

1. **Local fibrinolysis:** Fibrinolysis is an important potentiating factor in haemorrhage associated with menorrhagia and IUCD insertions and is an added complication in the management of upper gastro-intestinal haemorrhage and ulcerative colitis, subarachnoid haemorrhage and all forms of urinary tract surgery, particularly prostatectomy, and also cervical conisation for suspected carcinoma in situ. In addition, increased local fibrinolysis activity is associated with dental extractions in patients with haemophilia, Christmas disease and von Willebrand's disease.

2. **General fibrinolysis:** As in prostatic and pancreatic cancer, after thoracic and other major surgery; in obstetric complications such as abruptio placentae and post-partum haemorrhage; in leukaemia and liver diseases.

Dosage and administration *Route(s) of administration:* Effervescent powder: by mouth after reconstitution in water.

Syrup: By mouth.

1. **Local fibrinolysis:** The recommended standard dose is 3 g four to six times a day.

Menorrhagia: A sachet of 3.0 g aminocaproic acid (Epsikapron effervescent powder 50%) is dissolved in $\frac{1}{2}$ –1 glass of cold water and taken four to six times daily until menstruation has ceased (or 10 ml of syrup four to six times daily). Treatment should commence only when the menstrual flow has become profuse.

2. **General fibrinolysis:** The recommended standard dose is 6 g four to six times a day.

Children's dosage: This should be calculated according to body weight, at 100 mg/kg per dose.

Contra-indications, warnings, etc Epsikapron is contra-indicated in patients with thromboembolic disease.

Precautions:

1. If renal function is impaired, the dosage should be reduced because of the risk of accumulation.

2. In massive haematuria from the upper urinary tract (especially in haemophilia) since in a few cases ureteric obstruction has been reported.

3. In patients with recent history of a thromboembolic episode.

4. Although there is no evidence from animal studies of a teratogenic effect, the usual caution with the use of drugs in early pregnancy should be observed. Studies have shown the possibility of a reduction in fertility in the male rat. The significance of this in man is not known.

Side-effects: An acute myopathy with muscle pain, tenderness and sometimes myoglobinuria leading to secondary impairment of renal function has occurred rarely in patients who have had continuous therapy for longer than four weeks. Treatment should cease in any patient who complains of muscle pain. The condition is reversible following cessation of treatment. Dizziness, nausea or diarrhoea are occasional unwanted effects.

Antidote: In the case of overdose, stomach lavage and high fluid intake.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Box of 30 sachets, bottle of 250 ml.

Further information Nil.

Product licence numbers

Effervescent Powder 50% 0022/5004
Syrup 0022/5005

GAMMA GLOBULIN KABI*

Presentation Ampoules containing Human Normal Immunoglobulin solution 16%, a clear pale straw colour. The active constituent is gamma globulin.

Uses *Main pharmacological action:* Gamma Globulin is the source of antibodies.

Indications: Gamma globulins contain the main antibodies of normal adults as the preparation is produced from pooled plasma of not less than 15,000 blood donors. It is a reserve of antibodies for treatment and prophylaxis. Recommended as prophylaxis against infective hepatitis (hepatitis A) rubella (in pregnant women) and attenuation of measles. For the treatment of hypogammaglobulinaemia, agammaglobulinaemia and reduced immunity; following burns.

Dosage and administration *Route of administration:* By intramuscular injection only.

Recommended dosage: In infective hepatitis (hepatitis A) for prophylaxis against infective hepatitis on a weight and time basis for adults and children, 0.02–0.04 ml per kg body weight is recommended by WHO. In massive exposure, e.g. to people visiting highly endemic areas, 0.06–0.12 ml per kg body weight is recommended. The effect of the larger injection lasts normally four to six months and therefore the dosage should be repeated after this time.

In rubella: as soon as possible after exposure 20 ml are injected in pregnant women. The effect of an injection lasts about three weeks and therefore the dosage should be repeated after this time in case of a renewed exposure to the disease.

In measles: Prevention: 0.2 ml per kg body weight is injected within five days after date of exposure. The preventive effect of an injection normally lasts three weeks. The dosage should therefore be repeated after that period of time in case of a renewed exposure to the disease. Modification: 0.04 ml per kg body weight is injected within five days after date of exposure.

In hypogammaglobulinaemia and agammaglobulinaemia: as an initial dosage 1.3 ml per kg (maximum 60 ml) injected in divided doses over 48 hours. Half this dosage, 0.65 ml per kg (maximum 30 ml) is then given every three to four weeks.

In burns: during the first week after the trauma a total of about 50 g gamma globulin in the form of Gamma Globulin Kabi should be given in addition to plasma and blood. From the third up to the tenth day 15–30 ml (2.5–5.0 g gamma globulin) per day are injected.

Contra-indications, warnings, etc Gamma Globulin should not be given at the same time as live vaccines, such as measles, mumps, rubella and oral polio vaccines. If Gamma Globulin (2 ml) has been administered these vaccines should not be given for 3 months. This period should be increased to 6 months for the 5 ml injection. If these vaccines have been administered a period of 2 weeks should elapse before giving Gamma Globulin. Gamma Globulin may be given at the same time as

tetanus, typhus, diphtheria, polio (the inactivated form) and yellow fever.

Side-effects: In exceptional cases, intramuscular injections of gamma globulin may give rise to adverse reactions of the following type:

Local reactions: at the site of injection such as erythema, swelling, tenderness and induration, which generally subside within a few days after the injection.

General reactions: such as fever (38–40°C), chills and general malaise. These symptoms have appeared 6–8 hours after the injection and have generally subsided the day after the injection.

Hypersensitivity reactions: such as exanthema and pruritus. Flush, tachycardia and shock are rare. The reactions are more frequent in patients with hypogammaglobulinaemia or dysgammaglobulinaemia, generally occurring minutes or hours after the injection.

Pharmaceutical precautions Store between 4°C and 8°C.

Legal category POM.

Package quantities Ampoules of 2.0 and 5.0 ml.

Further information Concentration of antibodies many times higher than that of normal serum is obtained by precipitating the active fraction of immune bodies from a large pool of blood donors.

Gamma Globulin is used extensively as 'travel prophylaxis' against the risk of infective hepatitis (hepatitis A) in a standard dosage of 2.0 ml.

Product licence number 0022/5009.

INTRALIPID* 10%

INTRALIPID* 20%

Presentation A white, sterile, oil in water emulsion containing:

	<i>Intralipid</i> 10%	<i>Intralipid</i> 20%
Fractionated soya-bean oil	50 g	100 g
Fractionated egg phospholipids	6 g	6 g
Glycerol	11 g	11 g
Water for injections to 500 ml		
pH 7. The emulsion is sterile and pyrogen free		

Uses *Action:*

1. Intralipid is a concentrated source of energy for complete intravenous nutrition. Provision of a sufficient amount of energy in the form of carbohydrate is often restricted by such considerations as hypertonicity, hypervolaemia, tendency to thrombophlebitis and the limit beyond which further carbohydrate cannot be utilised. By the use of Intralipid it is possible to provide a high energy intake in a relatively small volume. One litre of Intralipid 20% provides 2,000 kcal (8.4 MJ) and one litre of Intralipid 10% 1,100 kcal (4.6 MJ).

2. Intralipid is a rich source of the essential fatty acids; linoleic and linolenic acids.

3. Intralipid has a protein-sparing effect when given in conjunction with amino acid and carbohydrate solutions.

4. Intralipid 20% has an osmolality of 350 mosmol per kg water.

Intralipid 10% has an osmolality of 300 mosmol per kg water. (Plasma ~290).

Therefore both these preparations are suitable for infusion into peripheral veins.

Indications: Intralipid should be used as part of a balanced intravenous feeding regimen in patients who are unable to receive sufficient amounts of nutrients enterally. Intralipid is especially valuable in providing a high energy intake to compensate for increased energy expenditure following trauma, infections, severe burns, etc.

Dosage and administration The dosage administered should be within the ranges recommended below and should be governed by the patient's ability to utilise fat.

Recommended dosage for adults: Intralipid 20%: 500–1000 ml per 24 hrs in conjunction with intravenous administration of amino acid and carbohydrate solutions. For lesser energy requirements Intralipid 10% 500–1500 ml per 24 hrs in conjunction with amino acid and carbohydrate solutions.

Intralipid 10% and 20% are administered by slow intravenous infusion. During the first 10 minutes the drip should be adjusted to 20 drops per minute and then gradually increased to a final rate after half an hour of 25–40 drops per minute for Intralipid 20% and 40–60 drops per minute for Intralipid 10%. 500 ml of Intralipid 20% should be given over a period of not less than five hours. 500 ml of Intralipid 10% should be given over a period of not less than three hours. On the first day of infusion it is advisable to administer 5 ml Intralipid 20% per kg body weight or 10 ml Intralipid 10% per kg body weight. Subsequently the dose is usually doubled and when a larger intake is indicated the dosage may be increased to 3 g fat per kg body weight per 24 hrs.

Recommended dosage for infants: Dosage is governed by the maturity and birth-weight of the infant. In mature infants dosage scheme 1. should be used. In small for gestational age and low birth-weight infants where the ability to handle fat may be impaired, dosage scheme 2. should be utilised.

In all cases the infant's ability to eliminate infused fat from the circulation should be checked daily as described in the fat elimination test in the precautions section. If lipaemia is present re-testing should be carried out after an interval of four hours.

When administered to infants Intralipid should, if possible, be infused continuously over twenty-four hours and to maintain a constant rate of infusion it is recommended that an appropriate pump is used.

1. **Infants:** 0.5–4 g fat per kg body weight in 24 hrs. In practice 0.02–0.17 g/kg body weight should be administered each hour. The equivalent volumes of Intralipid are 10% 0.21–1.70 ml/kg/hr; 20% 0.10–0.85 ml/kg/hr. The dosage should be gradually increased during the first week of administration.

2. In small for gestational age and low birthweight infants with impaired capacity to handle fat, commencing dosage should be 0.5 g fat per kg body weight in 24 hrs. In the absence of measurement of serum triglycerides the dosage should not exceed 2 g fat per kg body weight in 24 hrs.

Caution: The rates given are maximum rates and no attempt should be made to exceed these in order to compensate for missed doses.

Contra-indications, warnings, etc Intralipid is only contraindicated in severe disorders of fat metabolism such as in severe liver damage and acute shock.

Precautions: Fat metabolism may be disturbed in con-

ditions such as renal insufficiency, uncompensated diabetes, certain forms of liver insufficiency, metabolic disorders and sepsis. If intravenous administration of fat is considered in patients with the above mentioned disorders, the elimination of fat should be checked daily. In newborns with neonatal hyperbilirubinaemia Intralipid should be used with caution, especially in low birth weight infants, because of the risk of free fatty acids displacing bilirubin from albumin. Intralipid should be administered with caution to infants with known or suspected pulmonary hypertension.

Fat elimination test: In order to prevent the development of cumulative lipaemia the patient's capacity of fat elimination can be tested in the following manner. In the morning following the first day's infusion, a citrated blood sample is drawn, preferably when the patient is still in a fasting state. The blood sample is centrifuged at 1,200–1,500 rpm. If the plasma is found to be opalescent or milky, further infusion should be postponed. This test should be repeated at weekly intervals in patients in stable metabolic conditions. In the majority of patients, the plasma is completely clear 12 hours after the conclusion of an infusion of 2 g fat per kg body weight (corresponding to 10 ml of Intralipid 20% or 20 ml of Intralipid 10% per kg body weight). In patients with diagnosed or suspected metabolic disturbances (see precautions) the fat elimination capacity should be checked daily.

Side effects: In rare instances, initial administration of Intralipid has produced a rise in temperature with shivering. Infusion of Intralipid should be discontinued in such cases. Increased levels of transaminases, alkaline phosphatases and bilirubin have been observed after 6–8 weeks of infusion. All values return to normal if the dosage is reduced.

Pharmaceutical precautions Store at below 25°C. Do not freeze. After long periods of storage the bottle of Intralipid should be gently inverted two or three times before use.

Additives may only be added to Intralipid where compatibility is known.

Legal category POM.

Package quantities Intralipid 10% and 20%: 100 or 500 ml.

Further information Intralipid and Vamin solutions can be infused simultaneously, centrally or peripherally when the mixture reaches the vein through the same cannula. Evidence is also available to support the addition of Intralipid emulsion to single containers (eg 3 litre bags). Such mixing must follow defined formulae and mixing techniques, details of which are available on request. The manufacturer can be consulted for full information on balanced and complete intravenous feeding regimens.

Product licence numbers

Intralipid 10% 0022/0027

Intralipid 20% 0022/0028

KABIKINASE*

Presentation Vials containing a straw coloured lyophilised powder. Three preparations are available, vials of 100,000 or 600,000 i.u. of streptokinase. Human albumin and buffering agents are present as stabilisers.

Uses Action: Streptokinase is an activator of the fibrinolytic system in man, which will produce intravascular dissolution of thrombi and emboli.

Indications: Kabikinase is used as a thrombolytic agent in venous thrombosis; pulmonary embolism; acute arterial thromboembolism; chronic arterial occlusive disease; myocardial infarction; clotted haemodialysis shunts; occlusion of retinal vessels; haemothorax and empyema.

Dosage and administration Routes of administration: By intravascular infusion or injection; intrapleural instillation.

Recommended dosage: Adults: The standard intravascular dosage scheme is an initial dose of up to 600,000 i.u. over a period of 30–60 minutes and a maintenance dose of 100,000 i.u. hourly for three days. Response normally occurs within this period but if further therapy is considered it should not be for more than an additional 3 days. The initial dose and maintenance dose may be titrated according to the anti-streptokinase antibody level of the individual. For clotting in haemodialysis shunts: 100,000 i.u. of Kabikinase are dissolved in 100 ml of normal saline. 10,000–25,000 i.u. (10–25 ml) are deposited in the clotted part of the shunt and it is sealed on the venous side by forceps. A sterile single-dose syringe is attached on the arterial side to form an air cushion against which the artery can pulsate. If so required, the treatment is repeated after 30–45 mins. For intrapleural instillation: A solution of 250,000 units in 100 ml of normal saline is instilled into the pleura via a drainage tube. The tube should then be clamped for four hours before suction is applied to remove the fluid. Instillation is normally performed once daily until re-expansion of the lung occurs.

Children: Although the standard dosage scheme may be reduced proportionately to circulating volume, it may be preferable to titrate the initial dose, followed by a maintenance dose of 1300–1400 i.u./kg/hr body weight for 3 days. Response normally occurs within this period but if further therapy is considered it should not be for more than an additional 3 days.

Control of therapy: Therapy is controlled by the thrombin clotting time performed at intervals and should be within the limits two to four times the normal value.

Preparation of solution: The contents of a vial of Kabikinase are dissolved at room temperature (20°C) in 5 ml water for injections carefully avoiding the formation of a foam. The concentrated solution thus obtained is transferred aseptically into an infusion bottle of glucose or saline of suitable volume, according to the needs of the patient. The rate of infusion is then adjusted to give the dosage rate required.

For example, 1 vial of 600,000 i.u. Kabikinase may be made up in at least 100 ml 5% glucose or physiological saline for the initial infusion over a period of 30 minutes, and vials of 600,000 i.u. made up in 540 ml 5% glucose or physiological saline for maintenance infusion at the rate of 90 ml per hour (100,000 i.u. hourly).

If desired, smaller volumes can be employed, to suit use of a syringe pump.

Contra-indications, warnings, etc Since thrombolytic therapy increases the risk of bleeding, Kabikinase is contra-indicated in the following:

1. Surgery within the last 10 days.
2. Invasive diathesis procedures during the last 10 days.

3. Gastrointestinal bleeding within the last six months.
4. Thrombocytopenia or other evidence of defective haemostasis.
5. Liver or kidney disease.
6. Cerebrovascular accident.
7. Severe hypertension treated and untreated.
8. Parturition (within the last 10 days).
9. Ulcerative colitis.
10. Visceral carcinoma.
11. Menstrual bleeding.
12. Subacute bacterial endocarditis.
13. During the first 18 weeks of pregnancy.

Since the anti-streptokinase titre increases after 7–10 days of treatment, and only returns to normal values after three to six months, repeated therapy with Kabikinase should only be used with the utmost caution. In addition it is advisable to determine the titrated initial dose (T.I.D.) of Kabikinase from a measure of the smallest quantity of Kabikinase necessary for the lysis of a clot from 1.0 ml of the patient's blood in less than 10 minutes.

If heparin or oral anticoagulants have been given before commencing Kabikinase thrombolytic therapy, further administration should cease; it is not advisable to give Kabikinase and heparin simultaneously. The Kabikinase infusion can then be started after 4 hours. If immediate Kabikinase therapy is required the heparin in the blood should be neutralised with protamine sulphate.

At the end of Kabikinase thrombolytic therapy, the patient should be given anticoagulants in an attempt to prevent rethrombosis. Preferably heparin should be used, starting four hours after the end of thrombolysis, and then oral anticoagulants may be introduced in the usual manner. Salicylic acid preparations and pyrazolone or indole derivatives should never be given concurrently as they may affect blood platelet function and thereby increase the risk of bleeding. Old age is a relative contra-indication.

Intramuscular injections should not be given.

Side-effects: Kabikinase therapy may give rise to febrile reactions and some patients show signs of anaphylaxis. These reactions may be controlled by the prior administration of corticosteroids (25 mg prednisolone or a corresponding amount of other glucocorticoid) or 10 mg chlorpheniramine maleate.

Minor oozing or bleeding can occur and is readily controlled; exceptionally there may be severe haemorrhage. The administration of Kabikinase must then be stopped; if necessary, the antifibrinolytic agent Cyklokapron (tranexamic acid–10 mg/kg) can be given immediately by slow intravenous injection. Thrombolytic therapy should not be undertaken unless there are available adequate supplies of Cyklokapron for immediate use.

Antidote: Tranexamic acid 10 mg/kg by slow intravenous injection.

Pharmaceutical precautions Vials of Kabikinase should be stored below 25°C before reconstitution as a solution for injection. The vial containing a prepared concentrated solution will keep for 24 hours and preferably should be stored in a refrigerator (+5°C). The diluted infusion solution of Kabikinase should be used within 12 hours of preparation.

Legal category POM.

Package quantities Vials of: 600,000 i.u. 100,000 i.u.

Further information Kabikinase is prepared from culture filtrates of β -haemolytic streptococci, and by biochemical purifying processes virtually freed from streptodornase, streptolysin, hyaluronidase and other enzymes. Kabikinase is soluble in water, is non-toxic and non-pyrogenic, but weakly antigenic. Kabikinase is stabilised with sterile human albumin and this imparts a faint straw colour to the preparation. The activity of Kabikinase is measured in Christensen units.

Product licence numbers

600,000 i.u. 0022/5006

100,000 i.u. 0022/5013

PED-EL*

Presentation Sterile straw-coloured solution containing electrolytes and trace elements for addition to the Vamin amino acid solutions in the intravenous nutrition of neonates and infants. Ped-el corresponds to the following formula:

Calcium chloride $2H_2O$	22.06 mg
Magnesium chloride $6H_2O$	5.08 mg
Ferric chloride $6H_2O$	135 mcg
Zinc chloride	20.4 mcg
Manganese chloride $4H_2O$	49.5 mcg
Copper chloride $2H_2O$	12.8 mcg
Sodium fluoride	31.5 mcg
Potassium iodide	1.7 mcg
Phosphoric acid	8.65 mg
Sorbitol	0.3 g

Water for injection to 1 ml
pH 2.0

1 ml of Ped-el contains the following amounts of electrolytes and trace elements:

Ca^{2+}	0.15 mmol
Mg^{2+}	25 micromol
Fe^{3+}	0.5 micromol
Zn^{2+}	0.15 micromol
Mn^{2+}	0.25 micromol
Cu^{2+}	0.075 micromol
F^-	0.75 micromol
I^-	0.01 micromol
P	75 micromol
Cl^-	0.35 mmol

1 vial of Ped-el contains less than 1 micromol potassium and less than 1.5 mmol sodium.

Uses Ped-el is an integral part of the complete intravenous nutrition of neonates and infants. It should be used in conjunction with Vamin Glucose or Vamin N, Intralipid and a suitable phosphate preparation containing potassium. This will provide the infant's basal requirement of electrolytes and trace elements. As the requirements of electrolytes and trace elements may vary in different clinical conditions, these substances may have to be added as appropriate in the individual patient. Ped-el administration should not be started until kidney function is established – usually during the second day of life.

Dosage and administration Recommended dosage for neonates and infants: As part of a complete intravenous nutritional regimen 4 ml of Ped-el per kg body weight per day will cover the basal requirements of neonates and infants for electrolytes and trace elements. This preparation should be added to 30 ml of Vamin Glucose or Vamin N. This infusion should be given at a very slow rate and is best done with an appropriate

infusion pump or an automatic drop rate counter. The requirements of potassium and sodium vary with different patient conditions. Ped-el is not intended to meet these requirements.

Contra-indications, warnings, etc Should not be given undiluted.

Addition of other drugs is to be avoided due to the risk of precipitation.

Care should be taken in the administration of Ped-el to patients with impaired renal function.

Ped-el contains sorbitol which is metabolised to fructose and should therefore be given with caution to patients with fructose intolerance.

Pharmaceutical precautions Store at 6° to $15^\circ C$.

The addition of Ped-el should be performed aseptically immediately before the start of the infusion and should be used within 24 hours unless the mixture is refrigerated when it may be used within 48 hours of preparation.

Legal category POM.

Package quantities 20 ml vials packed in boxes of 10.

Further information The manufacturer can be consulted for full information on balanced and complete intravenous feeding regimens.

Product licence number 0022/0037.

SOLIVITO* ▼

Presentation A sterile, yellow lyophilised mixture of water-soluble vitamins to be added to glucose solution for i.v. infusion after dissolution in water for injections or glucose solution (pH of Solivito reconstituted in water is 5.6). Solivito corresponds to the following formula:

Thiamine mononitrate (B_1)	1.24 mg
Sodium riboflavine phosphate (B_2)	2.47 mg
Nicotinamide	10 mg
Pyridoxine hydrochloride (B_6)	2.43 mg
Sodium pantothenate	11 mg
Biotin	0.3 mg
Folic acid	0.2 mg
Cyanocobalamin (B_{12})	2 mcg
Sodium ascorbate	34 mg
Glycine	100 mg
Sodium edetate	0.5 mg
Methyl hydroxybenzoate	0.5 mg

One vial of Solivito contains the following quantities of water-soluble vitamins:

Vitamin B_1	1.2 mg
Vitamin B_2	1.8 mg
Nicotinamide	10 mg
Vitamin B_6	2 mg
Pantothenic acid	10 mg
Biotin	0.3 mg
Folic acid	0.2 mg
Vitamin B_{12}	2 mcg
Vitamin C	30 mg

Uses Solivito is intended as a supplement in intravenous nutrition in order to cover the daily requirements of the water-soluble vitamins in both adults and infants.

Dosage and administration

Recommended dosage for adults: The contents of 1 vial of Solivito are dissolved by the addition of 10 ml glucose solution (5–20%) or water for injections. This reconstituted mixture is aseptically transferred to 500 or 1,000 ml

of glucose solution (5–50%) for infusion. In this way the basal daily requirements of the water-soluble vitamins are provided.

Recommended dosage for infants: The contents of 1 vial of Solivito are dissolved by the addition of 5 ml of glucose solution (5–20%) or water for injections. The basal daily requirements of water-soluble vitamins in infants are provided by 0.5 ml of this reconstituted mixture per kg body weight. The reconstituted mixture is aseptically transferred to glucose solution (5–20%) for infusion.

1 vial of Solivito should be infused over a minimum of 2–3 hours in patients with normal renal function so as to avoid renal losses.

Contra-indications, warnings, etc Intravenous administration of vitamin B₁ can in exceptional cases cause hypersensitivity reactions, as can methyl-hydroxybenzoate.

Pharmaceutical precautions Store the lyophilised powder before reconstitution at 6 to 15°C, protected from light. The addition of Solivito should be performed aseptically immediately before the start of the infusion and should be used within 24 hours of preparation. Solutions containing Solivito should be protected from light, e.g. with a red plastic sleeve, which allows the level of the solution to be viewed directly or with aluminium foil.

Legal category POM.

Package quantities Vials packed in boxes of five.

Further information The manufacturer can be consulted for full information on balanced and complete intravenous feeding regimens.

Product licence number 0022/0035.

VAMIN® GLUCOSE

Presentation A clear straw-coloured solution for intravenous use of amino acids in the physiological L-form together with glucose and electrolytes to the following formula:

L-Alanine	3.0 g	}	70.2 g
L-Arginine	3.3 g		
L-Aspartic acid	4.1 g		
L-Cysteine/cystine	1.4 g		
L-Glutamic acid	9.0 g		
Glycine	2.1 g		
L-Histidine	2.4 g		
L-Isoleucine	3.9 g		
L-Leucine	5.3 g		
L-Lysine	3.9 g		
L-Methionine	1.9 g		
L-Phenylalanine	5.5 g		
L-Proline	8.1 g		
L-Serine	7.5 g		
L-Threonine	3.0 g		
L-Tryptophan	1.0 g		
L-Tyrosine	0.5 g		
L-Valine	4.3 g		
Glucose	100 g		
Sodium	50 mmol		
Potassium	20 mmol		
Calcium	2.5 mmol		
Magnesium	1.5 mmol		
Chloride	55 mmol		

in each 1,000 ml. pH 5.2. Free from antioxidant additives.

Osmolality: 1260 mosmol per kg water.

Nitrogen per litre: 9.4 g corresponding to about 60 g of first-class protein.

Energy content per litre 650 kcal (2.7 MJ) of which 400 kcal (1.7 MJ) are provided by the glucose.

Uses Vamin Glucose provides a balanced mixture of all essential and non-essential amino acids. Glucose is included to meet part of the carbohydrate requirements. Electrolytes are present, but may need supplementing according to patient needs. Vamin Glucose is indicated in conditions of protein depletion where sufficient enteral feeding is impossible or impracticable.

To achieve an optimal utilisation of administered amino acids adequate energy sources, e.g. glucose solutions, fat emulsions (Intralipid) should be provided during intravenous feeding with amino acid solutions. The simultaneous infusion of Intralipid with hypertonic solutions has the advantage of a reduced osmolality and therefore allows the use of peripheral veins by reducing the risk of thrombophlebitis.

Dosage and administration *Recommended dosage for Adults:* Depending upon patient requirements 0.5–2.0 litres intravenously per 24 hours.

Vamin Glucose is administered by slow intravenous infusion at approx 40–55 drops per minute corresponding to an infusion time of six to eight hours per litre.

Recommended dosage for infants: 30 ml per kg body weight in 24 hours to be achieved gradually during first week of administration.

For long-term feeding (i.e. a period of longer than one week) or in short-term feeding if a deficiency of trace elements exists, a trace element solution should be added. Addamel and Ped-el have been specifically designed for this purpose and are compatible with Vamin Glucose when used in the recommended proportions.

Vamin Glucose can be infused into a peripheral vein when given simultaneously with Intralipid through the same cannula.

Contra-indications, warnings, etc Vamin Glucose is contra-indicated in cases of irreversible liver damage and in severe uraemia when dialysis facilities are not available.

Side-effects: Vamin Glucose is well tolerated. In exceptional cases, nausea may occur. As with all hypertonic infusion solutions, thrombophlebitis may occur when peripheral veins are used. The incidence would be reduced by the simultaneous infusion of Intralipid as described above.

Pharmaceutical precautions Store at 5 to 25°C.

Legal category POM.

Package quantities Bottles of 100, 500 and 1,000 ml.

Further information The manufacturer can be consulted for full information on balanced and complete intravenous feeding regimens.

Product licence number 0022/0030.

VAMIN® N

Presentation A clear straw-coloured solution for intravenous use of amino acids in the physiological L-forms and electrolytes to the following formula:

L-Alanine	3.0 g	}	70.2 g
L-Arginine	3.3 g		
L-Aspartic acid	4.1 g		
L-Cysteine/cystine	1.4 g		
L-Glutamic acid	9.0 g		
Glycine	2.1 g		
L-Histidine	2.4 g		
L-Isoleucine	3.9 g		
L-Leucine	5.3 g		
L-Lysine	3.9 g		
L-Methionine	1.9 g		
L-Phenylalanine	5.5 g		
L-Proline	8.1 g		
L-Serine	7.5 g		
L-Threonine	3.0 g		
L-Tryptophan	1.0 g		
L-Tyrosine	0.5 g		
L-Valine	4.3 g		
Sodium	50 mmol		
Potassium	20 mmol		
Calcium	2.5 mmol		
Magnesium	1.5 mmol		
Chloride	55 mmol		

in each 1,000 ml. pH 5.2. Free from antioxidant additives.

Osmolality: 700 mosmol per kg water.

Nitrogen per litre: 9.4 g corresponding to about 60 g of first-class protein.

Energy content per litre 250 kcal (1.0 MJ).

Uses Vamin N provides a balanced mixture of all essential and non-essential amino acids. Electrolytes are present, but may need supplementing according to patient needs. Vamin N is indicated in conditions of protein depletion where sufficient enteral feeding is impossible or impracticable.

To achieve an optimal utilisation of administered amino acids adequate energy sources, e.g. glucose solutions, fat emulsions (Intralipid) should be provided during intravenous feeding with amino acid solutions. The simultaneous infusion of Intralipid with hypertonic solutions such as amino acid solutions has the advantage of a reduced osmolality and therefore allows the use of peripheral veins by reducing the risk of thrombophlebitis.

Dosage and administration *Recommended dosage for Adults:* Depending upon patient requirements 0.5–2.0 litres intravenously per 24 hours.

Vamin N is administered by slow intravenous infusion at approx. 40–55 drops per minute corresponding to an infusion time of six to eight hours per litre.

Recommended dosage for infants: 30 ml per kg body weight in 24 hours to be achieved gradually during first week of administration.

For long-term feeding (i.e. a period of longer than one week) or in short-term feeding if a deficiency of trace elements exists, a trace element solution should be added. Addamel and Ped-el have been specifically designed for this purpose and are compatible with Vamin N when used in the recommended proportions.

Vamin N can be infused into a peripheral vein when given simultaneously with Intralipid through the same cannula.

Contra-indications, warnings, etc Vamin N is contra-indicated in cases of irreversible liver damage and in severe uraemia when dialysis facilities are not available.

Side-effects: Vamin N is well tolerated. In exceptional cases, nausea may occur. As with all hypertonic infusion solutions, thrombophlebitis may occur when peripheral

veins are used. The incidence would be reduced by the simultaneous infusion of Intralipid as described above.

Pharmaceutical precautions Store at 5 to 25°C.

Legal category POM.

Package quantities Bottle of 500 ml, 1000 ml.

Further information The manufacturer can be consulted for full information on balanced and complete intravenous feeding regimens.

Product licence number 0022/0031.

VITLIPID ADULT* ▼

Presentation A white sterile oil in water emulsion containing the fat soluble vitamins A, D₂ and K₁, in the oil phase of the emulsion with a composition corresponding to that of Intralipid 10%. Vitlipid Adult is intended for addition to Intralipid 10% or 20% and for use in adults on intravenous nutrition. One ampoule of Vitlipid Adult contains:

Retinol palmitate	
corresponding to retinol	750 mcg (2,500 i.u.)
Calciferol	3 mcg (120 i.u.)
Phytomenadione	150 mcg
Fractionated soya-bean oil	1 g
Fractionated egg phospholipids	120 mg
Glycerol	225 mg
Water for injection to 10 ml	

Uses Vitlipid Adult is indicated as a supplement to Intralipid 10% or 20% in intravenous nutrition of adults in order to cover the daily requirements of the fat soluble vitamins A, D₂ and K₁.

Dosage and administration *Recommended dosage for adults:* One ampoule (10 ml) of Vitlipid Adult is added to 500 ml of Intralipid 10% or 20%. After gentle shaking, the emulsion is infused as described for Intralipid. The daily maintenance dosages of the vitamins A, D₂ and K₁ are thereby supplied.

Recommended dosage for infants: For infants the preparation Vitlipid Infant should be used.

Contra-indications, warnings, etc Should not be given undiluted.

Pharmaceutical precautions Store at 4 to 8°C protected from light. Do not freeze.

The addition of Vitlipid Adult should be performed aseptically immediately before the start of the infusion and should be used within 24 hours unless the mixture is refrigerated when it may be used within 48 hours of preparation.

Legal category POM.

Package quantities 10 ml ampoules packed in boxes of five.

Further information Vitlipid Adult is specially formulated for addition to either Intralipid 10% or 20%.

The manufacturer can be consulted for full information on balanced and complete intravenous feeding regimens.

Product licence number 0022/0036.

VITLIPID INFANT* ▼

Presentation A white sterile oil in water emulsion containing the fat soluble vitamins A, D₂ and K₁ in the oil phase of the emulsion with a composition corresponding to that of Intralipid 10%. Vitlipid Infant is intended for addition to Intralipid 10% or 20% and for use in infants on intravenous nutrition. One ml contains:

Retinol palmitate	
corresponding to retinol	100 mcg (333 i.u.)
Calciferol	2.5 mcg (100 i.u.)
Phytomenadione	50 mcg
Fractionated soya-bean oil	100 mg
Fractionated egg	
phospholipids	12 mg
Glycerol	22 mg
Water for injection to 1 ml	

Uses Vitlipid Infant is indicated as a supplement to Intralipid 10% or 20% in intravenous nutrition of infants in order to cover the daily requirements of the fat soluble vitamins A, D₂ and K₁.

Dosage and administration *Recommended dosage for infants:* Vitlipid Infant in a dosage of 1 ml per kg body weight per day is added to Intralipid 10% or 20%. The daily dosage must not exceed 4 ml. After gentle shaking the emulsion is infused as stated for Intralipid.

Recommended dosage for adults: For adults the preparation Vitlipid Adult should be used.

Contra-indications, warnings, etc Should not be given undiluted.

Pharmaceutical precautions Store at 4 to 8°C protected from light. Do not freeze.

The addition of Vitlipid Infant should be performed aseptically immediately before the start of the infusion and should be used within 24 hours unless the mixture is refrigerated when it may be used within 48 hours of preparation.

Legal category POM.

Package quantities 10 ml ampoules packed in boxes of five.

Further information Vitlipid Infant is specially formulated for addition to either Intralipid 10% or 20%.

The manufacturer can be consulted for full information on balanced and complete intravenous feeding regimens.

Product licence number 0022/0038.

*Trade Mark

Keymer Pharmaceuticals,

A Division of Schering Chemicals Limited.

The Brow, Burgess Hill,
West Sussex RH15 9NE

KEYMER
PHARMACEUTICALS

ANDROCUR*

Presentation Each round, white, 9 mm tablet is embossed on one side with 'BV' in a regular hexagon, and is scored on the other. It contains 50 mg cyproterone acetate (6-chloro-17 α -hydroxy-1 α , 2 α -methylene-pregna-4, 6-diene-3, 20-dione acetate).

Uses Control of libido in severe hypersexuality and/or sexual deviation in the male. Cyproterone acetate acts as an antiandrogen by blocking androgen receptors. It also has progestogenic activity which exerts a negative feedback effect on the hypothalamic receptors, so leading to a reduction in gonadotrophin release, and hence to diminished production of testicular androgens.

Dosage and administration The daily dose should be divided and taken after the morning and evening meals. The usual dose for adult males is 1 tablet twice daily.

Contra-indications, warnings, etc *Contra-indications:* Liver diseases. Malignant tumours and wasting diseases (because of transient catabolic action). A history of thrombosis or embolism. Severe chronic depression.

Warnings/side-effects: Liver, Cyproterone acetate has been found to cause liver abnormalities in animals, including the development of tumours. Androcur treatment has shown good liver tolerance in man. Nevertheless, liver function tests should be performed regularly during treatment.

Inhibition of spermatogenesis. The sperm count and the volume of ejaculate are reduced. Infertility is usual, and there may be azoospermia after eight weeks. There is usually slight atrophy of the seminiferous tubules. Follow-up examinations have shown these changes to be reversible, spermatogenesis usually reverting to its previous state about three to five months after stopping Androcur, or, in some users, up to 20 months. That spermatogenesis can recover even after very long treatment is not yet known. There is evidence that abnormal sperms which might give rise to malformed embryos are produced during treatment with Androcur.

Tiredness. Fatigue and lassitude are common in the first few weeks but become much less from the third month.

Gynaecomastia. About one patient in five develops transient or perhaps in some cases permanent enlargement of the mammary glands. In rare cases galactorrhoea and tender benign nodules have been reported. Symptoms mostly subside after discontinuation of treatment or reduction of dosage.

Bodyweight. During long-term treatment, changes in body weight have been reported, chiefly weight gains.

Other changes that have been reported include reduction of sebum production and consequently improvement of existing acne vulgaris, transient patchy loss and reduced growth of body hair, increased growth

of scalp hair, lightening of hair colour and female type of pubic hair growth.

Precautions and special information: Adrenocortical function: During treatment, adrenocortical function should be supervised, since suppression has been observed.

Diabetes: Androcur can influence carbohydrate metabolism. Parameters of carbohydrate metabolism should be examined carefully in all diabetics before and regularly during treatment.

Chronic alcoholism: Alcohol appears to reduce the effect of Androcur, which is of no value in chronic alcoholics.

Haemoglobin: Hypochromic anaemia has been found rarely during long-term treatment, and blood counts before and at regular intervals during treatment are advisable.

Nitrogen balance: A negative nitrogen balance is usual at the start of treatment, but does not persist.

Spermatogenesis: A spermatogram should be recorded before starting treatment in patients of procreative age, as a guard against attribution of pre-existing infertility to Androcur at a later stage.

It should be noted that the decline in spermatogenesis is slow, and Androcur should, therefore, not be regarded as a male contraceptive.

Immature youths: Androcur should not be given to youths whose bone maturation and testicular development are incomplete.

Medico-legal considerations: Doctors are advised to ensure that the fully informed consent of the patient to Androcur treatment is witnessed and can be verified.

Road safety: The marked lassitude and asthenia that may be experienced, particularly during the first few weeks of treatment, necessitate especial care while driving.

Overdosage: There have been no reports of ill-effects from overdosage, which it is, therefore, generally unnecessary to treat. If overdosage is discovered within two or three hours and is so large that treatment seems desirable, gastric lavage can safely be used. There are no specific antidotes, and further treatment should be symptomatic.

Pharmaceutical precautions Store in cool, dry conditions away from strong sunlight: shelf-life five years.

Legal category POM.

Package quantities Bottles of 50 tablets.

Further information Nil.

Product licence number 0053/0023.

BRONCHODIL ▼

Presentation Aerosol dispenser with metered-dose unit, containing 20 ml suspension. Each metered dose provides 0.5 mg reproterol hydrochloride.

White, half-scored, oral tablets containing reproterol hydrochloride 20 mg.

Uses Bronchodil, a selective β_2 -adrenergic stimulant with very little action on cardiac receptors, is indicated for the treatment of conditions involving reversible airways obstruction such as bronchial asthma, including that of an allergic origin, acute and chronic bronchitis and emphysema.

It is effective in the prophylaxis of acute attacks of bronchospasm.

Because of its selective action on the bronchi, Bronchodil may be used in the treatment of bronchospasm in patients with co-existing heart disease or hypertension.

Dosage and administration *Inhalation: Adults:* For acute attacks of bronchospasm the usual dose is 1 or 2 inhalations, repeated every 3–6 hours as required.

For chronic reversible obstruction of the airways, and the prophylaxis of recurrent attacks of acute bronchospasm, the usual dose is 2 inhalations three times a day.

Children: 6–12 years: No more than 1 inhalation every 3–6 hours for acute attacks, or three times a day for prophylaxis.

Oral: Adults: The usual adult dose is one tablet three times daily. If side-effects occur, the dosage should be reduced to half a tablet three times daily.

Children: 6–12 years: Usually half a tablet three times daily. Over 12 years, usually half to one tablet 3 times daily, according to weight.

Contra-indications, warnings, etc *Contra-indications:* There are no known contra-indications.

Side effects: Bronchodil is generally well tolerated, but, as with other beta-adrenergic stimulants, digital tremor, palpitations, slight tachycardia and restlessness may occasionally occur.

Precautions: Care should be taken with patients suffering from myocardial infarction, thyrotoxicosis or phaeochromocytoma. Bronchodil should be used with caution in patients already receiving sympathomimetic agents. Bronchodil should not be prescribed with beta-blocking drugs. Although no teratogenic effects have been observed in animal experiments, caution is recommended during the first trimester of pregnancy.

Exceeding the stated dose does not produce enhanced therapeutic effect, and should be avoided.

Overdosage: Reversal of the therapeutic action on the bronchi is never required, since excessive bronchodilation cannot result from overdosage. General blockade of the β -adrenergic stimulus is therefore never appropriate, and, if a β -blocker is used, it should be of the cardioselective type. Such a drug is the recommended antidote. However, β -blockade is not mandatory unless there is severe tachycardia or cardiac arrhythmia threatens, and β -blockers should be used with caution in patients with existing or potential cardiac failure, which may be precipitated by the negative inotropic effect of β -blockade on the myocardium. Muscle tremor and restlessness can be treated with benzodiazepines, which are particularly useful in children.

Pharmaceutical precautions Store in a cool, dry place. Shelf-life 3 years.

The aerosol canister should be kept away from heat, and must not be punctured or incinerated, even when empty.

Legal category POM.

Package quantities Each aerosol canister provides 400 metered doses.

The tablets are supplied as blister packs of 100.

Further information Nil.

Product licence numbers

aerosol 0053/0130

tablets 0053/0131

TRAVOGYN ▼

Presentation Vaginal tablets: White, almond-shaped vaginal tablets, impressed with CT in a regular hexagon on one side, and containing 300 mg isoconazole nitrate.

Uses Travogyn exhibits a broad spectrum of activity against fungal pathogens, including yeasts and yeast-like fungi (particularly those belonging to *Candida* spp. and *Torulopsis glabrata*), and against dermatophytes and hyphomycetes. Travogyn also has bactericidal activity against some gram-positive bacteria, including staphylococci, streptococci and micrococci, which may cause secondary infection of inflammatory skin lesions. Travogyn vaginal tablets may be used for vaginal mycoses, particularly those due to *Candida*, or for mixed infections with fungi and gram-positive bacteria.

Dosage and administration Two 300 mg vaginal tablets should be inserted together deep into the vagina. Only one application is required and may be done by the doctor at the time of consultation, or by the patient, preferably at night.

Contra-indications, warnings, etc There are no known contra-indications.

Pre-existing irritation of the vagina may be exacerbated in occasional patients. Although in order to avoid any possibility of adverse effects on the foetus, the general principle is now widely accepted that the administration of drugs to women during pregnancy should, as far as possible, be avoided, nothing that is known about the effect of isoconazole nitrate, either from animal experiments, or from clinical experience, suggests that Travogyn therapy should not be used during pregnancy.

Pharmaceutical precautions *Storage:* Cool conditions.

Shelf-life: Five years.

Legal category POM.

Package quantities Two vaginal tablets in foil-backed blister packs.

Further information Nil.

Product licence number 0053/0124

**Trade Mark*

Kirby-Warrick Pharmaceuticals Ltd
Mildenhall
Bury St Edmunds
Suffolk IP28 7AX



ACNEGEL®
ACNEGEL® FORTE

Presentation Acnegel contains 5% benzoyl peroxide in a gel base formulated with colloidal magnesium aluminium silicate, hydroxypropylmethyl-cellulose, ethyl alcohol, polyoxyethylene lauryl ether, citric acid and purified water.

Acnegel Forte contains 10% benzoyl peroxide in a gel base formulated as above.

Uses Acnegel and Acnegel Forte are indicated for the treatment of acne.

Benzoyl peroxide exerts an antibacterial effect on the acne bacillus, corynebacterium acnes, and provides a drying and desquamative action. Penetration is enhanced by the gel base, which is invisible on the skin.

Dosage and administration Treatment should normally commence with Acnegel. Apply the gel to the affected areas once daily. Washing with soap and water prior to application greatly enhances the efficacy of the preparation.

The reaction of the skin to benzoyl peroxide differs in individual patients and for this reason the higher percentage of benzoyl peroxide in Acnegel Forte may be required in order to provide a satisfactory drying and desquamative action.

Contra-indications, warnings, etc Patients with a known sensitivity to benzoyl peroxide should not use these products. For external use only. Take care to keep the product away from contact with the mouth, the eyes and other mucous membranes to avoid irritation. The product should only be applied to other sensitive areas, such as the skin of the neck, with caution.

In normal use a mild burning sensation will probably be felt on first application and a moderate reddening and peeling of the skin will occur within a few days. During the first few weeks of treatment a sudden increase in peeling will occur in most patients; this is not harmful and will subside within a day or two if treatment is temporarily discontinued. If discomfort such as burning, redness or excess peeling occur, discontinue treatment temporarily or consult a doctor. Keep away from children. The product may bleach dyed clothing and fabrics.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities Acnegel and Acnegel Forte are supplied in tubes each containing 50 g.

Further information Nil.

Product licence numbers
Acnegel 3478/0029
Acnegel Forte 3478/0030

AFRAZINE® NASAL SPRAY
AFRAZINE® NOSE DROPS
AFRAZINE® PAEDIATRIC NOSE DROPS

Presentation Each ml of Afrazine Nasal Spray/Nose Drops contains 0.5 mg Oxymetazoline hydrochloride INN in a buffered aqueous solution. Each ml of Afrazine Paediatric Nose Drops contains 0.25 mg Oxymetazoline hydrochloride INN in a buffered aqueous solution.

Uses Afrazine has a sympathomimetic action that constricts the smaller arterioles of the nasal passages, producing a prolonged gentle and predictable decongestant effect for up to 12 hours.

Afrazine is indicated for the relief of nasal congestion associated with a wide variety of allergic and infectious upper respiratory tract disorders.

Dosage and administration *Adults and children over 5 years of age:* 2–3 sprays or drops into each nostril with the patient in the lateral head-low position in the morning and at bed time.

Children up to 5 years of age: 2–3 drops of Afrazine Paediatric Nose Drops in each nostril in the morning and at bed time. With young children it is advisable for patients to be lying down with the head low and to one side.

Contra-indications, warnings, etc As with all sympathomimetic amines, Afrazine should be used with extreme care in patients who are receiving MAO inhibitors. Afrazine should be used with caution in patients with coronary artery disease, hypertension, hyperthyroidism, or diabetes mellitus.

Safety for use during pregnancy has not been established.

Overdosage: Overdosage may produce sedation in children, although no such occurrence has been reported with Afrazine.

Afrazine is generally well tolerated and side-effects, should they occur, are usually mild and transient. Possible side-effects include burning, stinging, dryness of nasal mucosa, sneezing, headache, light-headedness, insomnia and palpitations. Rebound congestion is not a problem but as with all topical nasal decongestants continuous use is not recommended for longer than two weeks.

Pharmaceutical precautions None.

Legal category P.

Package quantities 15 ml.

Further information Afrazine gives rapid relief from nasal congestion for up to 12 hours. The genuine long duration of action and simple twice daily dosage makes Afrazine highly acceptable to patients.

Product licence numbers
Afrazine Nose Drops 3478/0034
Afrazine Nasal Spray 3478/0036
Afrazine Paediatric Nose Drops 3478/0035

CONGESTEZE* ▼

Presentation *Congestez Tablets*: White sugar coated tablets. Each contain 1 mg azatadine maleate and 60 mg pseudoephedrine sulphate in the coating and 60 mg pseudoephedrine sulphate in the barrier coated core. The two active ingredients in the coating are quickly liberated, release of the decongestant in the core is delayed for several hours after ingestion.

Congestez Syrup: Clear, colourless to light yellow syrup. The syrup contains 1 mg/5 ml azatadine maleate and 30 mg/5 ml pseudoephedrine sulphate.

Uses Antihistamine and decongestant.

Azatadine maleate is a long acting antihistamine with anti-serotonin and anticholinergic properties. Pseudoephedrine, an orally administered vasoconstrictor, produces a gradual but sustained decongestant effect causing little, if any, 'rebound congestion' and facilitates shrinkage of congested mucosa in upper respiratory areas.

Congestez is indicated for the relief of symptoms of upper respiratory mucosal congestion in seasonal and perennial allergic rhinitis.

Dosage and administration

Adults and children over 12 years of age: Tablets: the usual dose is one tablet twice a day i.e. one tablet morning and evening.

Syrup: the usual dose is 5 ml (1 teaspoon) twice daily, but this may be increased to 10 ml (2 teaspoons) twice daily in severe cases.

Children, 6–12 years of age: Syrup: 2.5–5 ml ($\frac{1}{2}$ –1 teaspoon) twice a day. Graduated measure enclosed.

Analgesics, antibiotics or both may be administered concurrently when indicated.

Contra-indications, warnings, etc Congestez is contraindicated in patients receiving MAO inhibitor therapy.

Although pseudoephedrine causes virtually no pressor effect in patients with normal blood pressure, Congestez should be used with caution in patients with cardiovascular disorders and those being treated with beta-blocking agents.

Use with caution in patients with prostatic hypertrophy, urinary retention, glaucoma, stenosing peptic ulcer or pyloroduodenal obstructions.

Although drowsiness is infrequent and impairment of psychomotor function is not manifested at the recommended dosage of azatadine maleate, patients should be warned about engaging in mechanical operations requiring mental alertness, such as driving a car or operating machinery etc. until individual response has been determined.

Congestez should not be given to pregnant women or nursing mothers.

Side Effects: Congestez has caused no serious or unusual adverse effects either reported or determined by laboratory tests. The tablets and syrup are well tolerated and side effects are generally dose-related and transient. Side effects most frequently reported are those commonly associated with antihistamine/decongestant preparations such as drowsiness, epigastric distress, weakness and nervousness etc.

Overdosage: In the event of overdosage, emergency treatment should be started immediately. Treatment of signs and symptoms of overdosage is symptomatic and supportive.

Pharmaceutical precautions No special precautions.

Legal category POM.

Package quantities 100 tablets in cartons containing 10 blister strips of 10 tablets.
Bottles of 120 ml Syrup.

Further information Nil.

Product licence numbers

Tablets 3478/0042

Syrup 3478/0058

**GARAMYCIN* EYE/EAR DROPS
GARAMYCIN* EYE OINTMENT ▼**

Presentation Each ml of Garamycin Eye/Ear Drops contains gentamicin sulphate equivalent to 3.0 mg of gentamicin base in a sterile, aqueous isotonic solution. Benzalkonium Chloride is included as a preservative. Each gram of the sterile Garamycin Eye Ointment contains gentamicin sulphate, equivalent to 3.0 mg of gentamicin base, liquid paraffin, white soft paraffin and methylhydroxybenzoate and propylhydroxybenzoate as preservatives.

Uses Gentamicin is a bactericidal antibiotic active against a wide variety of pathogenic Gram-negative and Gram-positive bacteria. Garamycin Eye/Ear Drops and the Eye Ointment are indicated in the topical treatment of infections of the external structures of the eye and its adnexa caused by susceptible bacteria. Such infections include conjunctivitis, keratitis and kerato-conjunctivitis, corneal ulcers, blepharitis and blepharo-conjunctivitis, acute meibomianitis, episcleritis and dacryocystitis. Garamycin may be used for the prevention of ocular infection after: removal of a foreign body, burns or lacerations of the conjunctiva; damage from chemical or physical agents and after ocular surgery.

Garamycin Eye/Ear Drops are also indicated for the topical treatment of otitis externa caused by susceptible bacteria.

Dosage and administration For Adults and Children.

Eye: Instill 1–2 drops Garamycin Eye/Ear drops in affected eye every four hours as required.

Apply a sufficient amount of Garamycin Eye Ointment two or four times a day.

Ear: The ear canal should be cleaned thoroughly and 3–4 drops instilled three to four times a day.

After a favourable response is obtained, the dosage may be reduced and discontinued as cure is achieved.

Contra-indications, warnings, etc Garamycin Eye/Ear Drops and Garamycin Eye Ointment are contraindicated in patients with known hypersensitivity to any of the components of these preparations. Fungal and viral infections are contraindications to the use of these products. Prolonged use of topical antibiotics may give rise to overgrowth of non-susceptible organisms. If this occurs, appropriate therapy is indicated. Cross-allergenicity among aminoglycosides has been demonstrated. Transient eye irritation has been reported.

The safety of these products has not been established in children less than six years old or in pregnant women. Ophthalmic ointments may retard corneal healing.

Overdosage: A single overdosage of gentamicin would not be expected to produce symptoms.

Pharmaceutical precautions Store at room temperature.

Legal category POM.

Package quantities Garamycin Eye/Ear Drops are available in natural polyethylene dropper bottles containing 10 ml Garamycin Eye/Ear Drops. Garamycin Eye Ointment is available in 3 g tubes.

Further information Nil.

Product licence numbers

Garamycin Eye/Ear Drops 3478/0028
Garamycin Eye Ointment 3478/0027

GARAMYCIN* INJECTION

Presentation Garamycin for parenteral use is available as: Garamycin Injection in 2 ml ampoules, or 2 ml multiple-dose vials each containing the equivalent of 80 mg gentamicin base as the sulphate.

Uses Garamycin is gentamicin, an aminoglycoside antibiotic produced by the fermentation of *Micromonospora purpurea*. Gentamicin is active against a wide variety of pathogenic gram-negative and gram-positive bacteria, e.g. *Pseudomonas aeruginosa*, *Proteus* species, *Escherichia coli*, *Klebsiella* – *Enterobacter* – *Serratia* species, *Staphylococcus* species (including penicillin- and methicillin-resistant strains). It is also active against clinical isolates of bacteria resistant to other aminoglycoside antibiotics (kanamycin, neomycin, paromomycin and tobramycin).

Garamycin Injection is indicated in: urinary tract infections, respiratory tract infections, septicaemia, serious infections of the central nervous system (meningitis), gastro-intestinal tract infections, infected wounds, bone and soft tissue infections including peritonitis, septic abortion and burns complicated by sepsis, where susceptible organisms are involved or suspected.

Dosage and administration *Adult patients with normal renal function:* The recommended dosage of Garamycin Injection for adult patients with serious infections is 3 mg/kg/day administered intramuscularly eight-hourly for 7–10 days. For patients with life-threatening infections in the absence of impaired renal function, dosages up to 5 mg/kg/day in equally divided doses six or eight hourly are given. This dosage should be reduced to 3 mg/kg/day as soon as clinically indi-

cated. When systemic or urinary tract infections are of moderate severity and the causative organism is likely to be highly responsive, a dosage of 2 mg/kg/day given 12 hourly should be considered. However, if prompt clinical response is not apparent, dosage should be increased to 3 mg/kg/day given eight hourly.

Adult patients with impaired renal function: Approximate dosage guidelines for Garamycin Injection in adult patients based on renal function, are given in the table below.

In patients undergoing 14 hour haemodialysis twice weekly, the recommended dosage is 2 mg/kg of gentamicin at the end of each dialysis period.

Routes of administration: *GENTAMICIN SHOULD BE ADMINISTERED INTRAMUSCULARLY.* The intravenous route generally is reserved for patients in shock, with haemorrhagic disorders, with severe burns or reduced muscle mass. The recommended dosage and precautions for intramuscular and intravenous administration are identical.

Intravenous administration: *DIRECT INTRAVENOUS INJECTION:* A single dose of Garamycin may be given over a period of two to three minutes either directly into the vein or directly into i.v. tubing.

Infusion: A single dose is diluted into sterile isotonic saline or 5% dextrose solution and may be infused over a period of up to two hours.

Contra-indications, warnings, etc A history of hypersensitivity to gentamicin is a contra-indication to its use. Safety for use in pregnancy has not been established. Patients with impaired renal function treated with gentamicin injection may be exposed to an increased risk of ototoxicity. In these patients, renal, auditory and vestibular functions should be monitored. When feasible, gentamicin serum levels should be monitored; prolonged concentration above 12 mcg/ml should be avoided. The concurrent use of gentamicin with potent diuretics such as ethacrynic acid and frusemide should be avoided since these diuretics may by themselves cause ototoxicity. Concurrent use of other neurotoxic and/or nephrotoxic drugs, particularly streptomycin, neomycin, kanamycin, cephaloridine, viomycin, polymixin B, and polymixin E (colistin), should be avoided. Neuromuscular blockade and respiratory paralysis may occur with gentamicin especially if it is administered to patients receiving neuromuscular blocking agents. In some patients with impaired renal function,

Renal function tests

Body	Dose	Creatinine	Serum creatinine level	Blood urea nitrogen	Frequency of
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there has been reported a rise in BUN and NPN, serum creatinine and oliguria. These occur more frequently in patients with a history of renal impairment or eighth cranial nerve damage treated for longer periods or at higher doses than recommended.

When carbenicillin is used concurrently with gentamicin each should be injected at a separate site.

Overdosage: haemodialysis or peritoneal dialysis will aid the removal of gentamicin from the blood.

Pharmaceutical precautions Store at room temperature. Do not freeze. Each pack is clearly marked with an expiry date.

Legal category POM.

Package quantities 2 ml vials and ampoules in packs of 25.

Further information Nil.

Product licence number 3478/0005.

GARAMYCIN* PAEDIATRIC INJECTION

Presentation Garamycin for parenteral use in paediatrics is available as Garamycin Paediatric Injection in 2 ml multiple-dose vials each containing the equivalent of 20 mg gentamicin base as the sulphate.

Uses Garamycin is gentamicin, an aminoglycoside antibiotic produced by the fermentation of *Micromonospora purpurea*. Gentamicin is active against a wide variety of pathogenic gram-negative, and gram-positive bacteria. *Pseudomonas aeruginosa*, *Proteus* species, *Escherichia coli*, *Klebsiella* – *Enterobacter* – *Serratia* species, *staphylococcus* species (including penicillin- and methicillin-resistant strains). It is also active against clinical isolates of bacteria resistant to other aminoglycoside antibiotics (kanamycin, neomycin, paromomycin and tobramycin).

Gentamicin injection is indicated in: urinary tract infections, septicaemia, serious infection of the central nervous system (meningitis), gastro-intestinal tract infections, infected wounds, bone and soft tissue infections (including burns), where susceptible organisms are involved or suspected.

Dosage and administration *Children with moderate or severe infections:* 3–5 mg/kg/day in three equally divided doses. Neonates (premature or full term) require a dosage of 6 mg/kg/day given 12 hourly. Infants older than one week may be administered gentamicin in two equal doses, 12 hourly or three equal doses eight hourly. The usual duration of treatment for children, infants and neonates is 7–10 days.

Patients with impaired renal function: Dosage frequency should be reduced in accordance with gentamicin serum levels. The serum half-life (in hours) may be estimated by multiplying the serum creatinine (expressed in mg %) by four. The interval between doses, in hours, may be approximated by doubling the serum half-life or by multiplying serum creatinine (expressed in mg %) by eight.

In children undergoing 14 hour haemodialysis twice weekly, the recommended dosage is 2 mg/kg of gentamicin intramuscularly or intravenously at the end of each dialysis period.

Routes of administration: GENTAMICIN SHOULD BE ADMINISTERED INTRAMUSCULARLY. The intra-

venous route generally is reserved for patients in shock, with haemorrhagic disorders, with severe burns or reduced muscle mass. The recommended dosage and precautions for intramuscular and intravenous administration are identical.

Intravenous administration: DIRECT INTRAVENOUS INJECTION: A single dose of Garamycin may be given over a period of two to three minutes either directly into the vein or directly into i.v. tubing.

INFUSION: A single dose is diluted into sterile isotonic saline or 5% dextrose solution and may be infused over a period of up to two hours.

Contra-indications, warnings, etc A history of hypersensitivity to gentamicin is a contra-indication to its use. Patients with impaired renal function treated with gentamicin injection may be exposed to an increased risk of ototoxicity. In these patients, renal, auditory and vestibular functions should be monitored. When feasible, gentamicin serum levels should be monitored; prolonged concentration above 12 mcg/ml should be avoided. The concurrent use of gentamicin with potent diuretics such as ethacrynic acid and frusemide should be avoided since these diuretics may by themselves cause ototoxicity. Concurrent use of other neurotoxic and/or nephrotoxic drugs, particularly streptomycin, neomycin, kanamycin, cephaloridine, viomycin, polymixin B, and polymixin E (colistin), should be avoided. Neuromuscular blockade and respiratory paralysis may occur with gentamicin especially if it is administered to patients receiving neuromuscular blocking agents. In some patients with impaired renal function, there has been reported a rise in BUN and NPN, serum creatinine and oliguria. These occur more frequently in patients with a history of renal impairment or eighth cranial nerve damage treated with larger than recommended doses.

When carbenicillin is used concurrently with gentamicin each should be injected at a separate site.

Overdosage: Haemodialysis or peritoneal dialysis will aid the removal of gentamicin from the blood.

Pharmaceutical precautions Store at room temperature. Do not freeze. Each pack is clearly marked with an expiry date.

Legal category POM.

Package quantities 2 ml vials in packs of 5.

Further information Nil.

Product licence number 3478/0006.

GARAMYCIN* CHAINS

Presentation Polymethyl methacrylate – methylacrylate copolymer beads containing gentamicin and X-Ray contrast medium.

Each Methyl methacrylate – Methylacrylate copolymer bead (7mm in diameter) contains 7.5 mg gentamicin sulphate (corresponding to 4.5 mg gentamicin base) and 20 mg zirconium dioxide as X-Ray contrast medium. Each chain consists of 30 beads threaded on multiple-thread surgical wire.

Uses gentamicin is a proven broad spectrum antibiotic active against both gram-positive and gram-negative organisms. Following insertion of the Chains, gentamicin is released gradually from the beads over a prolonged period and the high bactericidal concentrations of the

antibiotic reached at the site of infection enable the infection to be controlled, or provide protection against infection when used prophylactically.

Garamycin Chains are indicated for short term and longer term administration in bone infection e.g. chronic forms of osteomyelitis, (post traumatic, hæmatogenous) infected pseudarthroses and infected osteosyntheses.

Preventative treatment of potentially infected bone injuries.

Directions for use: Garamycin chains have been sterilised in ethylene oxide. They are contained in a double sachet. The outer sachet (peel-off pack) is opened first and the inner sterile packaging then removed under aseptic conditions.

The cavity resulting after thorough surgical removal of the infected bone tissue sequestra is completely filled up with Garamycin Chains; the number of Chains used will depend on the size of the cavity. Usually 1-3 Chains are inserted but up to 5 Chains have been used. Inserted Chains will be completely enclosed by primary wound closure.

Garamycin Chains may be used as follows:

(a) Short Term Application

For the implantation of Chains, it is recommended to take into account the direction in which the Chain will later be pulled out and let the last bead project above the skin level in order that the Chain may be removed by careful, steady traction. The Chains are in general removed 10-14 days following insertion and preferably not more than 10 days after the operation.

The less the Chains are fixed to connective tissue, the easier it is to remove them; this procedure is thus also less painful and more comfortable for the patient. If the beads become fixed to connective tissue to an advanced extent, or if the traction of the beads is not adapted to the tissue conditions, one or several beads may rarely detach themselves from the multi-stranded wire or, in exceptional circumstances the wire may break on the removal of the Chain. In such an event one should generally try to remove the single beads (together with the remaining wire). Should however, extensive surgical procedures be necessary, the single beads may be left in the body, taking into consideration the comparative risk of reoperation.

(b) Longer Term Application

If circumstances require it, the Chains may be implanted completely below the skin level, and removed by reoperation up to 3 months later. Control of local infection allows subsequent surgical procedures, e.g. cancellous bone grafting.

Wherever possible, primary wound closure should be employed; this avoids excessive loss of secretion which would automatically reduce the gentamicin concentration at the site of infection.

An overflow drain may be employed only when considered necessary. Suction drainage is not employed but may be temporarily used in cases of obstructed wound secretion flow.

Contra-indications, warnings, etc There is no absolute contra-indication other than established intolerance of gentamicin.

Since the beads are strung on surgical wire containing chrome and nickel, there is a potential for local sensitivity reactions to these metals.

Garamycin may be used in all orthopaedic surgical procedures where gentamicin sensitive organisms are found to be present from routine bacteriological screen-

ing. Where resistant organisms are encountered to the standard 10 mcg disc test, an MIC determination is recommended. In view of the high bactericidal gentamicin concentration at the infection site, organisms found resistant to the standard 10 mcg sensitivity disc screen may in fact be sensitive and therefore results of such screening may not give a true reflection of clinical effectiveness.

Toxic effects due to the antibiotic are not anticipated; after use of Garamycin Chains, barely detectable gentamicin concentrations (no more than 0.5 mcg/ml) are found in serum for up to four days postoperatively following insertion of the Chains.

Pharmaceutical precautions Store at room temperature - DO NOT FREEZE.

Resterilisation of Garamycin Chains should not be attempted under any circumstances.

Legal category POM.

Package quantities Pack of 1 Chain.

Further information Nil.

Product licence number 3478/0038

LANCE B+C TABLETS

Presentation Each red, biconvex sugar coated tablet contains:

Thiamine Hydrochloride BP (Vitamin B ₁)	50 mg
Riboflavin BP (Vitamin B ₂)	5 mg
Pyridoxine Hydrochloride BP (Vitamin B ₆)	5 mg
Nicotinamide BP	200 mg
Ascorbic Acid BP (Vitamin C)	100 mg

Uses Deficiencies of the Vitamin B complex when encountered as (a) debility after illness such as influenza, measles, tonsillitis, acute bronchitis, enteritis, viral pneumonia (b) debility after operations: alcoholic psychoses.

Maintenance therapy after parenteral vitamin treatment. Acute deficiency states associated with broad spectrum antibiotic therapy.

Dosage and administration *Adults:* one tablet three times daily.

Contra-indications, warnings, etc Nil.

Precautions: Care should be exercised when Lance B+C tablets are prescribed for patients undergoing treatment with laevodopa since pyridoxine may antagonise the therapy.

Side-effects: Rarely, flushing of the face may occur.

Overdosage: Nil.

Pharmaceutical precautions Store in a cool place, keep containers tightly closed.

Legal category P.

Package quantities Containers of 100 and 1,000 tablets.

Further information The vitamins of the B group are converted in the body by phosphorylation reactions to give co-enzymes which play an important part in oxidative mechanisms and intracellular metabolism. Deficiency of the B and C vitamins can interfere with these reactions and give rise to certain disorders (see uses). The high concentrations of Vitamins B and C in Lance B+C tablets rapidly restore to normal altered

metabolic processes caused by deficiencies of these water-soluble vitamins.

Product licence number 0201/0038.

NETILLIN[®] Injection ▼

Presentation Netillin Injection for parenteral use is an aqueous solution of netilmicin sulphate. Each millilitre contains netilmicin sulphate equivalent to 100 mg, 50 mg or 10 mg of netilmicin base, and is available in ampoules and multiple-dose vials.

Uses Netilmicin sulphate is a semi-synthetic, water-soluble antibiotic of the aminoglycoside group. It is a rapidly acting bactericidal antibiotic which probably acts by inhibiting normal protein synthesis in susceptible organisms. It is active at low concentrations against many strains of a wide variety of pathogenic bacteria including *Escherichia coli*, *Klebsiella-Enterobacter-Serratia* species, *Citrobacter* species, *Proteus* species (indole-positive and indole-negative), including *Proteus mirabilis*, *Proteus morganii*, *Proteus rettgeri*, *Proteus vulgaris*; *Pseudomonas aeruginosa*, and *Staphylococcus* species (coagulase-positive and coagulase-negative, including penicillin and methicillin-resistant strains).

Netillin Injection is indicated in: bacteremia, septicemia (including neonatal sepsis), serious infections of the respiratory tract, kidney and genitourinary tract infections, skin and soft tissue infections, bone and joint infections, burns, wounds and peri-operative infections, intra-abdominal infections (including peritonitis) and infections of the gastro-intestinal tract.

Netillin Injection has also been effective in the treatment of infections caused by organisms resistant to other aminoglycosides, such as kanamycin, gentamicin, tobramycin and amikacin.

Dosage and administration The recommended dosage for intramuscular and intravenous administration is identical.

Patients with normal renal function.

Adults: The recommended dosage of Netillin Injection for patients with urinary tract or systemic infections with normal renal function is 4.0–6.0 mg/kg/day given in two equal doses every 12 hours. It may also be given in three equal doses every eight hours. In general, within this dose range, lower dosage will be used for urinary tract infections and higher dosage for systemic infections. For both uses, dosage should be adjusted depending on severity of infection and patient condition.

For adults weighing 50–90 kg, a dose of 150 mg may be given every twelve hours or 100 mg every eight hours. For adults smaller or larger than the above range, dosage should be calculated in mg/kg of lean body weight.

For patients with life-threatening infections, dosages up to 7.5 mg/kg/day may be administered in three equal doses every eight hours. This dosage should be reduced to 6 mg/kg/day or less as soon as clinically indicated, usually within 48 hours.

Children: 6.0–7.5 mg/kg/day (2.0 to 2.5 mg/kg administered every eight hours).

Infants and neonates over one week of age: 7.5 to 9.0 mg/kg/day (2.5 to 3.0 mg/kg administered every eight hours).

Premature or Full Term Neonates One Week of Age or Less: 6 mg/kg/day (3.0 mg/kg administered every 12 hours).

The usual duration of treatment is seven to fourteen days. Longer courses have been well tolerated but it is important that patients treated beyond the usual period be carefully monitored for changes in renal, auditory and vestibular function. Dosage should be reduced if clinically indicated. Netillin should usually be administered intramuscularly, but in certain circumstances a dose may be injected directly into a vein or I.V. tubing slowly over a period of 3 to 5 minutes.

Infusion: In adults a single dose of Netillin injection may be diluted in 50 to 200 ml of sterile normal saline or in a sterile solution of dextrose 5% in water; in infants and children the volume of diluent should be dependent on the patient's fluid requirements. The solution may be infused over a period of one half to two hours.

Netillin Injection should not be physically pre-mixed with other drugs, but should be administered separately in accordance with the recommended route of administration and dosage schedule.

Netillin Injection is physically compatible with the following parenteral solutions: Sterile Water for Injections, Normal Saline, 5% and 10% Dextrose in Water.

Patients with impaired renal function: Dosage must be adjusted and should be individualised on an eight hourly mg/kg basis as follows. The standard daily dose should be given at eight hourly intervals on the first day. Serum creatinine or creatinine clearance rate should then be measured and the dosage of netilmicin adjusted according to the table below. Monitor netilmicin serum concentrations and serum creatinine or creatinine clearance rates at regular intervals.

Hæmodialysis: the recommended dose at the end of each dialysis period is 2 mg/kg. In children a dose of 2 to 2.5 mg/kg may be administered, depending upon the severity of infection.

Dosages recommended above for patients with normal and impaired renal function should not be reduced when netilmicin is administered concomitantly with other antibiotics.

Contra-indications, warnings, etc Hypersensitivity to netilmicin contra-indicates its use. A history of hypersensitivity or serious toxic reactions to other aminoglycosides may also be a contra-indication.

Patients treated with aminoglycosides should be under close clinical observation because of the potential toxicity associated with their use. Monitoring of renal and eighth cranial nerve functions is desirable during therapy, particularly for patients with known or suspected reduced renal function.

Evidence of ototoxicity requires dosage adjustment or discontinuance of the drug.

Serum concentration assays of aminoglycosides are of value to assure adequate levels and to avoid potentially toxic levels. At the recommended dosage, peak levels will generally not exceed 12 mcg/ml. Prolonged levels above 16 mcg/ml should be avoided. If trough levels are monitored (just prior to next dose) they will usually be 3 mcg/ml or less with the recommended dosage. Increasing trough concentrations above 4 mcg/ml should be avoided.

Concurrent and/or sequential systemic or topical use of other potentially neurotoxic and/or nephrotoxic drugs, such as polymyxin B, colistin, cephaloridine, kanamycin, gentamicin, amikacin, tobramycin, neomycin, streptomycin and vancomycin should be avoided. Advanced age and dehydration may also increase the risk of toxicity.

Dosage adjustment guide for patients with renal function impairment

Loading Dose Administer initial standard daily dose as follows	Approx. creatinine clearance rate (ml/min/1.73 sq m)	Serum creatinine level		Percent of loading dose adjusted according to serum creatinine level
		mg/100 ml	S.I. Units μmol/l	
1. Adults with urinary tract and systemic infections 4–6 mg/kg/day	100	1.0	80	100
	71–100	1.1–1.3	100–120	80
2. Adults with life threatening infections 7.5 mg/kg/day	56–70	1.4–1.6	130–150	65
	46–55	1.7–1.9	160–175	55
3. Children 6–7.5 mg/kg/day	41–45	2.0–2.2	180–190	50
4. Infants & Neonates over 1 week of age 7.5– 9.0 mg/kg/day	36–40	2.3–2.5	210–220	40
	31–35	2.6–3.0	230–260	35
5. Premature or full-term neonates one week of age or less 6 mg/kg/day	26–30	3.1–3.5	270–310	30
	21–25	3.6–4.0	320–360	25
	16–20	4.1–5.1	365–450	20
	10–15	5.2–6.6	460–580	15
	< 10	6.7–8.0	600–700	10

The concurrent use of netilmicin with potent diuretics, such as ethacrynic acid or frusemide, should be avoided since these diuretics by themselves may cause ototoxicity. In addition, when administered intravenously, diuretics may enhance aminoglycoside toxicity by altering the antibiotic concentrations in serum and tissue.

Neurotoxic or nephrotoxic antibiotics may be absorbed from body surfaces after local irrigation or application. The potential toxic effect of such antibiotics administered in this fashion should be considered.

Increased nephrotoxicity has been reported following concomitant administration of aminoglycoside antibiotics and cephalothin.

Although neuromuscular blockade has been reported in animals receiving netilmicin at doses considerably above those clinically recommended, the possibility of this phenomenon occurring in man should be considered, particularly if aminoglycosides are administered to patients receiving anaesthetics, neuromuscular blocking agents (such as succinylcholine or tubocurarine), or massive transfusions of citrate-anticoagulated blood. If blockade occurs, calcium salts may reverse it.

Aminoglycosides should be used with caution in patients with neuromuscular disorders, such as myasthenia gravis or parkinsonism, since these drugs theoretically may aggravate muscle weakness because of their potential curare-like effects on neuromuscular junction.

Elderly patients may have reduced renal function which may not be evident by routine screening tests, such as BUN or serum creatinine. A creatinine clearance determination may be more useful. Monitoring of renal function during netilmicin treatment, as with other aminoglycosides, is particularly important in these patients.

Cross-allergenicity among aminoglycosides has been demonstrated. Patients should be well hydrated during treatment.

Although the *in vitro* mixing of netilmicin and carbenicillin results in a rapid and significant inactivation of netilmicin, this interaction has not been demonstrated in patients with normal renal function who received both drugs by different routes of administration. In patients with severe renal impairment receiving carbenicillin concomitantly with an aminoglycoside, a reduction in aminoglycoside serum half-life has been reported.

Treatment with netilmicin may result in overgrowth of non-susceptible organisms. If this occurs, appropriate therapy is indicated. Netilmicin is not intended for intrathecal use.

Side-effects: Adverse renal effects, generally mild in nature, have been reported infrequently after netilmicin administration. They occur more frequently in patients with a history of renal impairment, in patients treated with larger than the recommended dosage, and are most often reversible. While eighth cranial nerve toxicity has been reported with netilmicin, the incidence is lower and the severity appears milder than with other aminoglycosides. Some clinical studies indicate that at therapeutic dosage, netilmicin may have less effect than other aminoglycosides on eighth cranial nerve function. Adverse effects on both the vestibular and auditory branches of the eighth cranial nerve occur primarily in patients with renal impairment and in patients on high doses and/or prolonged therapy. Symptoms which are often transient may include dizziness, vertigo, tinnitus, roaring in the ears and hearing loss. The latter is usually manifested by diminution of high-tone acuity. Total deafness has not been reported.

Some patients who have had previous ototoxic reactions to other aminoglycosides have been treated safely with Netillin Injection.

Other rarely reported adverse reactions possibly related to netilmicin include: headache, malaise, visual disturb-

ances, disorientation, tachycardia, paraesthesia, rash, chills, fever, fluid retention, vomiting and diarrhoea.

Laboratory abnormalities possibly related to netilmicin include: increased blood sugar, increased alkaline phosphatase, increased SGOT or SGPT; other abnormal liver function studies; decreased haemoglobin, WBCs, and platelets; eosinophilia and increase in prothrombin time.

While local tolerance of Netillin Injection is generally excellent, there has been an occasional report of pain at the injection site or local reaction.

Safety for use in pregnancy has not been established.

Overdosage: In the event of overdose or toxic reaction, haemodialysis or peritoneal dialysis will aid the removal of netilmicin from the blood.

Pharmaceutical precautions Netillin Injection should be stored at 2°C to 30°C (35.6°F to 86°F). Protect from freezing.

Netillin Injections should not be physically premixed with other drugs, but should be administered separately in accordance with the recommended route of administration and dosage schedule.

Legal category POM.

Package quantities All the presentations of Netillin are colour coded on both cartons and the containers. The 100 mg/ml strength is available in 2 ml (colour coded red) and 1.5 ml (orange) ampoules and vials, and in 1 ml (yellow) ampoules. The 50 mg/ml and 10 mg/ml strengths are available in 1 ml (green) and 1.5 ml (blue) ampoules respectively. All ampoules and vials are supplied in packs of ten.

Further information Nil.

Product licence numbers

Netillin Injection 100 mg/ml	3478/0041
Netillin Injection 50 mg/ml	3478/0040
Netillin Injection 10 mg/ml	3478/0039

OPTIMINE*

Presentation *Optimine Tablets:* Each white tablet, with score mark on one side and Schering Corporation USA Trademark on the other, contains 1.0 mg azatadine maleate.

Optimine Syrup: Each 5 ml of syrup, which is a clear, orange colour with a characteristic odour and flavour of blackcurrant, contains 0.5 mg of azatadine maleate.

Indications Optimine tablets and syrup are indicated for the symptomatic relief of allergic conditions such as hayfever, vasomotor rhinitis, urticaria, pruritus of allergic origin and allergic reactions associated with insect bites and stings.

Dosage and administration *Adults:* In most conditions, 1 mg of azatadine maleate (1 tablet or 2 teaspoons – 10 ml of syrup) in the morning and evening is recommended in the majority of patients. In refractory or more severe cases, 2 mg twice daily may be used.

Children: 6–12 years of age, 0.5 to 1.0 mg of azatadine maleate ($\frac{1}{2}$ to 1 tablet or 1 to 2 teaspoons – 5 to 10 ml of syrup) twice daily.

Contra-indications, warnings, etc Until the safety of azatadine maleate concerning adverse effects on human foetal development has been established, the drug is not recommended for use in pregnant or lactating women.

Patients taking azatadine maleate should be cautioned against ingestion of alcohol. The drug may potentiate central nervous system depressants.

Although drowsiness is infrequent and impairment of psychomotor function is not manifested at the recommended dosage, patients should be cautioned against engaging in mechanical operations requiring mental alertness until individual response to azatadine maleate has been determined.

Due to the anticholinergic effect of azatadine maleate, the drug should be used with caution in patients with prostatic hypertrophy, urinary retention, glaucoma, stenosing peptic ulcer or pyloroduodenal obstructions.

Mono-amine oxidase inhibitors, which are known to intensify or prolong the anticholinergic and sedative action of drugs, should not be used concomitantly with azatadine maleate.

Azatadine maleate is well tolerated and side-effects are generally dose-related and transient. Among these are: weakness, nervousness, dry mouth, increased appetite, anorexia, nausea, headache, drowsiness, dysuria and blurring of vision.

Overdosage: Symptoms may vary from central nervous system depression to stimulation, the latter is particularly likely in children. Atropine-like symptoms may also occur. If vomiting has not occurred spontaneously the patient should be induced to vomit. If unsuccessful the stomach should be emptied by aspiration and lavage. Stimulants should not be used and vasopressors may be used to treat hypotension.

Pharmaceutical precautions There are no pharmaceutical precautions for Optimine tablets or syrup.

Legal category P.

Package quantities Optimine tablets are supplied in bottles containing 250 tablets and cartons of blister packs containing 10 tablets. Optimine syrup is supplied in a 120 ml bottle.

Further information Azatadine maleate possesses potent antihistamine and antiserotonin activity. It has an inherently long action which enables effective and sustained control of symptoms from twice a day administration.

Product licence numbers

Optimine Tablets	3478/0024
Optimine Syrup	3478/0025

PALACOS* R

Presentation Palacos R is a radiopaque rapidly setting bone cement formed from the mixture of two separate pre-measured sterilised components.

One component is supplied in a polyethylene coated paper packet and consists of 40 g of a powder (polymer) with the following composition:

Methyl methacrylate –	
methylacrylate copolymer	33.80 g
Benzoyl peroxide	0.20 g
Zirconium dioxide	6.00 g
Chlorophyll	0.008 g

The other component is supplied in an amber ampoule and consists of 20 ml of a liquid (monomer) with the following composition:

Methyl methacrylate (stabilised with hydroquinone)	18.40 g
--	---------

N,N-Dimethyl-p-toluidine 0.40 g
Chlorophyll 0.005 g

The liquid monomer is sterile filtered and the powder is sterilised by ethylene oxide. The polyethylene coated paper packet containing the powder as well as the exterior of the ampoule containing the liquid are also sterilised with ethylene oxide. Palacos R is pigmented light green in order to make it clearly visible in the operative field.

Note: Palacos R powder is double packaged. The outer aluminium protective foil which is NON-STERILE contains two polyethylene peel-packs. Each peel pack encloses a STERILE polyethylene paper coated packet of Palacos R Powder.

The ampoule containing the liquid monomer is packaged in a protective plastic blister pack.

When the powder (polymer) and the liquid (monomer) are mixed, the dimethyl-p-toluidine in the liquid activates the benzoyl peroxide catalyst in the powder. This initiates the polymerisation of the monomer which then binds together granules of polymer. As polymerisation proceeds, a dough-like mass is formed which, over a period of five to six minutes, hardens into a mechanically uniform solid. Polymerisation is an exothermic reaction with temperatures rising to as high as 80°C. Although the spontaneous generation of heat accelerates the reaction, the polymerisation of this self-curing resin occurs even if the temperature is reduced by irrigation with a cool physiologic saline solution.

Action Palacos R is a radiopaque cement-like substance which allows seating and fixation of prostheses to bone.

Indications Palacos R bone cement is indicated for fixation of prostheses to bone in partial or total arthroplastic procedures of the hip, knee or other joints.

Contra-indications, warnings, etc

Contra-indications: Palacos R is contra-indicated in patients allergic to any of its components.

Warnings: Prior to using Palacos R, surgeons should be thoroughly familiar with its properties, handling characteristics and application to arthroplasty. (See Presentation, Precautions, and Dosage and Preparation.) It is advisable for the surgeon to go through the entire mixing, handling and setting process before using the material in an actual surgical procedure.

The liquid monomer is highly volatile and flammable; therefore, appropriate precaution should be taken particularly with its use in the operating room. It is also a potent lipid solvent and should not be allowed to come into direct contact with the body. Contact of the liquid monomer, with rubber, including surgical rubber gloves, should also be avoided.

Care should be exercised during the mixing of the two components to prevent excessive exposure to the concentrated vapours of the monomer. These may irritate the respiratory tract and eyes, and may possibly be harmful to the liver. Skin reactions apparently resulting from contact with the monomer have been reported.

Long-term durability, wearability and stability of the polymerised bone cement in situ are unknown. This should be considered in light of the expected longevity of the patients for whom the substance will be used. The long-term effects of this preparation are unknown. Thus the physician should decide whether the benefits expected from its use outweigh any possible long-term adverse effects.

Precautions: Blood pressure, pulse and respiration should be carefully monitored during and immediately after implantation of the bone cement. Any significant alteration in these vital signs should be corrected with appropriate measures.

When Palacos R is used in total hip replacements, care should be taken to clean and aspirate the proximal portion of the femoral medullary canal just prior to insertion of the bone cement.

Adverse reactions: Transient fall in blood pressure immediately after implantation of the bone cement and endo-prosthesis is frequently observed. Rare cases have been reported in which the hypotension was associated with cardiac arrest and sudden death.

The following additional adverse reactions have been reported with the use of the methylmethacrylate bone cements:

Thrombophlebitis	Superficial wound infection
Pulmonary embolism	Deep wound infection
Haemorrhage and haematoma	Trochanteric bursitis
Loosening or displacement of the prosthesis	Trochanteric separation

Others which have been observed:

Heterotopic new bone	Myocardial infarction
Short-term irregularities in cardiac conduction	Cerebrovascular accident

Dosage and preparation A dose is prepared by mixing the entire contents of one packet of powder (40 g polymer) with one ampoule of liquid (20 ml monomer). One or two doses will usually suffice, although this will depend upon the specific surgical procedure and the techniques employed. (At least one extra unit of Palacos R should be available before starting a surgical procedure.) Each dose is prepared separately. The following are required for preparation of the bone cement:

Sterile working area
Sterile porcelain or stainless steel bowls
Sterile porcelain or stainless steel mixing spoons or spatulas.

The polyethylene package and the blister pack are opened by a circulating nurse or assistant and the sterile paper packet and ampoule are aseptically placed on a sterile table. The paper packet and the ampoule are opened under sterile conditions. *The liquid is poured into a bowl and the powder is added.* The mixture is then stirred vigorously, but carefully, for 30–40 seconds until a dough-like mass is formed which does not adhere to rubber gloves. At this stage, the mass is kneadable and will remain so for about four to five minutes. The ideal working consistency of the Palacos R for application to bone is best determined by the surgeon's experience in using the preparation. When the desired consistency is obtained, the preparation may be applied to bone and prosthesis as required. To assure adequate fixation, the prosthesis should be held securely in place without movement until the bone cement has fully hardened. Generally, this occurs seven to eight minutes after the onset of mixing the powder with the liquid. Excessive cement must be removed while it is still soft. The above doughing, working and setting times apply at approximately 23°C (73°F). Higher temperatures will shorten these times. Conversely, lowering of the ambient temperature or that of the material below 23°C will increase doughing, working and setting times. If, during the

surgical procedure, additional cement is required, another packet of powder and ampoule of liquid may be mixed as described above. The resulting kneadable mass may be applied to previously hardened bone cement.

Since each packet of powder contains a premeasured quantity of polymer to react with a premeasured quantity of monomer, care should be taken to mix the entire contents of one packet with the entire contents of one ampoule.

The mixing and subsequent kneading of the polymerising mass should be thorough and at least four (4) minutes in duration. Because of the volatile nature of the monomer, the above procedure may assist in causing its evaporation and thereby reduce the amount to which the patient is exposed. On the other hand, if the kneading process is extended too long, the polymerisation may proceed to a point where the mass is no longer soft and pliable, making manipulation and application to bone difficult.

The completion of polymerisation occurs in the patient and is associated with the liberation of heat. The long-term effects of this heat on the tissues surrounding the bone cement are not known. To more rapidly dissipate the heat, the polymerising cement may be irrigated with a cool physiologic saline solution.

Pharmaceutical precautions Do not store the liquid component above 30°C (86°F) or in direct sunlight to prevent premature polymerisation. Sterilisation shall only be performed by the manufacturer and is only guaranteed if the containers are undamaged. Resterilisation of any of the components should not be attempted under any circumstances.

Legal category POM.

Package quantities Carton consisting of: 2 packets, each containing 40 g sterilised powder (polymer); 2 ampoules, each containing 20 ml of sterilised liquid (monomer).

Further information Nil.

Product licence number 3478/0008.

PALACOS® R WITH GENTAMICIN PALACOS® R-20 WITH GENTAMICIN

Presentation Palacos R with gentamicin and Palacos R-20 with gentamicin is a radiopaque rapidly-setting bone cement containing the antibiotic gentamicin, it is formed from the mixture of two separate pre-measured sterilised components.

One component is supplied in a polyethylene coated paper packet consisting of powder (polymer) with the following composition.

	Palacos R with gentamicin	Palacos R-20 with gentamicin
Methyl methacrylate – methyl acrylate co- polymer	33.80 g	16.9 g
Benzoyl peroxide	0.20 g	0.10 g
Zirconium dioxide	6.00 g	3.00 g
Chlorophyll	0.008 g	0.004 g
with		
Gentamicin (as the sulphate)	0.50 g	0.25 g

The other component is supplied in an amber ampoule and consists of a liquid (monomer) with the following composition.

	Palacos R with gentamicin	Palacos R-20 with gentamicin
Methyl-methacrylate (stabilised with hydroquinone)	18.40 g	9.20 g
N,N-Dimethyl-p- toluidine	0.40 g	0.20 g
Chlorophyll	0.005 g	0.0025 g

The liquid monomer is sterile filtered and the powder polymer and gentamicin mixture is sterilised by ethylene oxide. The polyethylene coated paper packet containing the powder as well as the exterior of the ampoule containing the liquid are also sterilised with ethylene oxide.

Palacos R with gentamicin and Palacos R-20 with gentamicin are pigmented light green in order to make them clearly visible in the operative field.

Note: The powder polymer plus gentamicin is double packaged. The outer aluminium protective foil which is NON-STERILE contains two polyethylene peel-packs. Each peel-pack encloses a STERILE polyethylene paper coated packet of powder polymer plus gentamicin.

The ampoule containing the liquid monomer is packaged in a protective plastic blister pack.

When the powder (polymer) and liquid (monomer) are mixed, the dimethyl-p-toluidine in the liquid activates the benzoyl peroxide polymerisation catalyst in the powder. This initiates the polymerisation of the monomer which then binds together granules of polymer. As polymerisation proceeds, a dough-like mass is formed which subsequently, over a period of five to six minutes, hardens into a mechanically uniform solid. Polymerisation is an exothermic reaction with temperatures rising as high as 80°C. Although the spontaneous generation of heat accelerates the reaction, the polymerisation of this self-curing resin occurs even if the temperature is reduced by irrigation with a cool physiologic saline solution.

Gentamicin is a broad spectrum bactericidal aminoglycoside antibiotic having activity against gram-negative and gram-positive bacteria. It is water soluble and heat stable. *In vitro*, gentamicin has been shown to be released in active form from the bone cement complex for periods of greater than one year. After implantation in animals, the antibiotic is detected in the blood as well as in fluid removed from the site of implantation. In man, following total hip replacement in which Palacos R with gentamicin was used as a bone cement, the antibiotic was found in joint fluid, blood and urine. Concentrations in the urine have been detected for up to three weeks after surgery, suggesting good release of antibiotic.

Uses Palacos R with gentamicin and Palacos R-20 with gentamicin bone cement is indicated for fixation of prostheses to bone in partial or total arthroplastic procedures of the hip, knee or other joints in which infection by gentamicin-sensitive organisms is confirmed or suspected.

Contra-indications, warnings, etc

Contra-indications: Palacos R with gentamicin and Palacos R-20 with gentamicin is contra-indicated in patients allergic to any of its components.

Warnings: Prior to using Palacos R with gentamicin and Palacos R-20 with gentamicin surgeons should be thoroughly familiar with its properties; handling characteristics and application to arthroplasty (see Presentation, Precautions and Dosage and Preparation). It is advisable for the surgeon to go through the entire mixing, handling and setting process before using the materials in an actual surgical procedure.

The liquid monomer is highly volatile and flammable, therefore appropriate precautions should be taken particularly with its use in the operating room. It is also a potent lipid solvent and should not be allowed to come into direct contact with the body. Contact of the liquid monomer with rubber, including surgical gloves, should also be avoided.

Care should be exercised during the mixing of the two components to prevent excessive exposure to the concentrated vapours of the monomer. These may irritate the respiratory tract and eyes, and may possibly be harmful to the liver. Skin reactions apparently resulting from contact with the monomer have been reported.

Long term durability, wearability and stability of the polymerised bone cement *in situ* are unknown. This should be considered in light of the expected longevity of the patients for whom the substance will be used. The long-term effects of this preparation are unknown. Thus the physician should decide whether the benefits from its use outweigh any possible long-term adverse effects.

Precautions: Blood pressure, pulse and respiration should be carefully monitored during and immediately after implantation of the bone cement. Any significant alteration in these vital signs should be corrected with appropriate measures.

When Palacos R with gentamicin is used in total hip replacements, care should be taken to clean and aspirate the proximal portion of the femoral medullary canal just prior to insertion of the bone cement.

Adverse Reactions: Transient fall in blood pressure immediately after implantation of the bone cement and endo-prosthesis is frequently observed. Rare cases have been reported in which the hypotension was associated with cardiac arrest and sudden death.

The following additional adverse reactions have been reported with the use of methyl methacrylate bone cements:

Thrombophlebitis	Superficial wound infection
Pulmonary embolism	
Haemorrhage and haematoma	Deep wound infection
Loosening or displacement of the prosthesis	Trochanteric bursitis
	Trochanteric separation

Others which have been observed:

Heterotopic new bone	Myocardial infarction
Short-term irregularities in cardiac conduction	Cerebrovascular accident

Since the concentration of gentamicin reaching the VIII nerve and the kidney will be quite low, ototoxic and nephrotoxic reactions are very unlikely to result from the use of Palacos R with gentamicin and Palacos R-20 with gentamicin. Hypersensitivity to gentamicin is rare.

Dosage and preparation: A dose is prepared by mixing the entire contents of one packet of powder with one ampoule of liquid (40 g polymer plus 0.5 g gentamicin and 20 ml monomer OR 20 g polymer plus 0.25 g gentamicin and 10 ml monomer). The number of doses

and pack size required will depend upon the specific surgical procedure and technique employed. (At least one extra unit of the desired pack size should be available before starting a surgical procedure).

Each dose is prepared separately.

The following are required for preparation of the bone cement: sterile working area; sterile porcelain or stainless steel bowls; sterile porcelain or stainless steel mixing spoons or spatulas.

The polyethylene package and the blister pack are opened by a circulating nurse or assistant and the sterile paper packet and ampoule are aseptically placed on a sterile table. The paper packet and the ampoule are opened under sterile conditions. *The liquid is poured into a bowl and the powder is added.* The mixture is then stirred vigorously, but carefully, for 30–40 seconds until a dough-like mass is formed which does not adhere to rubber gloves. At this stage, the mass is kneadable and will remain so for about four to five minutes. The ideal working consistency of the Palacos R with gentamicin and Palacos R-20 with gentamicin for application to bone is best determined by the surgeon's experience in using the preparation. When the desired consistency is obtained the preparation may be applied to bone and prosthesis as required. To assure adequate fixation, the prosthesis should be held securely in place without movement until the bone cement has fully hardened. Generally, this occurs seven to eight minutes after the onset of mixing the powder with the liquid. Excessive cement must be removed while it is still soft. The above doughing, working and setting times apply at approximately 23°C (73°F). Higher temperatures will shorten these times. Conversely, lowering of the ambient temperature or that of the material below 23°C will increase doughing, working and setting times.

If, during the surgical procedure, additional cement is required, another packet of powder and ampoule of liquid may be mixed as described above. The resulting kneadable mass may be applied to previously hardened bone cement.

Since each packet of powder contains a premeasured quantity of polymer to react with a premeasured quantity of monomer, care should be taken to mix the entire contents of one packet with the entire contents of one ampoule.

The mixing and subsequent kneading of the polymerising mass should be thorough and at least four (4) minutes in duration.

Because of the volatile nature of the monomer, the above procedure may assist in causing its evaporation and thereby reducing the amount to which the patient is exposed. On the other hand, if the kneading process is extended too long, the polymerisation may proceed to a point where the mass is no longer soft and pliable, making manipulation and application to bone difficult.

The completion of polymerisation occurs in the patient and is associated with the liberation of heat. The long-term effects of this heat on the tissues surrounding the bone cement are not known. To more rapidly dissipate the heat, the polymerising cement may be irrigated with a cool physiologic saline solution.

Pharmaceutical precautions Do not store component above 30°C (86°F) or in direct sunlight to prevent premature polymerisation. Sterilisation shall only be performed by the manufacturer and is only guaranteed if the containers are undamaged. Resterilisation of any of the components should not be attempted under any circumstances.

Legal category POM.

Package quantities Palacos R with gentamicin is supplied in white cartons consisting of 2 packets each containing 40 g sterilised powder (polymer) with 0.5 g gentamicin (as the sulphate); 2 ampoules each containing 20 ml of sterilised liquid (monomer).

Palacos R-20 with gentamicin is supplied in blue cartons consisting of 2 packets each containing 20 g sterilised powder (polymer) with 0.25 g gentamicin (as the sulphate); 2 ampoules each containing 10 ml of sterilised liquid (monomer).

Further information Nil

Product licence number 3478/0009

TINADERM*

Presentation Tinaderm cream, powder and solution each contain 1% tolnaftate. The cream and powder are white in appearance and the solution is clear and colourless. Each ml of solution contains 10 mg tolnaftate, 1 mg of butylated hydroxytoluene in a non-aqueous, homogenous vehicle of polyethylene glycol-400.

Uses Tinaderm is recommended for the topical treatment of *Tinea pedis*, *Tinea cruris*, *Tinea corporis* and *Tinea manuum*, due to infection with *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Trichophyton tonsurans*, *Microsporum canis*, *Microsporum audouinii*, *Epidermophyton floccosum* and for *Tinea versicolor* due to *Malassezia furfur*. The solution is recommended for mild, recurrent fungal infections of the scalp (*tinea capitis*).

Dosage and administration Tinaderm cream should be massaged into the affected area twice a day. It does not usually sting or irritate even when applied to raw areas or when acute inflammation is present.

Symptomatic relief is usually rapid, often within two or three days and lesions generally clear within two or three weeks, but may take longer when palmar and plantar sites are involved. Removal of hardened skin or calluses from these areas is helpful.

Tinaderm powder is recommended for use on areas where perspiration is a problem, or where maceration is present. It should be sprinkled into footwear, socks and stockings, which may act as reservoirs of infection.

Tinaderm solution should be applied as two or three drops to the affected area two or three times daily and massaged gently to cover the entire area.

Contra-indications, warnings, etc There are no known contra-indications to the use of Tinaderm cream, powder and solution.

Pharmaceutical precautions Store Tinaderm cream and solution in a cool place.

Legal category GSL.

Package quantities Tinaderm cream in a tube of 15 g Tinaderm powder in a sprinkler tin of 50 g. Tinaderm solution in a 20 ml plastic bottle.

Further information Tolnaftate is a highly active fungicidal agent that is very effective in the treatment of superficial fungal infections of the skin. It is inactive systemically, nonsensitising, and the solution does not ordinarily sting or irritate intact or broken skin, even in the presence of acute inflammatory reactions. Optimum results are obtained if attention to hygiene is stressed.

Product licence numbers

Tinaderm Cream 3478/5900

Tinaderm Powder 3478/5901

Tinaderm Solution 3478/0001

TINADERM*-M CREAM

Presentation Each gram of Tinaderm-M Cream contains 10 mg of tolnaftate and 100,000 units of Nystatin in a white, water-washable, vanishing cream base.

Uses Tinaderm-M Cream is recommended for the topical treatment of cutaneous mycotic infections such as *Tinea pedis*, *Tinea cruris*, *Tinea corporis*, *Tinea barbae* and *Tinea manuum* due to *Trichophyton rubrum*, *T. mentagrophytes*, *T. tonsurans*, *Microsporum canis*, *M. audouinii*, *Epidermophyton floccosum*, *Candida (monilia) albicans* and *Tinea versicolor (Malassezia furfur)*.

If *Candida albicans* is the primary cause of infections, such conditions as 'Athlete's foot' (dermatophytosis), *perleche*, *paronychia*, *intertrigo*, 'nappy rash' and other cutaneous lesions can be successfully treated with Tinaderm-M.

Tinaderm-M is particularly recommended for the treatment of fungal infections localised in intertriginous and other moist areas of the skin where *Candida* infections are present or likely to develop.

Dosage and administration A sufficient quantity of Tinaderm-M should be applied to completely cover the affected area two or three times daily until healing is complete. Lesions generally begin to clear during the first treatment week and disappear completely after two to four weeks of treatment. In chronic or greatly hyperkeratotic lesions, more prolonged therapy may be necessary. The concomitant use of a mild keratolytic agent may be indicated in areas where the skin has become hyperkeratotic. Use of wet compresses prior to application of Tinaderm-M aids in the healing of exudative lesions and does not interfere with the fungicidal action of the medication. Surgical debridement of dead skin and treatment of calluses is advised when necessary.

If after four weeks of therapy there has not been a progressive improvement, diagnosis should be reconfirmed. Mycosis complicated by bacterial infections may require additional antibiotic treatment.

Contra-indications, warnings, etc Tinaderm-M should not be administered to patients with known hypersensitivity to any ingredients. Should sensitivity occur, discontinue use.

Keep out of eyes.

Tinaderm-M is for dermatological use only.

Pharmaceutical precautions There are no pharmaceutical precautions for Tinaderm-M.

Legal category POM.

Package quantities Tinaderm-M is available in 20 g tubes.

Further information Tolnaftate is a highly active, nonsensitising, fungicidal agent that is very effective in the treatment of superficial fungal infections of the skin. Nystatin, an antibiotic with antifungal activity, provides specific therapy for all localised forms of moniliasis.

Tinaderm-M Cream does not ordinarily sting or irritate intact or broken skin and is inactive systemically. Tinaderm-M Cream will not stain or discolour skin, hair, nails or clothing.

Product licence number 3478/0020.

*Trade Mark

Labaz
Regent House,
Heaton Lane,
Stockport, SK4 1AG



CALCIPARINE*

Presentation Disposable syringes, each containing 5,000 international units of heparin as the calcium salt in approximately 0.2 ml Water for Injections BP.

Uses As an anticoagulant for the prophylaxis of thromboembolic phenomena especially deep venous thrombosis and thromboembolic disease associated with major surgery or myocardial infarction.

Dosage and administration The recommended dose is 5,000 units by subcutaneous injection, two hours before operation, followed by 5,000 units by subcutaneous injection every eight hours for seven days. If the patient is still confined to bed at the end of this period, the same dosage should be continued until he is ambulant. In myocardial infarction the recommended dosage is 5,000 units twice daily for 10 days or until the patient is mobile. The injection is best carried out in the subcutaneous tissue of the lateral abdominal wall, inserting the specially designed needle of the pre-filled syringe vertically into a pinched up fold of skin.

Contra-indications, warnings, etc Calciparine is contra-indicated in patients hypersensitive to heparin. Calciparine is contra-indicated in patients with a condition in which there is an increased danger of haemorrhage. Such conditions include haemophilia, thrombocytopenia and other haemorrhagic diatheses, gastric and duodenal ulcer, sub-acute bacterial endocarditis, threatened abortion and major surgery involving the brain, spinal cord and eye.

Calciparine should not be used in patients with advanced renal or hepatic dysfunction, in severe hypertension, or patients in shock. Care should be taken in patients receiving salicylates, inhibitors of platelet aggregation, ulcerogenic drugs or any drug likely to prolong coagulation.

Special care should be taken when elderly patients and pregnant women are involved.

Side effects: Hypersensitivity reactions may occur, but are rare. Acute reversible thrombocytopenia has been reported but is rare. Osteoporosis and alopecia have occurred in patients treated over many months.

Treatment of overdosage: If overdosage or bleeding occurs, protamine sulphate should be used to neutralise the heparin. Enough Protamine Sulphate BP should be given to neutralise half the total amount of heparin given. 1 mg protamine sulphate will neutralise 100 units of calcium heparin. The protamine sulphate should be given at a rate not exceeding 5 ml of a 1% solution intravenously over 10 minutes and this neutralisation should be controlled by appropriate laboratory monitoring.

Pharmaceutical precautions Store in a cool place, below 25°C, but do not freeze. Other preparations should not be mixed with the heparin in the disposable syringe.

The injection and needle are sterile and the unit must not be autoclaved.

Legal category POM.

Package quantities Boxes of 10 pre-filled syringes.

Further information Nil.

Product licence number 0623/0010.

CORDARONE* X ▼

Presentation White to off-white scored round biconvex tablets approximately 10.5 mm in diameter each containing 200 mg amiodarone hydrochloride.

Uses Tachyarrhythmias associated with Wolff-Parkinson-White syndrome. All types of tachyarrhythmias of paroxysmal nature including: supraventricular, nodal and ventricular tachycardias; atrial flutter and fibrillation; ventricular fibrillation; when other drugs cannot be used.

Dosage and administration Treatment should be started with 1 tablet (200 mg) three times a day and continued for at least a week. Some patients may require up to 4 weeks at this dosage to reach a full response. When the desired effect is obtained the dose should be gradually reduced and adjusted to a maintenance dose, the dose being titrated to the individual patient's requirements. The maintenance dose is normally 1 tablet per day. Some patients can be controlled on a lower maintenance dose for example 1 tablet on 5 days out of 7, or even 1 tablet on alternate days.

Very rarely a patient may need a higher maintenance dose; for example 600 mg daily, or more, may be needed to control the arrhythmia.

In all cases, the patient's management must be judged on individual response and well being.

Contra-indications, warnings, etc Cordarone X is contra-indicated in sinus bradycardia, all degrees of A.V. block and episodes of bradycardia sufficient to cause syncope, unless used in conjunction with a pacemaker.

Cordarone X is not contra-indicated in patients with latent or manifest heart failure but caution should be exercised as existing heart failure may be worsened by Cordarone X. In this case, Cordarone X should be associated with the usual cardiotonic and diuretic treatments. However administration of Cordarone X to a patient already receiving digoxin may bring about an increase in the plasma digoxin concentration and thus precipitate symptoms and signs associated with high digoxin levels.

Cordarone X should be used with caution in combination with β -blocking agents or calcium antagonists, as any tendency to produce bradycardia may be potentiated. It may also potentiate anticoagulant therapy.

Cordarone X is contra-indicated in patients with evidence or a history of thyroid dysfunction. Both hyper- and hypo-thyroidism have occurred during treatment

with Cordarone X and thyroid function should be monitored before and during long-term administration. Cordarone X disturbs the classical thyroid function tests, (PBI,¹³¹I) and specific methods for measurement of plasma thyroxine levels (T_4 , T_3 and TSH) must be used.

U-Waves and deformed T-waves may occur in the ECG because of the fixing of Cordarone X in myocardial tissues. These are not signs of intoxication and administration may be continued.

Although no teratogenic effects have been observed in animals, there are insufficient data on the use of Cordarone X during pregnancy in humans to judge any possible toxicity.

Too high a dosage may lead to severe bradycardia and to conduction disturbances with the appearance of an idioventricular rhythm, particularly in elderly patients or during digitalis therapy. In these circumstances, Cordarone X treatment should be withdrawn. If necessary, β -adrenostimulants or glucagon may be given.

Side-effects: Patients on continuous therapy may develop microdeposits in the cornea. The deposits are usually discernible only by slit-lamp examination and very rarely give rise to symptoms such as visual haloes. They regress with reduction of dose or termination of treatment and are considered essentially benign in nature. No associated ophthalmic pathology has been reported, but during long term administration regular ophthalmological examination is recommended.

Peripheral neuropathy has been reported in some patients, in all cases this has been reversible on withdrawing the drug. Tremor of an extrapyramidal type has also infrequently been reported with complete regression after reduction of dose or withdrawal of the drug.

Cordarone X may induce photosensitization in some patients; this can usually be alleviated by the use of barrier creams and other protective measures. Rarely a slate grey discoloration of the skin has been reported.

Diffuse pulmonary alveolitis has been reported, sometimes presenting as unexplained or disproportionate dyspnoea. This has usually been reversible with corticosteroid therapy and/or reduction or withdrawal of amiodarone therapy.

Other unwanted effects occasionally reported include nightmares, vertigo, headaches, sleeplessness, fatigue, nausea, vomiting and metallic taste. When these effects occur, they usually do so at the beginning of therapy and disappear on reduction of the dose.

Treatment of overdosage: Animal studies indicate that Cordarone X has a high LD₅₀ hence it is most unlikely that a patient will ingest an acute toxic dose. In such an event gastric lavage may be employed to reduce absorption, in addition to general supportive measures. The patient should be monitored and if bradycardia ensues β -adrenostimulants or glucagon may be given.

Pharmaceutical precautions Tablets should be protected from light.

Legal category POM.

Package quantities Carton of 30 tablets (in blister pack of 10 tablets).

Further information Cordarone X is strongly protein bound and its pharmacokinetic and pharmacodynamic half-lives are both very long, of the order of 14–28 days.

High doses of Cordarone X, usually 3 tablets/day, should be given initially to achieve effective tissue levels as rapidly as possible. Owing to the long half-life of the

drug, a maintenance dose of only one tablet/day, or less, is usually necessary. Sufficient time must be allowed for a new distribution equilibrium to be achieved between adjustments of dose.

The long half-life is a valuable safeguard for patients with potentially lethal arrhythmias as omission of occasional doses does not significantly influence the protection afforded by the drug.

The electrophysiological properties of Cordarone X may be summarised as follows:

1. Prolongation without flattening of the action potential in atrial and ventricular muscle and, to a lesser extent, in Purkinje fibres, without change in the resting membrane potential. (Class III activity – Singh and Vaughan Williams).
2. Reduction in the maximum rate of repolarization.
3. Marked antifibrillatory action.
4. No significant depression of spontaneous diastolic depolarization of the His-Purkinje fibres.
5. Lengthening the refractory period of the myocardium and conducting system, including accessory pathways.

This electrophysiological profile explains the marked efficacy of Cordarone X in the treatment of arrhythmias where the refractory period of the accessory pathway is very short.

Product licence number 0623/0007.

EPILIM*

Presentation

1. *Epilim 200 enteric-coated:* A lilac-coloured enteric-coated tablet containing 200 mg sodium valproate.
2. *Epilim 500 enteric-coated:* A lilac-coloured enteric-coated tablet containing 500 mg sodium valproate.
3. *Epilim Syrup:* A red cherry-flavoured syrup containing 200 mg sodium valproate per 5 ml.
4. *Epilim tablets:* A white scored tablet containing 200 mg sodium valproate.

Uses In the treatment of generalised, focal or other epilepsy. In women of childbearing age, Epilim should be used only in severe cases or in those resistant to other treatment.

Dosage and administration Epilim should preferably be taken with or after food; enteric-coated and plain tablets should be swallowed whole, if necessary with a little water, but not aerated water. It is recommended that optimum dosage be established using the 200 mg enteric-coated tablet. Epilim 500 enteric-coated is recommended for patients requiring high dosages.

Adults: Dosage should start at 600 mg/day, in divided doses, increasing by 200 mg/day at three-day intervals until control is achieved; this is generally within the range 1,000–1,600 mg/day. If adequate control has not been achieved after two weeks, the dose may be further increased, by stages, to a maximum of 2,600 mg/day, or one other anti-epileptic agent may be added, at a low dosage.

In patients already receiving other therapy the same pattern should be followed. If increased sedation is observed, dosage of barbiturates should be reduced as that of Epilim is increased; the respective dosages should be adjusted, during the stabilisation period, to give optimum control at the lowest possible combined-dose

level, and it may be found possible to maintain control with Epilim alone.

In sole therapy the dose/plasma level ratio is between 1:2.5–3 in children, and 1:3.5–4 in adults. In combination therapy the ratios are reduced to 1:1.2–1.5 in children, and 1:2.1–2.4 in adults. Therefore when added to existing therapy higher doses of Epilim may be required to maintain therapeutic plasma levels than when it is used as sole therapy. Conversely, when changing from combined therapy to sole therapy a dosage reduction of Epilim may be required.

Once known enzyme-inducers (e.g. phenytoin, phenobarbitone, carbamazepine) have been withdrawn, it may be possible to maintain seizure control on a reduced dose of Epilim. A method of measuring plasma levels is available, should this be considered helpful; however, optimum dosage must ultimately be determined by seizure-control.

Children over 20 kg: Initial dosage should be 400 mg/day (irrespective of weight) in divided doses, with spaced increases until control is achieved; this is usually within the range 20–30 mg/kg of body weight per day.

Children under 20 kg: 20 mg/kg of body weight per day; in severe cases, this may be increased up to 30 mg/kg/day but should be undertaken only in patients in whom plasma valproate levels, clinical chemistry and haematological parameters can be monitored.

Contra-indications, warnings, etc Liver dysfunction, including hepatic failure resulting in fatalities has occurred in patients whose treatment included valproic acid or sodium valproate. The incidents mainly occurred during the first six months of therapy, the period of maximum risk being 2–12 weeks.

Biochemical tests may not always become abnormal early in the evolution of hepatic failure; non specific findings such as loss of seizure control, malaise, anorexia and vomiting, developing after a period of satisfactory epilim treatment may alert the clinician to the possibility of hepatic damage.

Epilim should not be administered to patients with pre-existing hepatic dysfunction.

All patients for whom treatment with Epilim is contemplated should have base line liver function assessed (including serum fibrinogen and albumin levels) prior to commencement of therapy. Liver function should be carefully monitored, particularly during the first six months of therapy, and when dosage is being titrated upwards.

Patients with a prior history of liver disease or with severe or unusual seizure disorders, e.g. those accompanied by mental retardation and/or organic brain disease, should be followed particularly carefully. Transient elevations of liver enzymes are not uncommon during early treatment with Epilim. However, if liver enzyme elevations are accompanied by other evidence of hepatic dysfunction, especially raised serum bilirubin or lowered serum fibrinogen, then the drug should be immediately withdrawn.

Hypermonaemia without hepatic damage can occur in patients during treatment with valproic acid or sodium valproate. It has been suggested that this may be related to interference with propionic acid metabolism. This may manifest clinically as vomiting, ataxia and increasing clouding of consciousness. Should these symptoms occur, Epilim should be discontinued.

Valproic acid inhibits second stage of platelet aggregation.

Reversible prolongation of bleeding time and thrombocytopenia have been reported, but have usually been associated with doses above those recommended. Spontaneous bruising or bleeding is an indication for withdrawal of medication pending investigations; it is recommended that patients receiving Epilim be monitored for platelet function before major surgery. Red cell hypoplasia and leucopenia have been reported with sodium valproate. The blood picture returned to normal when the drug was discontinued.

There have been reports of pancreatitis occurring in patients receiving valproic acid or sodium valproate. Patients experiencing acute abdominal pain should have the serum amylase estimated.

No cardiac effects attributed to Epilim have been reported. Minor gastric irritation and, less frequently, nausea have been observed in some patients at the start of treatment, but these problems can usually be overcome by administering Epilim tablets or syrup with or after food, or by transferring the patient to the Epilim enteric-coated formulations.

Transient hair loss has been noted in some patients. This effect does not appear to be dose-related and regrowth normally begins within six months, although the hair may become more curly than previously. Tremor has occasionally been observed at high dosage; this may be controlled by reduction of dosage. Oedema has been reported. Increase in alertness, appetite and weight may occur.

Combined medication: Epilim is generally well tolerated in combination with other anti-epileptic agents; however owing to the interaction known to occur between these compounds, it may sometimes be necessary to reduce the dosage of other drugs when adding Epilim to existing anti-convulsant therapy. Epilim may block the metabolism of barbiturates giving rise to raised plasma barbiturate level. Like many other drugs, Epilim may also potentiate the effect of monoamine oxidase inhibitors and other anti-depressants, and dosage of such compounds should, therefore, also be reduced. Epilim does not induce liver enzymes, and there have been no reports of loss of efficacy of oral contraceptive agents.

Diabetic patients: Epilim is eliminated mainly through the kidneys, partly in the form of ketone bodies; this may give false positives in the urine testing of possible diabetics. In addition, care should be taken when treating diabetic patients with Epilim Syrup, as this contains 3.6 g sucrose per 5 ml.

Women of childbearing age: Valproic acid or sodium valproate, like certain other anti-convulsants, have been shown to be teratogenic in animals. In women of childbearing age, the benefits of these compounds should be weighed against the possible hazard suggested by these findings.

Overdosage Nine cases of accidental and fourteen cases of suicidal overdosage have been reported. Full recovery occurred in 22 following treatment which included induced vomiting, gastric lavage, assisted ventilation, forced diuresis and other supportive measures; naloxone was used successfully in one patient.

The only known fatality followed a massive suicidal overdose resulting in a plasma level of 1970 mg/litre.

Pharmaceutical precautions Epilim tablets are hygroscopic and must be kept in their protective foil until taken; they should be stored in a cool, dry place. Epilim Syrup should be kept cool and away from direct sunlight.

Dilutions: If it is necessary to dilute Epilim Syrup, the recommended diluent is Syrup BP, but syrup containing SO₂ as a preservative should not be used. The diluted product will have a 14-day shelf-life.

Legal category POM.

Package quantities Epilim tablets, Epilim 200 enteric-coated and Epilim 500 enteric-coated tablets are packed in foil, in cartons of 100 tablets. Epilim Syrup is packed in 200 ml bottles.

Further information Although the beneficial effects of Epilim may not be clearly correlated with the total plasma valproic acid levels, anticonvulsant activity may be optimal when the percentage of free drug in the plasma is 9–15% of the total level. Above this range an increase in the percentage of the free drug may be associated with a higher incidence of adverse effects.

When plasma valproic acid is within the recommended range of 50–120 mg/litre (350–840 mcg mol/litre) and serum albumin levels are normal, about 90% of the drug is bound to albumin. If the total plasma valproic acid rises above the upper range of normal, or if there is hypoalbuminaemia, the percentage of free valproic acid may rise markedly and in disproportion to any dosage increase.

Facilities for the direct measurement of free valproic acid levels are not readily available, however the amounts of bound and free drug may be calculated approximately by assuming that 1 gram of serum albumin will bind 2 mg of valproate (maximum binding 90%).

Product licence numbers

Epilim 200 enteric-coated tablets	0623/0006
Epilim 500 enteric-coated tablets	0623/0005
Epilim Syrup	0623/0004
Epilim Tablets	0623/0001

OSSOPAN*

Presentation The active ingredient of Ossopan preparations is microcrystalline hydroxyapatite compound (MCHC), which provides calcium, phosphorus and essential trace elements in a protein base. Ossopan powder is pale brown, granular, with an aromatic odour. Each gram of powder contains 820 mg MCHC, providing 176 mg calcium and 82 mg phosphorus. One level 5 ml spoonful contains approximately 4 grams.

Ossopan tablets are yellow, sugar-coated. Each tablet contains 200 mg MCHC, providing 43 mg calcium and 20 mg phosphorus.

Uses Provision of calcium and phosphorus in all defects of skeletal metabolism, including:

- (i) most forms of osteoporosis with or without corticosteroid therapy;
- (ii) osteogenesis imperfecta;
- (iii) rickets and osteomalacia;
- (iv) fractures and conditions requiring orthopaedic surgery; and
- (v) dental conditions associated with mineral disturbances.

Dosage and administration *Ossopan powder:* One to two level 5 ml spoonfuls daily in divided doses with or before food.

Ossopan tablets: Up to 16 tablets daily, to be taken in divided doses, before meals.

Contra-indications, warnings, etc *Contra-indications:* Hypercalcaemia, hypercalciuria.

Precautions: Care should be exercised in patients with severe immobilisation, e.g. paraplegia, and in patients with a history of renal calcium stone formation.

Pharmaceutical precautions Store in a cool, dry place.

Legal category P.

Package quantities *Ossopan powder:* jars containing 50 grams.

Ossopan tablets: packs of 150 and 1,000.

Further information Hydroxyapatite is the complex biological calcium salt which forms the basis of skeletal structure; its overall formula is Ca₁₀(PO₄)₆(OH)₂. MCHC contains about 50 per cent hydroxyapatite, and X-ray diffraction studies have confirmed the presence and microcrystalline nature of the salt. It also contains many essential trace elements together with natural skeletal protein (collagen), substituent amino acids and glycosaminoglycans. Clinical studies suggest that MCHC may be more readily assimilable than synthetic calcium supplements.

Product licence numbers

Ossopan powder: 0376/5001

Ossopan tablets: 0376/5000.

*Trade Mark

Laboratories for Applied Biology Limited

11 Amhurst Park
London N16 5DR



CERUMOL* EAR DROPS

Presentation A clear oily preparation containing p-chlorobenzene BPC (1949) 2% Chlorbutol BP 5%, Oil of Eucalyptus BP 10%.

Uses Occlusion or partial occlusion of external auditory meatus by either a collection of soft wax or a harder wax plug.

Dosage and administration Approximately 5 drops should be instilled into the ear with the head kept inclined for 5 minutes or, better still, with the patient lying down. Should the Cerumol tend to run out when the head is held up again, a small plug of cotton wool moistened with Cerumol could then be applied. Ten to thirty minutes after the softened and disimpacted cerumen can be very easily removed by using a probe tipped with cotton wool or by gentle syringing.

Alternatively, the patient can himself instil the drops as described above) two or three times a day for a few days in order to loosen the wax. In many cases this procedure is sufficient as frequently the wax will run out of its own accord, making further attendance at the surgery unnecessary.

Contra-indications, warnings, etc Otitis externa, eczematous dermatitis and eczema affecting the external ear.

Overdosage: Accidental ingestion although unlikely to occur should not give rise to any clinical disturbance. The amounts of the various ingredients in the 11 ml bottle are too small to give rise to toxic effects.

Pharmaceutical precautions No special storage precautions.

Legal category P

Package quantities 11 ml vial with separate dropper. 5 ml (for hospital use only).

Further information Nil.

Product licence number 0118/0013.

DUROMORPH*

Presentation A long-acting aqueous suspension of morphine in microcrystalline form presented in ampoules each containing 64 mg morphine in 1 ml 1.3% sodium chloride solution. The ampoules are light amber marked ml Duromorph (64 mg morphine) for subcutaneous or intramuscular injection LAB LTD London.

Uses Duromorph is indicated for relief of severe pain in alignment conditions and for post operative analgesia. Sedative, narcotic and analgesic effects are produced within 10–30 minutes and last for up to nine hours.

Dosage and administration The standard dose is ml of Duromorph (64 mg of morphine base). This can

safely be increased to 96 mg where necessary. Administration is by subcutaneous or intramuscular injection. Not intended for administration to children.

Contra-indications, warnings, etc Because of the effect on respiration, caution should be exercised where there is likelihood of hypoxia due to respiratory or cardiac disease, or post operative ventilation difficulty. Also, alcohol, hypnotics, phenothiazines and especially monoamine oxidase inhibitors intensify the depressant effects of morphine on the respiratory centre. Disease of the liver must be taken into consideration since conjugation of the morphine is impaired in hepatic insufficiency.

Overdosage: Treatment is as for morphine, i.e. to maintain respiration and circulation. Oxygen should be administered and assisted ventilation may be necessary. The effective antidote is naloxone hydrochloride 0.4 mg given intravenously which could be repeated at intervals of 2–3 minutes if necessary. In view of the prolonged action of Duromorph such treatment is better sustained with a naloxone infusion: 0.4 mg–2 mg per hour according to response.

Pharmaceutical precautions Protect from heat and light.

Legal category POM; MDA.

Package quantities 10 ampoules containing 1 ml Duromorph (64 mg morphine) per box.

Further information Nil.

Product licence number 0118/5001.

EMESIDE* CAPSULES AND SYRUP

Presentation Soft yellow gelatin capsules each containing 250 mg of Ethosuximide BP.

Blackcurrant or orange-flavoured syrup containing 250 mg of Ethosuximide BP per 5 ml.

Uses Emeside gives selective control of petit-mal either alone or when complicated by grand-mal. The reduction of seizure frequency is thought to be achieved by depression of the motor cortex and elevation of the threshold to convulsive stimuli as seen by the suppression of the characteristic spike and wave EEG pattern. Emeside may be prescribed together with other anticonvulsants such as phenobarbitone, phenytoin, primidone or sodium valproate where grandmal or other forms of epilepsy may require additional treatment.

Dosage and administration *Adults and children over 6 years:* Start with a small dose – 500 mg daily with increments of 250 mg every five to seven days until control is achieved usually with 1,000–1,500 mg (4–6 capsules) daily. Occasionally 2,000 mg daily in divided dose may be necessary.

The half-life of ethosuximide in the plasma is more

than 24 hours but the daily dose if large is more comfortably divided between morning and evening.

If Emeside is being substituted for another anti-epileptic drug the latter must not be withdrawn abruptly but the replacement made gradually with overlap of the preparations otherwise petit mal may break through.

Children and infants under six years: Begin with a daily dose of 250 mg (5 ml syrup) and increase the dose gradually by small increments every few days until control is achieved, the maximum dose should be 1,000 mg.

Plasma levels of ethosuximide to be effective lie between 40 and 85 mcg per ml but the clinical response should be the criterion for regulation of dosage.

Contra-indications, warnings, etc Known hypersensitivity to succinimides. Exercise caution with regular appropriate tests in patients with hepatic or renal disease. Ethosuximide may be excreted into breast milk. There is a recognised small increase in the incidence of congenital malformations in children born to mothers receiving anti-convulsants. For women planning pregnancy or who are already pregnant the risk should be weighed carefully against the benefit of the treatment.

Side Effects: Nausea, vomiting, anorexia and epigastric pain are common at first and generally subside. Unusual symptoms are headache, fatigue, drowsiness, dizziness, ataxia, dyskinesia, hiccup, photophobia, depression and skin rash. Isolated reports have been made of erythema nodosum, erythema multiforme, agranulocytosis and systemic lupus.

Drug Interaction: There is no interaction with other anticonvulsants and no effect on liver enzymes.

Overdosage: Where more than 2 g has been thought to be ingested gastric lavage may be employed, if the time lapse is less than four hours.

Routine observation of respiration and circulation will indicate the need for supportive measures.

Pharmaceutical precautions Store in a cool dry place.

Legal category POM.

Package quantities Capsules: 100 and 500 in aluminium cylinders.

Syrup (blackcurrant or orange flavour): Bottles of 200 ml and 1,000 ml.

Further information Nil.

Product licence numbers

Emeside Capsules	0118/5002
Emeside Syrup orange	0118/5003
Emeside Syrup blackcurrant	0118/5004.

HALYCITROL* VITAMIN EMULSION ▼

Presentation Orange flavoured emulsion containing 27,600 mcg (92,000 iu)/100 ml Vitamin A and 230 mcg (9,200 iu) Vitamin D per 100 ml. This is equivalent to 1380 mcg (4,600 iu) of Vitamin A and 11.5 mcg (460 iu) of Vitamin D in a 5 ml daily dose.

Uses For prevention of Vitamin A and D deficiency.

Dosage and administration Adults and children above 6 months: 5 ml daily.

Infants up to six months: 2 ml daily.

Contra-indications, warnings, etc Prolonged ex-

cessive ingestion of Vitamins A and D can lead to hypervitaminosis states.

Hypervitaminosis A: Symptoms include dry rough skin, painful joint swellings, anorexia and vomiting.

Hypervitaminosis D: Infants already receiving vitamin D from such sources as vitaminised margarine and cereals can develop infantile hypercalcaemia from excessive Vitamin D intake.

In children and adults the symptoms of hypercalcaemia are weakness, anorexia, abdominal pain, constipation, thirst and polyuria with the development of nephrocalcinosis, renal stones and renal failure. Individuals with renal disease and Sarcoidosis are particularly susceptible.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities Bottles of 114 ml.

Further information This is a preparation of fish oil devoid of any fish odour or taste.

Product licence number 0118/0015.

LABITON* TONIC

Presentation A brown liquid containing vitamin B₁ 0.75 mg, dried extract of kola nuts 6.05 mg, alcohol 2.78 ml, caffeine (total) 7 mg, p-aminobenzoic acid 4 mg, Syrup BP 3 g, glycerophosphoric acid (20%) 0.02 ml, caramel 10 mg per 10 ml.

Uses The kola nut contains complex catecholcaffeinates which give central stimulation, increase muscular performance and reduce fatigability. Vitamin B₁ is included to make up deficiency resulting from recent illness or anorexia. Labiton is indicated for use as a tonic for fatigue, anorexia and debility in convalescence after infections such as influenza and after operations.

Dosage and administration 10–20 ml twice daily, before or after meals, with or without water.

Not intended for administration to children.

Contra-indications, warnings, etc Undesirable in cases of hepatitis and patients taking sedatives. Car drivers should be made aware of the presence of alcohol and should be advised not to exceed the recommended dosage, especially if taking tranquilisers or remedies for allergies that have sedative side effects.

Drug interactions: With correct dosage, the alcohol content should give no interaction. With excessive dosage there could be potentiation of CNS depressants and potentiation of the hypoglycaemic effect of insulin.

Overdosage: Treatment is that for alcohol with correction dehydration, attendance to the airway and other supportive measures for coma.

Pharmaceutical precautions Store in a cool place. Use within nine months, after which time sediment may form.

Legal category GSL.

Package quantities Supplied in bottles of 200 ml and 1 litre.

Further information Nil.

Product licence number 0118/5005.

.ABOPHYLLINE*

Presentation Beige tablets embossed 'LAB' containing 100 mg theophylline and 74 mg lysine.

Uses Bronchodilator to prevent or relieve bronchospasm in chronic bronchitis and asthma. As an aid to diuretics in cardiac failure.

Dosage and administration *Adults:* 1–2 tablets three or four times per day.

Children over 6 years old: $\frac{1}{2}$ –1 tablet three times per day. Not intended for administration to children under 6 years old.

Contra-indications, warnings, etc Known hypersensitivity to Xanthene preparations.

The margin between therapeutic and toxic plasma levels of theophylline is small so that overdosage as shown by tachycardia and fall in blood pressure is easily elicited. The concurrent use of ephedrine is best avoided and, similarly, care must be taken with β -adrenergic antagonists and other xanthene drugs especially aminophylline suppositories.

Side-effects of nausea and vomiting are unusual.

Drug Interactions: Erythromycin raises the serum theophylline levels.

Overdosage: The toxic effects of excessive treatment concern the cardiovascular system (tachycardia, hypertension) and the CNS (anxiety, insomnia and agitation). Treatment is symptomatic.

Gastric lavage should be undertaken with single overdosage.

Pharmaceutical precautions Requires cool dry storage.

Legal category P.

Package quantities Bottles containing 100 tablets.

Further information Nil.

Product licence number 0118/5014.

ABOPRIN*

Presentation A round, bi-convex tablet, white with brown flecks, containing 300 mg aspirin and 245 mg lysine.

Uses For the relief of headache, musculo-skeletal pains, arthralgia, pain and inflammation due to rheumatoid and other forms of arthritis.

Dosage and administration 1–2 tablets at a time; possibly repeated in a few hours or as prescribed.

Dosage for children at the physician's discretion.

Contra-indications, warnings, etc Peptic ulcer. Allergy to aspirin. In common with other forms of aspirin there is clinical and epidemiological evidence that it is safe in pregnancy. Drug interaction: there is a potentiation of the action of anticoagulants. Also increased tendency to gastric ulceration if given with non-steroidal anti-inflammatory agents or cortico-steroids. The action of Probenecid is prolonged.

Overdosage: Treatment is that of salicylate poisoning; gastric aspiration and lavage, correction of dehydration and of hypokalaemia; cautious use of sodium bicarbonate or the acidosis; intravenous Vitamin K. If salicylate level exceeds 500 mg/l administer forced alkaline diuresis but greater than 900 mg/l consider haemoperfusion and

haemodialysis. Self-poisoning has been successfully treated by resin or charcoal haemoperfusion.

Pharmaceutical precautions These tablets are extremely hygroscopic. They should be kept in the manufacturer's original container. The inner seal and screw cap should be replaced immediately after use. If discoloration or swelling takes place, the tablets should not be used.

Legal category P.

Package quantities 24 tablets per bottle.

Further information Nil.

Product licence number 0118/5006.

LABOSEPT* PASTILLES

Presentation Hexagonal red pastilles each containing Dequalinium Chloride BP 0.25 mg in a slow dissolving gelatine base.

Uses For bacterial and fungal infections of the mouth and throat.

Dosage and administration *Adults and children:* To be sucked slowly every three or four hours. For maximum benefit pastilles should be lodged comfortably between gum and cheek rather than be chewed. The daily dose should not exceed eight pastilles.

Contra-indications, warnings, etc Side effects and ill-effects from overdosage have not been reported.

Pharmaceutical precautions No special precautions.

Legal category P.

Package quantities Carton containing 20 pastilles.

Further information Contains no sugar.

Product licence number 0118/0012.

MONPHYTOL*

Presentation A colourless, rapidly drying, non-greasy paint containing boric acid 2%, chlorbutol 3%, methyl undecylenate 5%, propyl undecylenate 1%, salicylic acid (free and methyl ester) 31%.

Uses Monphytol is indicated for chronic paronychia, intertrigo, erosio interdigitalis, tinea pedis, tinea circinata, tinea unguium.

Dosage and administration Four times a day, moisten brush with Monphytol and apply to the affected parts, reaching gently into the folds of the skin. Treatment should be repeated from time to time after the condition has subsided to prevent reinfection.

Contra-indications, warnings, etc Monphytol may sting sensitive weeping areas of acutely inflamed skin. Other treatment (to reduce inflammation and exudation) may first be necessary. Although there is only a small amount of boric acid present, caution is advised in the repeated application of Monphytol to extensive areas of the skin.

Pharmaceutical precautions Store away from heat.

Legal category P.

Package quantities Bottles containing 18 ml with brush fitted in cap.

Further information Nil.

Product licence number 0118/5010.

PERNOMOL* CHILBLAIN PAINT

Presentation A quick-drying, colourless solution contained in a small pencil-shaped glass vial with a narrow opening to permit direct application. The solution contains per 100 ml: Chlorbutol BP 2 g, Phenol BP 0.95 g, Camphor BP 10 g, Tannic Acid BP 2.2g, Sp. Sap. Meth. BP 34 ml.

Uses Pernomol is indicated for the treatment of chilblains. The different substances promote vaso-dilatation and give an anaesthetising and soothing effect. Being readily absorbed below the skin surface, Pernomol gives immediate relief of irritation and rapid reduction of the inflammatory swelling.

Dosage and administration Pernomol is applied directly from its container to the affected areas three to four times daily. Pernomol may be applied to chilblains at any stage, including broken chilblains. Early treatment will prevent this complication.

Contra-indications, warnings, etc None known.

Pharmaceutical precautions Protect from light.

Legal category P.

Package quantities Glass vial containing 2½ ml in aluminium tube.

Further information Nil.

Product licence number 0118/5011.

VOLITAL*

Presentation Round white, bi-convex tablets scored and marked P9 and containing 20 mg pemoline.

Uses For treatment of tiredness, lassitude due to stress, or in convalescence after illness or surgery. To combat drowsiness induced by anti-convulsants, antihistamines

and anti-depressants. Pemoline is used in association with amantidine in extra-pyramidal disorders also to treat children with hyperkinetic syndrome or minimal brain dysfunction.

A non-addictive CNS stimulant possibly acting through dopaminergic mechanisms. Pemoline is structurally different from amphetamines, methylphenidate and xanthenes and does not affect the cardiovascular system.

Dosage and administration *Adults:* 1 tablet Volital (20 mg) in the morning. This can be increased to 60 mg daily given as 2 tablets in the morning and 1 in the afternoon.

Children over 6 years: ½–1 tablet morning and again in the afternoon.

Contra-indications, warnings, etc Nervousness and tachycardia may result from large doses. The drug should not be given in the evening, otherwise insomnia is likely to occur.

The safe use of pemoline during pregnancy has not been established and therefore the physician must use his judgement in prescribing it.

Side Effects: With prolonged use in children, anorexia and loss of weight have been reported. Other symptoms such as dizziness or headache seem to have been just as common as the placebo in reported trials.

Overdosage: Acute accidental overdosage has been reported in a child who became overactive and had choreiform movements. Pulse rate and blood pressure were unaffected and recovery took place in 48 hours.

Treatment with diazepam and fluids intravenously may be needed.

Pharmaceutical precautions To be kept cool and dry.

Legal category POM.

Package quantities Glass tubes containing 25 tablets. Plastic bottles containing 500 tablets.

Further information Nil.

Product licence number 0118/5012.

*Trade Mark

Lederle Laboratories

(A Division of Cyanamid of
Great Britain Limited) Fareham Road
Gosport, Hants PO13 0AS



ABSTEM*

Presentation Tablets 50 mg. Each white tablet contains 50 mg citrated calcium carbimide.

Uses Abstem acts by interfering with the metabolic oxidation of alcohol. It is indicated as an adjunct in the treatment of alcoholism.

Dosage and administration *Adults:* 1 tablet once or twice daily. This is usually taken in the morning and the second dose 12 hours later. It is not recommended for administration to children.

Contra-indications, warnings, etc

Contra-indications: Abstem should not be given to a patient in a state of intoxication.

Precautions: Abstem should be used with caution in patients with myocardial or coronary artery disease.

In cases of severe reaction or idiosyncrasy, discontinue the drug and take appropriate measures such as oxygen by mask or antihistamines intravenously.

Patients on long-term therapy should be watched for hypothyroidism as depression of thyroid function has been noted in some patients.

Patients should be made aware that certain medicines and household items such as cider vinegar, salad dressings contain alcohol and ingestion of these substances together with Abstem may cause the typical Abstem-alcohol reaction.

Concomitant administration of paraldehyde may precipitate the symptoms of an Abstem-alcohol reaction, and concurrent use of metronidazole may exacerbate an Abstem-alcohol reaction.

Side-effects: Drowsiness, fatigue, rash, tinnitus, impotence or frequent micturition may occur in some patients. An increase in white cell count has been noted during therapy with Abstem, but the count returns to pre-treatment level when the therapy is discontinued.

Overdosage: No specific antidote. Normal supportive measures should be taken.

Pharmaceutical precautions The product should be stored at room temperature in containers which prevent access of moisture.

Legal category POM.

Package quantities Bottles of 100.

Further information Nil.

Product licence number 0095/5049.

ACHROMYCIN* (ORAL PREPARATIONS)

Presentation *Capsules 250 mg:* Each opaque, orange capsule printed 'Lederle 4874' contains 250 mg tetracycline hydrochloride.

Tablets 250 mg: Each orange tablet printed 'Lederle 1745' contains 250 mg tetracycline hydrochloride.

Syrup 125 mg/5 ml: Each 5 ml of cherry-red suspension contains tetracycline equivalent to tetracycline hydrochloride 125 mg.

Powder 25 g: Each bottle contains 25 g tetracycline hydrochloride.

Uses Achromycin is a broad-spectrum antibiotic used for the treatment of infections caused by tetracycline-sensitive organisms. Typical indications include: Ear, nose and throat infections. Acute and chronic bronchitis. Pneumonia. Venereal Diseases. Non-Gonococcal Urethritis. Gastro-intestinal Infections. Urinary tract infections. Soft tissue infections. Acne. Typhus fever. Psittacosis. Other infections due to Achromycin-sensitive organisms. Achromycin is also indicated for prophylaxis before or after surgical and dental procedures.

Dosage and administration *Adults: (tablets, capsules):* 1 tablet or capsule four times a day. This may be increased to 6 or 8 tablets or capsules daily in severe infections.

Children: 20–40 mg/kg daily in divided doses. A table of suggested dosages for children is given at the foot of the page.

Administration: Achromycin should be taken an hour before or two hours after meals and therapy should be continued for up to three days after characteristic symptoms of the infection have subsided.

Contra-indications, warnings, etc

Contra-indications: A history of hypersensitivity to tetracyclines. Overt renal insufficiency. Systemic lupus erythematosus.

Warnings: Tetracyclines may cause a yellow to brown discoloration of the teeth in the developing foetus or child and therefore Achromycin should only be administered if considered essential to pregnant women and young children under eight years of age. Achromycin should be used with caution in patients with renal or hepatic dysfunction, or in conjunction with other potentially hepatotoxic drugs. Cross-resistance between tetracyclines may develop in micro-organisms and cross-sensitisation in patients.

Precautions: Absorption of Achromycin is impaired by the concomitant administration of calcium, magnesium, iron and particularly aluminium salts commonly used as

Syrup 125 mg/5 ml

Age (years)	Weight lb	Weight kg	Suggested total mg per day	Suggested daily dose
2–4	28–37	12.7–16.8	280–370	5 ml three times
5–7	41–49	18.6–22.2	410–490	5 ml four times
8–9	55–61	25.0–27.7	550–610	5 ml five times
10–12	67–79	30.4–35.8	670–790	10 ml three times
Adults			1,000	10 ml four times

antacids. Tetracyclines depress plasma prothrombin activity therefore reduced dosages of concurrent anti-coagulants may be required. Lower doses are indicated in cases of renal impairment to avoid excessive systemic accumulation, and if therapy is prolonged, serum level determinations are advisable.

Side-effects: Gastro-intestinal disturbances may occur and as with all antibiotics overgrowth of resistant organisms may cause glossitis, stomatitis, vaginitis, or staphylococcal enterocolitis. Photosensitivity and dermatological reactions are rare. Occurrences of enamel hypoplasia have been reported. Rarely increased intracranial pressure with bulging fontanelles, has been observed in infants which disappears rapidly upon cessation of treatment.

Overdosage: No specific antidote. Gastric lavage plus oral administration of milk or antacids.

Pharmaceutical precautions The products should be stored at room temperature (except Achromycin syrup which should be stored in a cool place) in either the original pack or in containers which prevent access of light and moisture.

Achromycin Syrup may be diluted with Syrup BP, provided the dilution is freshly prepared and not used after more than two weeks.

Legal category POM.

Package quantities Capsules 250 mg: Bottles of 20, 100 and 1,000.

Tablets 250 mg: Bottles of 100 and 1,000.

Syrup 125 mg/5 ml: Bottles of 100 ml and 500 ml.

Powder: Bottle of 25 g.

Further information Achromycin Syrup contains 0.181 millimoles of sodium per 5 ml

Product licence numbers

Capsules 250 mg 0095/0041

Tablets 250 mg 0095/5026

Syrup 125 mg/5 ml 0095/5027

Powder 0095/5037

ACHROMYCIN* (TOPICAL PREPARATIONS)

Presentation Achromycin Ointment 3%: Each gram of yellow ointment contains tetracycline hydrochloride 30 mg, methylparaben 2.4%, propylparaben 0.6%, in a white soft paraffin and wool-fat base.

Achromycin Eye and Ear Ointment 1%: Each gram of yellow ointment contains 10 mg tetracycline hydrochloride in a white soft paraffin and wool-fat base.

Achromycin Ophthalmic Oil Suspension 1%: Each millilitre of yellow oily suspension contains 10 mg tetracycline hydrochloride in a vehicle of sesame oil.

Uses Achromycin is a broad-spectrum antibiotic.

Achromycin Ointment 3% is indicated for the treatment of superficial pyogenic infections of the skin and for the prevention of infection in wounds, abrasions and after surgery. It is indicated for local infections caused by both Gram-positive and Gram-negative organisms including Streptococci, Staphylococci and the Coli-aerogenes group.

Achromycin Eye and Ear Ointment and Achromycin Ophthalmic Oil Suspension are indicated for the treatment of susceptible ocular infections caused by Staphylococci, Pneumococci, H. influenzae, Diplococcus of Morax-Axenfeld (*H. lacunatus*), Streptococci, A. aero-

genes, Proteus vulgaris, Proteus morganii, E. coli, Alcaligenes faecalis and Pseudomonas aeruginosa.

Achromycin Eye and Ear Ointment is also indicated in the treatment of external otitis due to tetracycline-susceptible organisms.

Dosage and administration Adults and children: Achromycin Ointment 3%: Apply the ointment directly to the involved area, preferably on sterile gauze once or more daily as the condition indicates. In severe local infections, local treatment should be supplemented by oral therapy.

Achromycin Eye and Ear Ointment 1%: Apply directly to the affected area every two hours. Severe ocular infections may require treatment for many days, and may also require oral therapy.

Achromycin Ophthalmic Oil Suspension 1%: In most bacterial infections gently squeeze the plastic dropper bottle to instil 1 or 2 drops in the affected eye, two to four times daily, or more often if the severity of the infection merits this. Chronic trachoma may require extensive treatment (one to two months).

Contra-indications, warnings, etc

Contra-indications: Achromycin Ointment, Achromycin Eye and Ear Ointment, and Achromycin Ophthalmic Oil Suspension are contra-indicated in patients with a history of hypersensitivity to tetracycline hydrochloride or any other ingredient.

Precautions: The use of antibiotics may result in overgrowth of non-susceptible organisms. Constant observation of the patient is essential. If new infections appear during therapy, appropriate measures should be taken.

Side-effects: Some patients may be allergic to any of the components.

If adverse reaction or idiosyncrasy occurs, discontinue medication.

Pharmaceutical precautions The products should be stored in a cool place in the original pack. Dilution is not recommended.

Achromycin Ointment may cause a yellow staining of clothes. Following extended use a similar local staining of the skin may occur which disappears on cessation of treatment.

Legal category POM.

Package quantities Achromycin Ointment 3%: Tubes of 30 g.

Achromycin Eye and Ear Ointment 1%: Tubes of 3.5 g.

Achromycin Ophthalmic Oil Suspension 1%: Plastic dropper bottle containing 6 ml.

Further information Nil.

Product licence numbers

Achromycin Ointment 3% 0095/5031

Achromycin Eye and Ear Ointment 0095/5032

Achromycin Ophthalmic Oil Suspension 0095/5033

ACHROMYCIN* INTRAMUSCULAR

Presentation Achromycin Intramuscular 100 mg. Each vial contains:

Tetracycline hydrochloride	100 mg
Procaine hydrochloride	40 mg
Magnesium chloride	46.84 mg
Ascorbic acid	250 mg

Uses Achromycin is a broad spectrum antibiotic indicated alone or adjunctively in the treatment of infections caused by tetracycline-sensitive organisms, and for prophylaxis before or after dental and surgical procedures.

For example, Achromycin is highly effective in the treatment of infections caused by *Borrelia recurrentis* (relapsing fever), *Calymmatobacterium granulatis* (granuloma inguinale), *Chlamydia* species (psittacosis, lymphogranuloma venereum, trachoma, inclusion conjunctivitis), *Francisella tularensis* (tularemia), *Haemophilus ducreyi* (chancroid), *Leptospira* (meningitis, jaundice), *Mycoplasma pneumoniae* (non-gonococcal urethritis), *Pseudomonas mallei* and *pseudomallei* (glanders and melioidosis), *Rickettsiae* (typhus fever, Q fever, rocky mountain spotted fever), *Vibrio* species (cholera). It is also highly effective alone or in combination with streptomycin, in the treatment of infections due to *Brucella* species (brucellosis), and *Yersinia pestis* (bubonic plague).

Other sensitive organisms include: *Actinomyces israelii*, *Bacillus anthracis* (pneumonia), *Bordetella pertussis* (whooping cough), *Clostridium* species (gas gangrene, tetanus), *Entamoeba histolytica* (dysentery), *Haemophilus influenzae* (pharyngitis, otitis media), *Listeria monocytogenes* (bacteraemia), *Neisseria gonorrhoeae*, *Shigella* species (acute gastroenteritis), *Streptococcus pyogenes*, *pneumoniae* and anaerobic species, *Treponema pallidum* and *pertenue* (syphilis and yaws).

Dosage and administration *Adults:* By intramuscular injection only.

100 mg two or three times a day. In severe infections 100 mg every four to six hours.

Children: 10 mg per kg of body weight per day, in divided doses, by intramuscular injection.

Administration: Dissolve the contents of each vial, immediately before use, by the addition of 2 ml of Water for Injection. The appropriate dose of the resulting solution (50 mg/ml) should be injected deeply into the gluteal region.

Oral Achromycin medication should replace parenteral as soon as practical, and be continued for up to three days after characteristic symptoms of the infection have subsided. Streptococcal infections should be treated for 10 days to prevent the development of rheumatic fever or glomerulonephritis, and acute staphylococcal infections for 10–14 days.

Contra-indications, warnings, etc

Contra-indications: Known hypersensitivity to tetracyclines or procaine hydrochloride. Overt renal insufficiency. Systemic lupus erythematosus.

Precautions: Achromycin may cause a yellow to brown discoloration of the teeth in the developing foetus or child and therefore should only be administered if considered essential to pregnant women and young children under eight years of age. Achromycin should be used with caution in patients with renal or hepatic dysfunction or in conjunction with other potentially hepatotoxic drugs. Lower doses are indicated in cases of renal impairment to avoid excessive systemic accumulation, and, if therapy is prolonged, serum level determinations are advisable. Patients who are pregnant or who have known liver disease should not receive more than 1 g daily. Tetracyclines depress plasma prothrombin activity therefore reduced dosages of concurrent anticoagulants may be required. Concurrent use with the

anaesthetic methoxyflurane increases the risk of kidney failure.

Warnings and adverse effects: As with all antibiotics, overgrowth of resistant or non-susceptible organisms may occur. Excessive systemic accumulation, due to renal impairment or other reasons, will cause a rise in blood urea nitrogen leading to uraemia, hyperphosphataemia and acidosis. Rarely, increased intracranial pressure with bulging fontanelles has been observed in infants which disappears rapidly upon cessation of treatment. Enamel hypoplasia has been reported.

Cross-resistance between tetracyclines may develop in micro-organisms, and cross-sensitisation in patients.

Overdosage: No specific antidote. Use appropriate supportive treatment.

Pharmaceutical precautions No special handling or storage requirements are necessary. The increase in injection volume, caused by displacement, during dissolution of the powder with 2 ml of Water for Injection, is clinically insignificant when calculating dosage and volume to be injected. The brown appearance of the vial is produced when the injection is sterilised by irradiation and does not indicate any degradation.

Legal category POM.

Package quantities 6 × 100 mg vials.

Further information Nil.

Product licence number 0095/5033.

ACHROMYCIN* INTRAVENOUS

Presentation Achromycin Intravenous 250 mg and 500 mg. Each vial contains tetracycline hydrochloride 250 mg or 500 mg buffered with 625 mg or 1,250 mg of ascorbic acid respectively.

Uses

1. Achromycin is a broad spectrum antibiotic indicated alone or adjunctively in the treatment of infections caused by tetracycline-sensitive organisms, and for prophylaxis before or after dental and surgical procedures.

For example, Achromycin is highly effective in the treatment of infections caused by *Borrelia recurrentis* (relapsing fever), *Calymmatobacterium granulatis* (granuloma inguinale), *Chlamydia* species (psittacosis, lymphogranuloma venereum, trachoma, inclusion conjunctivitis), *Francisella tularensis* (tularemia), *Haemophilus ducreyi* (chancroid), *Leptospira* (meningitis, jaundice), *Mycoplasma pneumoniae* (non-gonococcal urethritis), *Pseudomonas mallei* and *pseudomallei* (glanders and melioidosis), *Rickettsiae* (typhus fever, Q fever, rocky mountain spotted fever), *Vibrio* species (cholera). It is also highly effective, alone or in combination with streptomycin, in the treatment of infections due to *Brucella* species (brucellosis), and *Yersinia pestis* (bubonic plague).

Other sensitive organisms include: *Actinomyces israelii*, *Bacillus anthracis* (pneumonia), *Bordetella pertussis* (whooping cough), *Clostridium* species (gas gangrene, tetanus), *Entamoeba histolytica* (dysentery), *Haemophilus influenzae* (pharyngitis, otitis media), *Listeria monocytogenes* (bacteraemia), *Neisseria gonorrhoeae*, *Shigella* species (acute gastroenteritis), *Streptococcus pyogenes*, *pneumoniae*, and anaerobic species, *Treponema pallidum* and *pertenue* (syphilis and yaws).

2. The treatment of recurrent pleural effusions, secondary to neoplastic disease or end stage cirrhosis, by intrapleural administration.

Dosage and administration

1. *For Antibiotic use by Intravenous Infusion: Adults:* 500 mg every 12 hours by intravenous infusion. Maximum daily dosage should not exceed 2 g.

Children: Up to 10 mg/kg body weight per day in divided doses by intravenous infusion.

Administration: Achromycin should be reconstituted and diluted immediately before administration by intravenous infusion. The use of a terminal filter (suitable pore size 0.22 micron) in line with the IV giving set is recommended. Reconstitute the injection by adding 5 ml of Water for Injection to the 250 mg vial (or 10 ml of Water for Injection to the 500 mg vial) and then dilute the resulting solution (50 mg/ml) to at least 100 ml (up to 1,000 ml) with any of the following diluents immediately before administration by intravenous infusion at a rate not exceeding 100 ml in five minutes: Sodium Chloride Injection BP 0.9%, Dextrose Injection BP, Sodium Chloride and Dextrose Injection BP, Sodium Lactate Compound Injection BP.

Oral Achromycin medication should replace parenteral as soon as practical, and be continued for up to three days after characteristic symptoms of the infection have subsided. Streptococcal infections should be treated for 10 days, to prevent the development of rheumatic fever or glomerulonephritis, and acute staphylococcal infections for 10–14 days.

2. *For Pleural Effusions by Intrapleural Administration: Adults:* A single dose of 500 mg by intrapleural administration.

Administration: The pleural space should first be completely drained with a thoracostomy tube which should be positioned to give optimum drainage. 500 mg of Achromycin in 30–50 ml of sterile saline is then instilled through the tube into the pleural space followed by flushing of the thoracostomy tube with more saline. The patient's position must then be altered frequently to ensure contact of the Achromycin with both the visceral and parietal pleural surfaces. It is recommended that initially the patient should be rotated to the left and right lateral decubitus, prone and supine positions for intervals of 2–3 minutes and then left in each of these positions for 30 minutes with the tube clamped. The thoracostomy tube should then be reconnected to negative pressure and the tube removed when drainage is complete or minimal. This can take up to 48–72 hours.

This procedure has been reported to produce pleural symphysis in up to 90% of cases.

Contra-indications, warnings, etc

Contra-indications: Known hypersensitivity to tetracyclines. Overt renal insufficiency. Systemic lupus erythematosus.

Precautions: Achromycin may cause a yellow to brown discoloration of the teeth in the developing foetus or child and therefore should only be administered if considered essential to pregnant women and young children under eight years of age. Achromycin should be used with caution in patients with renal or hepatic dysfunction or in conjunction with other potentially hepatotoxic drugs. Lower doses are indicated in cases of renal impairment to avoid excessive systemic accumulation, and, if therapy is prolonged, serum level determinations are advisable. Patients who are pregnant or who

have known liver disease should not receive more than 1 g daily. Tetracyclines depress plasma prothrombin activity therefore reduced dosages of concurrent anticoagulants may be required. Concurrent use with the anaesthetic methoxyflurane increases the risk of kidney failure.

Warnings and adverse effects: As with all antibiotics, overgrowth of resistant or non-susceptible organisms may occur. Excessive systemic accumulation, due to renal impairment or other reasons, will cause a rise in blood urea nitrogen leading to uraemia, hyperphosphataemia and acidosis. Rarely, increased intracranial pressure with bulging fontanelles has been observed in infants which disappears rapidly upon cessation of treatment. Enamel hypoplasia has been reported. Cross-resistance between tetracyclines may develop in micro-organisms, and cross-sensitisation in patients.

Intrapleural administration may be associated with transient local pain (which can be controlled by analgesics) and/or pyrexia.

Overdosage: No specific antidote. Use appropriate supportive treatment.

Pharmaceutical precautions No special handling or storage requirements are necessary. The increase in injection volume, caused by displacement, during dissolution of the powder with Water for Injection, is clinically insignificant when calculating dosage and volume to be injected. The brown appearance of the vial is produced when the injection is sterilised by irradiation and does not indicate any degradation.

The following substances are incompatible in solution with Achromycin Intravenous, and should not be administered in the same drip:

Aminophylline, amphotericin, barbiturates, cephalothin, chloramphenicol, chlorothiazide, chlorpromazine, cyanocobalamin, dimenhydrinate, erythromycin, heparin, hydrocortisone, methicillin, methohexitone, methyl-dopa, nitrofurantoin, novobiocin, penicillins, phenytoin, polymixin B, prochlorperazine, riboflavin, sodium bicarbonate, sulphadiazine, sulphafurazole, thiopentone sodium, vitamin B complex, warfarin, various inorganic ions (Ca, Mg, Al, Mn, Fe) and donor blood.

Note: The use of solutions containing calcium should be avoided as these tend to form precipitates (especially in neutral to alkaline solution) and therefore should not be used unless necessary. However, Sodium Lactate Compound Injection BP may be used with caution since the calcium ion content in this diluent does not normally precipitate tetracycline in an acid medium.

Legal category POM.

Package quantities *Achromycin Intravenous*
250 mg: 6 × 250 mg vials.

Achromycin Intravenous 500 mg: 6 × 500 mg vials.

Further information Nil.

Product licence numbers

Achromycin Intravenous 250 mg 0095/5034

Achromycin Intravenous 500 mg 0095/5035

ACHROMYCIN* V

Presentation *Capsules* 250 mg: Each pink capsule, printed 'Lederle 4885', contains tetracycline equivalent to 250 mg of tetracycline hydrochloride buffered with sodium metaphosphate.

Syrup 125 mg/5 ml: Each 5 ml of rose-red suspension contains tetracycline equivalent to 125 mg of tetracycline.

line hydrochloride buffered with citric acid and sodium citrate.

Uses Achromycin V is a broad-spectrum antibiotic used for the treatment of infections caused by tetracycline-sensitive organisms. Typical indications include: Ear, nose and throat infections. Acute and chronic bronchitis. Pneumonia. Venereal Diseases. Non-Gonococcal Urethritis. Gastro-intestinal Infections. Urinary tract infections. Soft tissue infections. Acne. Typhus fever. Psittacosis. Other infections due to Achromycin-sensitive organisms. Achromycin V is also indicated for prophylaxis before or after surgical and dental procedures.

Dosage and administration *Adults:* Capsules: 1 capsule four times a day. This may be increased to 6 or 8 capsules daily in severe infections.

Syrup: 10–20 ml two to four times daily.

Children: 20–40 mg/kg daily in divided doses. A table of suggested dosages for children is given below.

Syrup: 125 mg per 5 ml

Age (years)	Weight (kg)	Total mg/day	Suggested daily dosage
5–9	20–30	500–800	5–7.5 ml four times
9–15	35–40	800–1,000	7.5–10 ml four times
	45	1,000	10 ml four times
Adult	—	1,000–2,000	10–20 ml two to four times

Administration: Achromycin V should be taken an hour before or two hours after meals and therapy should be continued for up to three days after characteristic symptoms of the infection have subsided.

Contra-indications, warnings, etc

Contra-indications: A history of hypersensitivity to tetracyclines. Overt renal insufficiency. Systemic lupus erythematosus.

Warnings: Tetracyclines may cause a yellow to brown discoloration of the teeth in the developing foetus or child and therefore Achromycin V should only be administered if considered essential to pregnant women and young children under eight years of age. Achromycin V should be used with caution in patients with renal or hepatic dysfunction, or in conjunction with other potentially hepatotoxic drugs. Cross-resistance between tetracyclines may develop in micro-organisms and cross-sensitisation in patients.

Precautions: Absorption of Achromycin V is impaired by the concomitant administration of calcium, magnesium, iron and particularly aluminium salts commonly used as antacids. Tetracyclines depress plasma prothrombin activity therefore reduced dosages of concurrent anticoagulants may be required. Lower doses are indicated in cases of renal impairment to avoid excessive systemic accumulation, and if therapy is prolonged, serum level determinations are advisable.

Side-effects: Gastro-intestinal disturbances may occur and as with all antibiotics overgrowth of resistant organisms may cause glossitis, stomatitis, vaginitis, or staphylococcal enterocolitis. Photosensitivity and dermatological reactions are rare. Occurrences of enamel hypoplasia have been reported. Rarely increased intracranial pressure with bulging fontanelles has been observed in infants which disappears rapidly upon cessation of treatment.

Overdosage: No specific antidote. Gastric lavage plus oral administration of milk or antacids.

Pharmaceutical precautions Achromycin V capsules should be stored at room temperature. Achromycin V Syrup should be stored in a cool place in either the original pack or in containers which will prevent access of light or moisture.

Dilution of Achromycin V Syrup is not recommended as it will affect the stability of the product.

Legal category POM.

Package quantities Capsules 250 mg: Bottles of 20, 100 and 1,000.

Syrup 125 mg/5 ml: Bottles of 100 ml and 500 ml.

Further information Achromycin V Syrup contains 1.169 millimoles of sodium per 5 ml.

Product licence numbers

Capsules 250 mg 0095/0061

Syrup 125 mg/5 ml 0095/5067

AQUAMOX*

Presentation Tablets. Each white tablet coded 'Lederle 4458' contains quinethazone 50 mg.

Uses Aquamox is a non-mercurial diuretic agent. It is indicated as adjunctive therapy in oedema associated with congestive heart failure, hepatic cirrhosis, and corticosteroid and oestrogen therapy. Aquamox has also been found useful in oedema due to various forms of renal dysfunction such as nephrotic syndrome; acute glomerulonephritis, and chronic renal failure. Aquamox is indicated in severe oedema when due to pregnancy (see 'Contra-indications' and 'Precautions').

Diuretics are indicated in the management of hypertension either as the sole therapeutic agent or to enhance the effect of other antihypertensive drugs in the more severe forms of hypertension and in the control of hypertension in pregnancy.

Aquamox is also indicated in toxæmia of pregnancy (eclampsia); angina due to congestive heart failure and/or hypertension, and 'drug-induced' oedema.

Dosage and administration *Average adult dosage:* One or two 50 mg tablets, orally, once a day. Because of its relatively prolonged duration of activity, a single daily dose is generally sufficient. Occasionally 1 tablet (50 mg) is administered twice a day. Infrequently, a total daily dose of 3–4 tablets (150–200 mg) may be necessary. The dosage employed depends upon the severity of the condition being treated and the responsiveness of the patient, and often must be adjusted at the beginning or during the course of therapy. When Aquamox is used in combination with other antihypertensive agents, the dosage of each drug may often be reduced because of potentiation. Aquamox is not recommended for administration to children.

Contra-indications, warnings, etc

Contra-indications: Aquamox is contra-indicated in:

- Anuria.
- Hypersensitivity to this and other sulphonamide derived drugs.
- Progressively impaired renal function.
- The routine use in otherwise healthy pregnant women with or without mild oedema.

Precautions: Available information tends to implicate

enteric-coated potassium salts with or without thiazides in the etiology of non-specific small bowel lesions consisting of ulceration with or without stenosis, causing obstruction, haemorrhage and perforation and frequently requiring surgery. Deaths due to these complications have been reported. Enteric-coated potassium salts should be used only when adequate dietary supplementation is not practical and should be discontinued immediately if abdominal pain, distension, nausea, vomiting or gastro-intestinal bleeding occur. Aquamox itself does not contain enteric-coated potassium.

Usage of Aquamox in women of childbearing age requires that the potential benefit of the drug be weighed against its possible hazards to the foetus. These hazards include jaundice, thrombocytopenia and possibly other adverse reactions which have occurred in the adult.

Aquamox should be used with caution in patients with impaired hepatic function or progressive liver disease since minor alterations of fluid and electrolyte balance may precipitate hepatic coma.

Whereas electrolyte abnormalities are often present in conditions such as heart failure and cirrhosis as a result of underlying disease process, they may also be aggravated or may be produced independently by any potent diuretic affecting electrolyte excretion. Caution is especially important during prolonged or intensive therapy and when salt intake is restricted or during concomitant use of steroids or ACTH. Hypokalaemia attributable to Aquamox therapy has been mild and infrequent, and other electrolyte abnormalities have been rare.

The possibility of potassium depletion and its toxic results must be kept in mind, particularly in cirrhotics and patients receiving digitalis. As a preventive measure, the use of foods rich in potassium, such as orange juice, or supplements of potassium chloride may be desirable.

In patients with impaired renal function, azotaemia and/or excessive drug accumulation may occur.

When Aquamox is added to a regimen that includes ganglionic blocking agents, the dosage of these latter preparations should be reduced to avoid a sudden drop in blood pressure. Reduction of dosage is also necessary when one or more of these antihypertensive agents is added to an established Aquamox regimen.

Increases of serum uric acid may occur, but precipitation of gout has been rare.

A decreased glucose tolerance as evidenced by hyperglycaemia and glycosuria thus aggravating or provoking diabetes mellitus has occurred.

Aquamox may decrease arterial responsiveness to noradrenaline and therefore should be withdrawn 48 hours before elective surgery. If emergency surgery is indicated, pre-anaesthetic and anaesthetic agents should be administered in reduced dosage. Aquamox may also increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the post-sympathectomy patient.

Sensitivity reactions may be more likely to occur in patients with a history of allergy or bronchial asthma.

The possibility of exacerbation or activation of systemic lupus erythematosus has been suggested for sulphonamide derived drugs.

Side-effects: The following adverse reactions have been reported with diuretic drugs and some may be expected to occur with Aquamox.

Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhoea, constipation, jaundice, pancreatitis, hyperglycaemia, glycosuria, dizziness, vertigo, paraesthesias, headache, xanthopsia, leukopenia, thrombo-

cytopenia, agranulocytosis, aplastic anaemia, purpura photosensitivity, rash, urticaria, necrotising angitis. Orthostatic hypotension may occur and be potentiated by alcohol, barbiturates or narcotics.

Muscle spasm, weakness, restlessness.

Overdosage: No specific treatment. Rapid evacuation of stomach and general supportive measures.

Pharmaceutical precautions The product should be stored at room temperature in either the original pack or in containers which prevent access of moisture.

Legal category POM.

Package quantities Bottles of 100.

Further information Nil.

Product licence number 0095/5052.

ARTANE* TABLETS

Presentation *Tablets 2 mg:* Each white scored tablet coded 'Lederle 4434' contains benzhexol hydrochloride 2 mg.

Tablets 5 mg: Each white scored tablet coded 'Lederle 4436' contains benzhexol hydrochloride 5 mg.

Uses Artane is an antispasmodic drug which exerts a direct inhibitory effect on the parasympathetic nervous system. It also has a relaxing effect on smooth muscle.

It is indicated in all forms of Parkinsonism – post-encephalitic, arteriosclerotic and idiopathic – as well as to prevent and control extrapyramidal disorders due to central nervous system drugs such as reserpine and the phenothiazines. These disorders include tremor, rigidity and increased salivation as commonly encountered in Parkinson's disease; akathisia manifested by extreme restlessness; and dyskinesia characterised by spastic contractions and involuntary movements.

Artane is especially effective in reducing the rigidity or muscle spasm and is useful in relieving the depressor and mental inertia characteristic of this syndrome. It decreases sialorrhoea and is a particularly valuable adjunct in the treatment of arteriosclerotic Parkinsonism.

Dosage and administration *Adults only:* Optimal dosage should always be determined empirically, usually by initiating therapy at a relatively low level and by subsequent graduated increments. Patients over 65 years of age tend to be relatively more sensitive and require smaller amounts of the drug.

Normal dosage for Parkinsonism is 6–10 mg per day although some patients chiefly in the post-encephalitic group may require an average total dose of 12–15 mg daily. It should be given orally either three or four times a day at mealtimes. The total daily milligram dose may be replaced by the slow release Artane Sustets.

Normal dosage for drug-induced Parkinsonism is usually between 5 mg and 15 mg per day, although some cases have been controlled by 1 mg daily.

In all cases, Artane dosage should be increased or decreased only by small increments over a period of several days. In initial therapy the dose should be 1 mg the first day, 2 mg the second day with further increase of 2 mg per day at three to five-day intervals until the optimum dose is reached.

If patients are already being treated with other parasympathetic inhibitors, Artane should be substituted as part of the therapy.

Artane may be taken before or after meals according to the way the patient reacts. If Artane tends to dry the mouth excessively, it may be better to take it before meals, unless it causes nausea. If taken after meals, induced thirst can be allayed by peppermint, chewing gum or water.

Contra-indications, warnings, etc

Precautions: Since the use of Artane must, of necessity, continue indefinitely, the patient should be under careful observation over the long term. It should be administered with care to avoid allergic or other untoward reactions.

Incipient glaucoma may be precipitated by parasympatholytic drugs such as Artane.

Hypertension, cardiac, liver or kidney disorders are not contra-indications, but such patients should be followed closely.

Artane should be used with caution in patients with glaucoma, obstructive disease of the gastro-intestinal or genito-urinary tracts, and in elderly males with possible prostatic hypertrophy.

Side-effects: Minor side-effects such as dryness of mouth, blurring of vision, dizziness, mild nausea or nervousness will be experienced by 30–50% of all patients. These reactions tend to become less pronounced as treatment continues.

Patients with arteriosclerosis or with a history of other drug idiosyncrasies may exhibit reactions of mental confusion, agitation, or nausea and vomiting. Such patients should be allowed to develop a tolerance using the smaller initial dose, with gradual increases until the effective level is reached.

Overdosage: No specific antidote. Gastric lavage, emetic, high enema. Usual general treatment plus cold compresses and forcing of fluid are mandatory. Atropine antagonists may be useful.

Pharmaceutical precautions The products should be stored at room temperature in either the original pack or in containers which prevent the access of moisture.

Legal category POM.

Package quantities *Artane Tablets 2 mg:* Bottles of 100, 1,000 and 5,000.

Artane Tablets 5 mg: Bottles of 100, 1,000 and 5,000.

Further information Nil.

Product licence numbers

Artane Tablets 2 mg 0095/5041

Artane Tablets 5 mg 0095/5042

ARTANE* SUSTETS*

Presentation Each aquamarine, transparent ovoid gelatine capsule, printed A14, contains benzhexol hydrochloride 5 mg in a sustained release formulation. The preparation has been specially compounded to release 1.25 mg of benzhexol hydrochloride immediately and the remaining 3.75 mg gradually over a period of 6–8 hours.

Uses Artane is an antispasmodic drug which exerts a direct inhibitory effect on the parasympathetic nervous system. It also has a relaxing effect on smooth muscle.

It is indicated in all forms of Parkinsonism – post-encephalitic, arteriosclerotic and idiopathic – as well as to prevent and control extrapyramidal disorders due to central nervous system drugs such as reserpine and the

phenothiazines. These disorders include tremor, rigidity and increased salivation as commonly encountered in Parkinson's disease; akathisia manifested by extreme restlessness; and dyskinesia characterised by spastic contractions and involuntary movements.

Artane is especially effective in reducing the rigidity of muscle spasm and is useful in relieving the depression and mental inertia characteristic of this syndrome. It decreases sialorrhoea and is a particularly valuable adjunct in the treatment of arteriosclerotic Parkinsonism.

Dosage and administration *Adults only:* One to three capsules daily as a single dose in the morning, or in divided doses, depending upon the stabilising dose required.

The stabilising dose may be determined by treatment with Artane Tablets, whose dosage should be increased or decreased only by small increments over a period of several days. In initial therapy the dose should be 1 mg the first day, 2 mg the second day with further increases of 2 mg per day at three to five-day intervals until the optimum dose is reached.

The optimum daily dose can then be administered in a once daily dosage regime with Sustets.

If patients are already being treated with other parasympathetic inhibitors, Artane should be substituted as part of the therapy. Artane may be taken before or after meals according to the way the patient reacts. If Artane tends to dry the mouth excessively, it may be better to take it before meals, unless it causes nausea. If taken after meals, induced thirst can be allayed by peppermint, chewing gum or water.

Contra-indications, warnings, etc *Precautions:* Since the use of Artane Sustets must, of necessity, continue indefinitely, the patient should be under careful observation over the long term. It should be administered with care to avoid allergic or other untoward reactions.

Incipient glaucoma may be precipitated by parasympatholytic drugs such as Artane Sustets.

Hypertension, cardiac, liver or kidney disorders are not contra-indications, but such patients should be followed closely.

Artane Sustets should be used with caution in patients with glaucoma, obstructive disease of the gastro-intestinal or genito-urinary tracts, and in elderly males with possible prostatic hypertrophy.

Side-effects: Minor side-effects such as dryness of mouth, blurring of vision, dizziness, mild nausea or nervousness will be experienced by 30–50% of all patients. These reactions tend to become less pronounced as treatment continues.

Patients with arteriosclerosis or with a history of other drug idiosyncrasies may exhibit reactions of mental confusion, agitation, or nausea and vomiting. Such patients should be allowed to develop a tolerance using the smaller initial dose, with gradual increases until the effective level is reached.

Overdosage: No specific antidote. Gastric lavage, emetic, high enema. Usual general treatment plus cold compresses and forcing of fluid are mandatory. Atropine antagonists may be useful.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Bottles of 100.

Further information Artane tablets are available as scored, white tablets containing 2 mg or 5 mg of

benzhexol hydrochloride in bottles of 100, 1,000 and 5,000.

Product licence number 0095/5050.

AUDICORT*

Presentation Ear drops. Each millilitre contains:

Triamcinolone acetonide 1.0 mg
Neomycin undecylenate equivalent to:
3.5 mg neomycin base and
7.0 mg undecylenic acid
Benzocaine 50 mg

Uses Audicort is an anti-inflammatory, antibacterial, and antifungal preparation.

It is indicated in the treatment of acute and chronic otitis externa due to or complicated by bacterial or fungal infection; for eczematous or seborrhoeic dermatitis of the external auditory meatus; as an adjunct to systemic therapy in chronic otitis media and for the treatment of cavities after mastoidectomy and fenestration operations.

Dosage and administration *Adults and children:* After careful cleansing of the ear, Audicort is administered in doses of 2–5 drops, usually three or four times daily. If desired, the drops may be used to saturate a gauze or cotton wick placed in the ear. Excessive heating of the solution should be avoided.

Contra-indications, warnings, etc

Contra-indications: Audicort is contra-indicated in tuberculosis of the skin, viral exanthemata, herpes simplex, smallpox vaccination reactions, and in patients with a history of hypersensitivity to any of the ingredients.

It should not be used in the eyes.

Precautions: Use of an antibiotic may occasionally result in an overgrowth of non-susceptible micro-organisms, while the presence of an anti-inflammatory steroid may encourage their spread. If superinfection does occur, the drug should be stopped and appropriate therapy instituted.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in early pregnancy i.e. in large amounts for long periods.

In infants, long term continuous topical steroid therapy should be avoided. Adrenal suppression can occur even without occlusion.

In the adjunctive treatment of otitis media, the benefit expected from the use of Audicort in patients with a perforated eardrum should outweigh the risk of neomycin ototoxicity.

Side-effects: Adverse local effects from triamcinolone acetonide are rare, but neomycin and benzocaine have occasionally been responsible for localised skin sensitisation. If local reactions occur, such as irritation, erythema and oedema, discontinue medication.

Pharmaceutical precautions Audicort should be stored at room temperature in the original pack.

Audicort should not be diluted.

Legal category POM.

Package quantities 5 ml or 10 ml of sterile solution in plastic dropper bottle.

Further information Nil.

Product licence number 0095/5069.

AUREOCORT* CREAM AUREOCORT* OINTMENT AUREOCORT* AEROSOL SPRAY

Presentation *Ointment:* Each gram of yellow ointment contains:

Chlortetracycline hydrochloride 30 mg
Triamcinolone acetonide 1 mg

in a greasy base of anhydrous wool fat and white soft paraffin, with 0.16% methylparaben and 0.04% propylparaben as preservative.

Cream: Each gram of yellow cream contains:

Chlortetracycline equivalent to
chlortetracycline hydrochloride 30 mg
Triamcinolone acetonide 1 mg

in a smooth yellow water-miscible cream, with 0.2% chlorocresol as preservative.

Aerosol Spray: Each can contains:

Chlortetracycline hydrochloride 600 mg
Triamcinolone acetonide 15 mg

in a vehicle/propellant of isopropyl myristate and fluorinated hydrocarbons.

Uses Aureocort combines the anti-inflammatory action of triamcinolone acetonide with the anti-infective properties of chlortetracycline.

It is indicated in the treatment of atopic dermatitis contact dermatitis, eczema, infected wounds and ulcers neurodermatitis, otitis externa, seborrhoeic dermatitis septic types of contact dermatitis, varicose eczema vesiculo-pustular dermatitis. It may also be used in the treatment of infection and inflammation associated with burns, abrasions, lacerations, contact dermatoses, industrial dermatoses, insect bites, etc.

Dosage and administration *Adults and children.* Ointment. Aureocort Ointment should be applied sparingly to the affected area either directly or on sterile gauze two or three times daily.

In varicose ulcers the ointment should be applied to the ulcer on sterile gauze, and the surrounding skin edges smeared thinly prior to dressing and pressure bandaging.

Cream. Aureocort Cream should be applied sparingly to the affected areas two or three times daily.

Aerosol Spray. Aureocort Spray should be applied sparingly to the affected area two or three times daily. Hold the nozzle four to six inches from the affected area and depress the button for one to three seconds.

Contra-indications, warnings, etc

Contra-indications: The use of Aureocort is contra-indicated in tuberculous, fungal or viral lesions of the skin (herpes simplex, vaccinia and varicella).

Precautions: The use of antibiotics topically may result in overgrowth of non-susceptible organisms; if new infections appear during therapy appropriate measures should be taken.

The use of corticosteroids on infected areas should be continuously and carefully observed, bearing in mind the potential spreading of infection by anti-inflammatory corticosteroids (caused by organisms not sensitive to chlortetracycline) and the possible advisability of discontinuing corticosteroid therapy and/or initiating alternative antibacterial measures. Generalised dermatological conditions may require systemic corticosteroid therapy.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development

The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in early pregnancy, i.e. in large amounts or for long periods.

In infants, long term continuous topical steroid therapy should be avoided. Adrenal suppression can occur even without occlusion.

Side-effects: A few patients may be allergic to any of the components. If adverse reaction or idiosyncrasy occurs discontinue medication.

The use of corticosteroids over extensive body areas, with or without occlusive non-permeable dressings, may result in systemic absorption of the corticosteroid, and the physician should be aware of such possible absorption and take appropriate precautions. When occlusive non-permeable dressings are used, miliaria, folliculitis and pyoderma may sometimes develop beneath the occlusive material. Localised atrophy and striae have been reported with the use of corticosteroids by the occlusive technique.

Pharmaceutical precautions Aureocort Cream should be stored in a cool place. Dilution of Aureocort Ointment and Cream is not recommended as it will affect the stability of the product.

Aureocort Cream and Ointment may cause a yellow staining of clothes. Following extended use a similar local staining of the skin may occur which disappears on cessation of treatment.

Legal category POM.

Package quantities *Aureocort Ointment:* Tubes of 15 g.

Aureocort Cream: Tubes of 15 g.

Aureocort Aerosol Spray: Spray can of 60 g.

Further information Nil.

Product licence numbers

Aureocort Ointment 0095/5076

Aureocort Cream 0095/0019

Aureocort Aerosol Spray 0095/5077

AUREOMYCIN* CAPSULES

AUREOMYCIN* POWDER

Presentation *Capsules 250 mg:* Each yellow capsule, printed 'Lederle 4739' contains chlortetracycline hydrochloride 250 mg.

Powder 25 g: Each bottle contains 25 g of chlortetracycline hydrochloride as a micropulverised yellow powder.

Uses Aureomycin is a broad-spectrum antibiotic used for the treatment of infections caused by chlortetracycline-sensitive organisms. Typical indications include:

Ear, nose and throat infections. Acute and chronic bronchitis. Pneumonia. Gastro-intestinal infections. Amoebic Hepatitis. Urinary tract infections. Soft tissue infections. Venereal diseases. Acne. Typhus fever.

Other infections due to Aureomycin-sensitive organisms.

Aureomycin is also indicated for prophylaxis before or after surgical and dental procedures.

Dosage and administration *Dosage: Adults:* 1 capsule four times a day. This may be increased to 6 or 8 capsules daily in severe infections.

In the treatment of amoebiasis, at least 2 capsules four times daily for 10–14 days is recommended.

Administration: Aureomycin should be taken an hour before or two hours after meals and therapy should be continued for up to three days after characteristic symptoms of the infection have subsided.

Contra-indications, warnings, etc

Contra-indications: A history of hypersensitivity to tetracyclines. Systemic lupus erythematosus.

Warnings: Tetracyclines may cause a yellow to brown discoloration of the teeth in the developing foetus or child and therefore Aureomycin should only be administered if considered essential to pregnant women and young children under eight years of age. Aureomycin should be used with caution in patients with renal or hepatic dysfunction, or in conjunction with other potentially hepatotoxic drugs. Cross-resistance between tetracyclines may develop in micro-organisms and cross-sensitisation in patients.

Precautions: Absorption of Aureomycin is impaired by the concomitant administration of calcium, magnesium, iron and particularly aluminium salts commonly used as antacids. Tetracyclines depress plasma prothrombin activity therefore reduced dosages of concurrent anticoagulants may be required. Lower doses may be required in cases of renal impairment to avoid excessive systemic accumulation, although this is unlikely due to the high biliary excretion of Aureomycin. If therapy in such cases, is prolonged, serum level determinations are advisable.

Side-effects: Gastro-intestinal disturbances may occur and as with all antibiotics overgrowth of resistant organisms may cause glossitis, stomatitis, vaginitis, or staphylococcal enterocolitis. Photosensitivity and dermatological reactions are rare. Occurrences of enamel hypoplasia have been reported. Rarely, increased intracranial pressure with bulging fontanelles has been observed in infants which disappears rapidly upon cessation of treatment.

Overdosage: No specific antidote. Gastric lavage plus oral administration of milk or antacids.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities *Capsules:* Bottles of 20 and 100.

Powder: Bottles containing 25 g.

Further information Nil.

Product licence numbers

Capsules 250 mg 0095/0051

Powder 25 g 0095/5022

AUREOMYCIN* OINTMENT

AUREOMYCIN* CREAM

AUREOMYCIN* OPHTHALMIC OINTMENT

Presentation *Aureomycin Ointment 3%:* Each gram of yellow ointment contains Chlortetracycline hydrochloride 30 mg in a greasy base of anhydrous wool fat and white soft paraffin with 2.4% methylparaben and 0.6% propylparaben as preservatives.

Aureomycin Cream 3%: Each gram of yellow cream contains Chlortetracycline equivalent to chlortetracycline.

line hydrochloride 30 mg in a smooth yellow water-miscible cream, with 0.2% chlorocresol as preservative.

Aureomycin Ophthalmic Ointment 1%: Each gram of yellow ointment contains Chlortetracycline hydrochloride 10 mg in a greasy base of anhydrous wool fat and white soft paraffin.

Uses Aureomycin is a broad-spectrum antibiotic.

Aureomycin Ointment 3% and Aureomycin Cream 3%: Aureomycin topical preparations are indicated for the treatment of superficial pyogenic infections of the skin. They are effective against Gram-positive cocci (Streptococci, Staphylococci and Pneumococci) and Gram-negative bacteria (Coli-aerogenes group).

Aureomycin Ophthalmic Ointment 1%: Aureomycin Ophthalmic Ointment 1% is indicated in the treatment of susceptible ocular infections caused by Staphylococci, Pneumococci, *Haemophilus influenzae*, Diplococcus of Morax-Axenfeld, the Friedlander bacillus, Streptococci, *Aerobacter aerogenes*, *Proteus vulgaris*, *Proteus morganii*, *Escherichia coli*, *Alcaligenes faecalis*, *Pseudomonas aeruginosa*, and in the treatment of trachoma (in conjunction with oral therapy).

Dosage and administration *Adults and children:* **Aureomycin Ointment 3% and Cream 3%:** In the treatment of local skin infections, apply the preparation directly to the involved area, preferably on sterile gauze, one or more times daily as the condition warrants. In severe local infection, topical application should be supplemented by oral administration.

Aureomycin Ophthalmic Ointment 1%: Aureomycin Ophthalmic Ointment should be applied to the infected eye every two hours or more often as the condition warrants and response indicates. Severe or stubborn infections may require treatment for many days or oral administration in addition to local treatment. Mild infections may respond in as little as 48 hours.

Contra-indications, warnings, etc

Contra-indications: Aureomycin topical preparations are contra-indicated in patients with a history of hypersensitivity to chlortetracycline hydrochloride or any other ingredient.

Precautions: The use of antibiotics may result in the overgrowth of non-susceptible organisms. If new infections appear during therapy appropriate measures should be taken.

Side-effects: A few patients may be allergic to any of the components. If adverse reaction or idiosyncrasy occurs, discontinue medication.

Pharmaceutical precautions **Aureomycin Ointment 3%:** The product should be stored in a cool place. The ointment may be diluted with a base of 10% wool-fat in white soft paraffin.

Aureomycin Cream 3%: The product should be stored in a cool place. Dilution is not recommended.

Aureomycin Ophthalmic Ointment: The product should be stored in a cool place. Dilution of Aureomycin Ophthalmic Ointment is not recommended.

Aureomycin Cream and Ointment may cause a yellow staining of clothes. Following extended use a similar local staining of the skin may occur which disappears on cessation of treatment.

Legal category POM.

Package quantities **Aureomycin Ointment 3%:** Tubes of 30 g.

Aureomycin Ophthalmic Ointment 1%: Tubes of 3.5 g.

Aureomycin Cream 3%: Tubes of 30 g.

Further information Nil.

Product licence numbers

Aureomycin Ointment 3%	0095/5019
Aureomycin Ophthalmic Ointment 1%	0095/5020
Aureomycin Cream 3%	0095/0018

CALCIUM LEUCOVORIN

Presentation *Injection:* Ampoules containing 3 mg/ml folinic acid as the calcium salt.

Powder for Injection 30 mg: Vials containing a lyophilised powder of 30 mg folinic acid as the calcium salt.

Tablets 15 mg: Each yellowish-white scored tablet contains 15 mg folinic acid as the calcium salt.

Uses Calcium Leucovorin is the calcium salt of a formyl derivative of tetrahydrofolic acid, the metabolite of folic acid, and an essential coenzyme for nucleic acid synthesis. Calcium Leucovorin is used therefore to diminish the toxicity and counteract the action of folic acid antagonists such as Methotrexate in cytotoxic therapy. This procedure is commonly known as Calcium Leucovorin Rescue.

Calcium Leucovorin has also been demonstrated to be effective in producing amelioration of the blood picture in a number of megaloblastic anaemias due to folate deficiency.

Dosage and administration *Calcium Leucovorin Rescue: Adults and children:* Dosage regimes vary, depending upon the dose of Methotrexate administered. In general, up to 120 mg are usually given in divided doses, over 12–24 hours, by intramuscular injection, bolus intravenous injection, or intravenous infusion followed by 12–15 mg intramuscularly or 15 mg (1 tablet) orally, every 6 hours for the next 48 hours. Rescue therapy is usually started following a delay of up to 24 hours, after the beginning of the Methotrexate infusion. One tablet (15 mg) of Calcium Leucovorin every 6 hours for 48–72 hours may be sufficient when lower doses (less than 100 mg) of Methotrexate have been given. Where overdosage of Methotrexate is suspected, the dose of Calcium Leucovorin should be equal to or higher than the offending dose of Methotrexate, and should be administered within the first hour.

Treatment of Folate Deficiency:

Children up to 12 years of age: 0.25 mg/kg/day.

Adults: 10–20 mg daily. Oral therapy with one tablet of Calcium Leucovorin daily is more usual.

Contra-indications, warnings, etc

Contra-indications: None.

Precautions: Calcium Leucovorin should not be given simultaneously with an anti-neoplastic folic acid antagonist, e.g. Methotrexate to modify or abort clinical toxicity, as the therapeutic effect of the antagonist may be nullified. Concomitant Calcium Leucovorin will not however inhibit the antibacterial activity of other folic acid antagonists such as trimethoprim and pyrimethamine.

Calcium Leucovorin should not be used for the treatment of pernicious anaemia or other megaloblastic anaemias where vitamin B₁₂ is deficient.

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Dosage: Tablets (adults
rs.
r 4 tablets daily for short
ns.

Gonorrhoea: 1,200 mg (4 tablets) followed by a similar
dose six hours later.

Non-gonococcal urethritis: One tablet twice daily for
10–21 days.

Syrup: Adults: 20 ml twice daily.

Children: 5–9 years (18–27 kg) 5 ml twice daily.

9–15 years (< 40 kg) 5 ml three times daily.

9–15 years (> 40 kg) 10 ml twice daily.

These paediatric dosages are based on an average
daily dose of 6 mg/kg, but may be adjusted according to
the severity of infection and weight of the patient.

Administration: Deteclo should be taken an hour before
or two hours after meals and therapy should be continued
for up to three days after characteristic symptoms of the
infection have subsided.

Contra-indications, warnings, etc

Contra-indications: A history of hypersensitivity to
tetracyclines. Overt renal insufficiency, Systemic lupus
erythematosus.

Warnings: Tetracycline may cause a yellow to brown
discoloration of the teeth in the developing foetus or
child and therefore Deteclo should only be administered
if considered essential to pregnant women and young
children under eight years of age. Deteclo should be
used with caution in patients with renal or hepatic
dysfunction, or in conjunction with other potentially
hepatotoxic drugs. Cross-resistance between tetra-
cyclines may develop in micro-organisms and cross-
sensitisation in patients.

Precautions: Absorption of Deteclo is impaired by the
concomitant administration of calcium, magnesium, iron
and particularly aluminium salts commonly used as
antacids. Tetracyclines depress plasma prothrombin
activity therefore reduced dosages of concurrent anti-
coagulants may be required. Lower doses are indicated
in cases of renal impairment to avoid excessive systemic
accumulation, and, if therapy is prolonged, serum level
determinations are advisable.

Side-effects: Nausea, diarrhoea and dermatitis may
occur and, as with all antibiotics, overgrowth of resistant
organisms may cause glossitis, stomatitis, vaginitis, or
staphylococcal enterocolitis. Photoallergic reactions
may occur in hypersensitive persons and such patients
should be warned to avoid direct exposure to natural or
artificial sunlight and to discontinue treatment at the first
sign of skin discomfort. Rarely, increased intracranial
pressure with bulging fontanelles has been observed in
infants which disappears rapidly upon cessation of
treatment.

Overdosage: No specific antidote. Gastric lavage plus
oral administration of milk or antacids.

Pharmaceutical precautions The powder for Dete-
clo Syrup should be stored in a cool dry place, and when
dispensed should be used within seven days. Dilution of
Deteclo Syrup is not recommended since it will affect
the stability of the product.

Legal category POM.

Package quantities *Tablets:* Bottles of 100 and 500.
Syrup: Bottles of 100 ml.

Further information Deteclo is a unique combination
of three effective tetracycline broad-spectrum anti-
biotics. The ratio of the different tetracyclines has been
carefully chosen to ensure that high therapeutic blood
levels are rapidly realised and maintained with a reduced

potential for side-effects, on a twice daily dosage regime, because of their different rates of absorption and excretion.

Product licence numbers

Tablets 0095/5070
Syrup 0095/0004

DIAMOX*

Presentation *Tablets 250 mg:* Each white tablet coded 'Lederle 4395' contains acetazolamide 250 mg.

Sodium Parenteral 500 mg: Each vial contains 500 mg of acetazolamide as the sodium salt with sodium hydroxide to adjust the pH to approximately 9.2.

Uses Diamox is an enzyme inhibitor and acts specifically on carbonic anhydrase. It is indicated in the treatment of:

1. *Glaucoma:* It is felt that Diamox is useful in glaucoma, because it acts on inflow, decreasing the amount of aqueous secretion.

2. *Abnormal retention of fluid:* Diamox is a diuretic whose effect is due to the effect on the reversible hydration of carbon dioxide and dehydration of carbonic acid reaction in the kidney. The result is renal loss of HCO_3^- -ion which carries out sodium, water and potassium.

Diamox is therefore indicated in the treatment of toxæmia and oedema of pregnancy, pre-menstrual tension, drug-induced oedema, obesity, and congestive heart failure in each case where fluid retention is a problem.

3. *Epilepsy:* Best results with Diamox have been seen in petit mal in children. Good results, however, have been seen in patients, both children and adults, with other types of seizures such as grand mal, mixed seizure patterns, myoclonic jerk patterns, etc.

4. *Other fields:* Certain patients with Ménière's disease have shown a good response, but this is probably limited to those patients who have a component of oedema in the labyrinth mechanism of the inner ear.

Similarly, there have been varying reports on the use of Diamox in hydrocephalus in the infant.

Dosage and administration *Tablets:*

1. *Glaucoma (acute congestive and secondary):*
Adults: 250–1,000 mg (1–4 tablets) per 24 hours, usually in divided doses for amounts over 250 mg daily.

Children: 125–750 mg ($\frac{1}{2}$ –3 tablets) daily in divided doses.

Infants: 125 mg daily ($\frac{1}{2}$ tablet).

Diamox should be used as an adjunct to the usual therapy.

2. *Abnormal retention of fluid:* Congestive heart failure, toxæmia and oedema of pregnancy, drug-induced oedema. (Adults only.)

For diuresis, the starting dose is usually 1–1½ tablets (250–375 mg) once daily in the morning. If, after an initial response, the patient fails to continue to lose oedema fluid, do not increase the dose but allow for kidney recovery by omitting a day. Best results are often obtained on a regime of 1–1½ tablets daily for two days, rest a day, and repeat, or merely giving the Diamox every other day. The use of Diamox does not eliminate the need for other therapy, e.g. digitalis, bed rest and salt restriction in congestive heart failure and proper supple-

mentation with elements such as potassium in drug-induced oedema.

For cases of pre-menstrual tension where fluid retention is a problem a daily dose (single) of 125–375 mg is suggested beginning 5–10 days prior to onset of menstruation, or at onset of symptoms. Therapy may be alternated with days of rest.

For obesity the recommended dosage is 250–375 mg daily. For some patients therapy may be on an alternate week basis. Diamox is not intended for use in curbing appetite.

3. *Epilepsy: Adults:* 250–1,000 mg daily in divided doses.

Children: 125–750 mg daily in divided doses.

Infants (less than 2 years old): 125 mg daily.

The change from other medication to Diamox should be gradual.

Sodium Parenteral: Intravenous or intramuscular administration may be employed in the same dosage as indicated for oral use. The direct intravenous route is preferred as the intramuscular use is limited by the alkaline pH of the solution.

Each vial should be reconstituted with at least 5 ml of Water for Injection prior to use.

Contra-indications, warnings, etc

Contra-indications: Since Diamox may induce a mild acidosis, its use is contra-indicated in idiopathic renal hyperchloraemic acidosis. Because of the nature of its action, Diamox may be contra-indicated in conditions in which there is a known depletion of sodium and potassium at least until after successful preliminary medication with sodium and potassium salts. It is also contra-indicated in Addison's disease or all types of suprarenal gland failure.

Long-term administration is contra-indicated in patients with chronic congestive angle-closure glaucoma since it may permit organic closure of the angle to occur while the worsening glaucoma is masked by lowered intra-ocular pressure.

Precautions: Increasing the dose does not increase the diuresis and may increase the incidence of drowsiness and/or paraesthesia. Less commonly, fatigue, excitement, gastro-intestinal upsets and increased polyuria have been reported. Disorientation has been observed in a few patients with oedema due to hepatic cirrhosis. Such cases should be under close supervision.

When Diamox is prescribed for long-term therapy, special precautions are advisable. The patient should be cautioned to report any unusual skin rash. Periodic blood cell counts are recommended. A precipitous drop in formed blood cell elements or the appearance of toxic skin manifestations should call for diminution or cessation of Diamox therapy. The transitory loss of hearing calls for immediate cessation of medication.

Side-effects: Instances of flushing, thirst, headache, drowsiness, dizziness, fatigue, irritability, excitement, polydipsia and polyuria, paraesthesia of extremities and face, ataxia, hyperpnoea, and gastro-intestinal upsets such as anorexia and vomiting have been reported. These side-effects have normally disappeared during continued medication or upon diminution or cessation of Diamox therapy.

However, Diamox is a sulphonamide derivative and therefore some side-effects similar to those caused by sulphonamides have occasionally been reported. These include fever, agranulocytosis, thrombocytopenia,

thrombocytic purpura, leukopenia, and aplastic anaemia, skin toxicity, crystalluria, calculus formation, renal and ureteral colic, and renal lesions.

Transient myopia has been reported. This condition invariably subsides upon diminution or discontinuance of the medication.

Drug interactions: Possible potentiation of the effects of folic acid antagonists, hypoglycaemics and oral anticoagulants.

Overdosage: No specific antidote. Supportive measures with correction of electrolyte and fluid balance. Force fluids.

Pharmaceutical precautions The products should be stored at room temperature in either the original pack or in containers which prevent access of moisture.

Reconstituted solutions of Diamox Sodium Parenteral contain no preservative and should be used or discarded within 24 hours.

Legal category POM.

Package quantities *Diamox Tablets 250 mg:* Bottles of 100 and 1,000.

Diamox Sodium Parenteral: Vials, 500 mg.

Further information Diamox Sodium Parenteral contains 2.36 millimoles of sodium per vial.

Product licence numbers

Diamox Tablets 250 mg	0095/5075
Diamox Sodium Parenteral	0095/5073

DIAMOX* SUSTETS*

Presentation Each orange transparent capsule contains acetazolamide 500 mg formulated to release 125 mg immediately and 375 mg gradually over a six to eight hour period.

Uses Diamox is an enzyme inhibitor and acts specifically on carbonic anhydrase which affects the reversible hydration of carbon dioxide and dehydration of carbonic acid in the kidney and other sites. The result is renal loss of HCO_3^- -ion which carries out sodium, water and potassium.

Indications Glaucoma.

Dosage and administration *Adults:* 1 Capsule at night and in the morning. The product is not intended for administration to children.

Contra-indications, warnings, etc

Contra-indications: Since Diamox Sustets may induce a mild acidosis, its use is contra-indicated in idiopathic renal hyperchloraemic acidosis. Because of the nature of its action, Diamox Sustets may be contra-indicated in conditions in which there is a known depletion of sodium and potassium at least until after successful preliminary medication with sodium and potassium salts. It is also contra-indicated in Addison's disease or all types of suprarenal gland failure.

Long-term administration is contra-indicated in patients with chronic congestive angle-closure glaucoma since it may permit organic closure of the angle to occur while the worsening glaucoma is masked by lowered intra-ocular pressure.

Precautions: Increasing the dose does not increase the diuresis and may increase the incidence of drowsiness and/or paraesthesia. Less commonly, fatigue, excitement, gastro-intestinal upsets and increased polyuria

have been reported. Disorientation has been observed in a few patients with oedema due to hepatic cirrhosis. Such cases should be under close supervision.

When Diamox Sustets is prescribed for long-term therapy, special precautions are advisable. The patient should be cautioned to report any unusual skin rash. Periodic blood cell counts are recommended. A precipitous drop in formed blood cell elements or the appearance of toxic skin manifestations should call for diminution or cessation of Diamox Sustets therapy. The transitory loss of hearing calls for immediate cessation of medication.

Side-effects: Instances of flushing, thirst, headache, drowsiness, dizziness, fatigue, irritability, excitement, polydipsia and polyuria, paraesthesia of extremities and face, ataxia, hyperpnoea, and gastro-intestinal upsets such as anorexia and vomiting have been reported. These side-effects have normally disappeared during continued medication or upon diminution or cessation of Diamox Sustets therapy.

However, Diamox Sustets is a sulphonamide derivative and therefore some side-effects similar to those caused by sulphonamides have occasionally been reported. These include fever, agranulocytosis, thrombocytopenia, thrombocytic purpura, leukopenia, and aplastic anaemia, skin toxicity, crystalluria, calculus formation, renal and ureteral colic, and renal lesions.

Transient myopia has been reported. This condition invariably subsides upon diminution or discontinuance of the medication.

Drug interactions: Possible potentiation of the effects of folic acid antagonists, hypoglycaemics and oral anticoagulants.

Overdosage: No specific antidote. Supportive measures with correction of electrolyte and fluid balance. Force fluids.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Bottles of 30, 100 and 500.

Further information Nil.

Product licence number 0095/5074.

FOLVRON*

Presentation Tablets. Each red, sugar-coated tablet contains folic acid 1.7 mg, dried ferrous sulphate 194 mg (supplying 57 mg of elemental iron).

Uses Folvron is indicated for the treatment and prevention of iron-deficiency anaemias and of the megaloblastic anaemias of pregnancy. Pernicious anaemia should be excluded before instituting therapy with folic acid.

Dosage and administration *Adults and children above the age of 6 years:* 1 tablet three times daily after meals is indicated in most cases. In severe cases this dose may be doubled. Treatment should be continued until haematopoiesis is adequate to maintain a relatively normal haemoglobin concentration in the blood, as determined by blood examinations. Folvron is not recommended for children below the age of 6.

Contra-indications, warnings, etc Folic acid may obscure pernicious anaemia in that the peripheral blood picture may revert to normal while neurological manifestations remain progressive. Iron salts diminish the absorption of tetracyclines given concomitantly. Admin-

istration of this product should be made with care to avoid allergic and other untoward reactions.

Side-effects: Folvron may cause gastro-intestinal discomfort, diarrhoea and vomiting in a few patients. Prolonged use may sometimes cause constipation.

Overdosage: Induce emesis immediately followed by gastric lavage with a 1% solution of sodium bicarbonate. Inject intramuscularly 2 g of desferrioxamine dissolved in Water for Injection. Give 5 g of desferrioxamine in 50–100 ml of water by mouth or stomach tube to chelate any iron left in the stomach.

Pharmaceutical precautions The product should be stored at room temperature in either the original pack or in containers which prevent access of moisture.

Legal category POM.

Package quantities Bottles of 100.

Further information Nil.

Product licence number 0095/5000.

GEVRAL*

Presentation Each brown gelatine capsule coded 'Lederle 4981' contains:

Vitamin A (acetate)	5,000 i.u.
Vitamin D	500 i.u.
Vitamin B ₁ (as thiamine mononitrate)	5.0 mg
Vitamin B ₂ (riboflavine)	5.0 mg
Vitamin B ₆ (pyridoxine hydrochloride)	0.5 mg
Vitamin B ₁₂	1 mcg
Vitamin C (ascorbic acid)	50.0 mg
Vitamin E (<i>d</i> - α -tocopheryl acetate)	10 i.u.
Niacinamide	15.0 mg
Calcium pantothenate	5.0 mg
Calcium (as dibasic calcium phosphate)	145.0 mg
Phosphorus (as dibasic calcium phosphate)	110.0 mg
Elemental iron (as ferrous fumarate)	10.0 mg
Magnesium (as magnesium oxide)	1.0 mg
Potassium (as potassium sulphate)	5.0 mg
Iodine (as potassium iodide)	0.1 mg
Copper (as copper oxide)	1.0 mg
Manganese (as manganese dioxide)	1.0 mg
Zinc (as zinc oxide)	0.5 mg
Inositol	50.0 mg
L-Lysine monohydrochloride	25.0 mg
Choline bitartrate	50.0 mg

Uses Gevral is indicated for the prevention of deficiencies of the vitamins and minerals contained.

Dosage and administration *Adults and children:* 1 capsule daily, preferably after a meal, or as prescribed by the physician.

Contra-indications, warnings, etc There are no contra-indications, side-effects or adverse reactions. Overdosage does not apply.

Pharmaceutical precautions The product should be stored at room temperature in either the original pack or in containers which prevent access of moisture.

Legal category P.

Package quantities Packs of 30.

Further information Gevral Capsules contain 0.129 millimole of potassium per capsule.

Product licence number 0095/5078.

LEDERCORT* CREAM AND OINTMENT

Presentation *Ledercort Cream 0.1%:* Each gram of white cream contains triamcinolone acetonide 1.0 mg in a water-miscible base with methylparaben 0.16% and propylparaben 0.04% as preservatives.

Ledercort Ointment 0.1%: Each gram of pale yellow ointment contains triamcinolone acetonide 1.0 mg in a greasy base with methylparaben 0.16% and propylparaben 0.04% as preservatives.

Uses Triamcinolone acetonide is a corticosteroid with anti-inflammatory, antipruritic and anti-allergic effects.

Ledercort Cream 0.1% and Ledercort Ointment 0.1% are indicated in the treatment of inflammatory skin conditions such as atopic dermatitis; contact dermatitis; eczematous psoriasis; eczematous dermatitis; generalised erythroderma; neurodermatitis; nummular eczema; otitis externa; pruritus ani; pruritus vulvae, and seborrhoeic dermatitis.

Dosage and administration *Adults and children:* Apply in small quantities to the affected areas three or four times daily; the cream or ointment may be rubbed in or applied as a thin film.

Some cases of psoriasis may be treated more effectively by application under an occlusive non-permeable dressing.

Contra-indications, warnings, etc

Contra-indications: The use of Ledercort Cream 0.1% and Ledercort Ointment 0.1% is contra-indicated in tuberculous, fungal or viral lesions of the skin (herpes simplex, vaccinia and varicella).

Precautions: In infants, long-term continuous topical steroid therapy should be avoided. Adrenal suppression can occur even without occlusion.

The use of corticosteroids on infected areas should be cautiously and carefully observed, bearing in mind the potential spreading of infection by anti-inflammatory corticosteroids and the possible advisability of discontinuing corticosteroid therapy and/or initiating antibacterial measures. Generalised dermatological conditions may require systemic corticosteroid therapy. If infection of the tissues is present, the use of a broad-spectrum systemic antibiotic may be desirable.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in early pregnancy, i.e. in large amounts or for prolonged periods.

Side-effects: A few patients may be allergic to any of the components. If adverse reaction or idiosyncrasy occurs, discontinue medication.

Side-effects are not ordinarily encountered with topical application of corticosteroids; but as with all drugs some patients react unfavourably under certain conditions. The use of corticosteroids over extensive body areas, with or without occlusive non-permeable dressings, may result in systemic absorption of the corticosteroid being used, and the physician should be aware of such possible absorption and take appropriate precautions. When occlusive non-permeable dressings are used, miliaria, folliculitis and pyoderma may sometimes develop beneath the occlusive material. Localised atrophy and striae have been reported with the use of corticosteroids by the occlusive technique.

Pharmaceutical precautions *Ledercort Cream 0.1%:* Ledercort Cream should be stored in a cool place, in

either the original pack or in containers with complete closure.

The cream may be diluted, taking hygienic precautions, with aqueous cream. The diluted cream must be freshly prepared and not used more than one month after issue.

Ledercort Ointment 0.1%: Ledercort Ointment should be stored in a cool place, in either the original pack or in containers which prevent access of moisture. The ointment may be diluted with a basis consisting of 1 part wool fat and 9 parts white soft paraffin.

Legal category POM.

Package quantities *Ledercort Cream 0.1%:* 15 g tube and 250 g jar.

Ledercort Ointment 0.1%: 15 g tube and 250 g jar.

Further information Nil.

Product licence numbers

Ledercort Cream 0.1% 0095/5004

Ledercort Ointment 0.1% 0095/5005

LEDERCORT* TABLETS

Presentation *Tablets 2 mg:* Each blue, oblong tablet coded 'LL1' contains triamcinolone 2 mg.

Tablets 4 mg: Each white, oblong tablet coded 'LL4406' contains triamcinolone 4 mg.

Uses Ledercort is a potent glucocorticoid indicated in the treatment of rheumatoid arthritis; rheumatic fever; disseminated lupus erythematosus and other collagen diseases; nephrotic syndrome; bronchial asthma and respiratory allergy; pulmonary emphysema and fibrosis; allergic and inflammatory dermatoses, and haemolytic diseases.

Dosage and administration

1. *General. Adults and children:* Ledercort is administered orally in a wide range of dosages. The doctor should individualise the dosage according to the condition. In adults and children over 75 lb body weight, the usual initial dose ranges from 8 mg to 16 mg per day in single or divided doses. For children under 75 lb the range is from 4 to 12 mg.

When a satisfactory response is obtained the initial dosage should be reduced gradually by 2 mg every two to three days until the smallest dosage is achieved which will adequately maintain the patient.

2. Dosage in specific conditions:

- Rheumatoid arthritis:* The initial suppressive dose usually ranges from 8 to 16 mg per day, although an occasional patient may require larger doses to suppress the disease adequately. Once the acute manifestations of the disease have subsided (usually within two to seven days) the dosage should gradually be reduced until the smallest maintenance dose is achieved. The daily maintenance dose has ranged from 2 to 16 mg per day, although an occasional patient may require more.
- Rheumatic fever:* The initial dose is 16–20 mg daily; maintenance dosage is 6–20 mg daily. Dosage varies considerably according to the severity of the carditis and its complications.
- Disseminated lupus erythematosus:* The initial suppressive dose in collagen diseases should be 20–30 mg daily, reducing gradually to maintenance levels when the desired response is noted. Maintenance dosage varies from 3 to 30 mg daily. In

severely ill patients, larger doses may be necessary to control the disease.

- Nephrotic syndrome:* 16–20 mg daily should be administered until diuresis occurs, usually by the fourteenth day. After diuresis begins it is advisable to continue treatment until maximum or complete chemical and clinical remission occurs; then dosage should be reduced gradually and finally discontinued.
- Bronchial asthma and respiratory allergy, pulmonary emphysema and fibrosis:* In acute bronchial asthma, initial suppressive doses of 8–16 mg should be given to bring the disease under control within 24–48 hours. Rarely, more than 16 mg may be necessary.
The initial suppressive dose for pulmonary emphysema and pulmonary fibrosis is 8–12 mg daily; the maintenance dose varies and may be as little as 2–4 mg daily.
- Dermatoses:* The initial suppressive dosage should be 8–16 mg daily, or higher in the rare case. The maintenance dose can be as little as 1–2 mg daily.
- Haemolytic diseases:* Where steroid therapy is indicated in haemolytic diseases, the average initial dose of Ledercort is 12–24 mg daily.

3. *Change in maintenance from other glucocorticoids:* Because the variation in response to each glucocorticoid varies considerably with each type of disease, the following schedule should be adjusted according to individual response – 4 mg Ledercort for each:

25 mg cortisone
20 mg hydrocortisone
5 mg prednisone or prednisolone
4 mg methylprednisolone
0.75 mg dexamethasone
0.60 mg betamethasone

4. *Short-term therapy in asthma:* Ledercort can control exacerbations of asthma via a short-term dosage regimen that reduces as it progresses.

Short-term courses of either ten or four days duration may be prescribed, in the following schedules (using the 4 mg tablet):

	Number of tablets	
	Ten-day course	Four-day course
1st day	4	4
2nd day	4	3
3rd day	4	2
4th day	3	1
5th day	3	
6th day	3	
7th day	2	
8th day	2	
9th day	1	
10th day	1	

Contra-indications, warnings, etc

Contra-indications: Tuberculosis and herpes simplex are usually considered to be absolute contra-indications. Active peptic ulcer, acute glomerulonephritis, myasthenia gravis, osteoporosis, fresh intestinal anastomoses, diverticulitis, thrombophlebitis, psychic disturbances, pregnancy and local or systemic infections, including fungal and exanthematous diseases, are relative contra-indications.

Precautions: General precautions common to all corticosteroid therapy should be observed. Daily doses over 32 mg are seldom indicated. Patients should be kept

under careful observation because a few may react with side-effects under certain conditions; in such an event, the drug should be discontinued.

Since adrenal cortical function may be suppressed by glucocorticoids, it is important that therapy be withdrawn gradually after long-term treatment. Adequate supporting measures, ACTH supplementation or increase in dosage, are indicated when undue stress occurs during or after Leder cort therapy. Leder cort is not the treatment of choice in adrenocortical insufficiency.

The possibility of development of infectious disease during glucocorticoid therapy requires careful observation of the patient, because initial signs of the infection may be obscured. Appropriate antibiotic therapy should be instituted in such cases.

Side-effects: Leder cort may produce the side-effects common to all cortisone-like drugs: moon face, striae, acne, buffalo hump, osteoporosis, spontaneous fractures, amenorrhoea, aggravation of infection, psychic disturbances, thrombo-embolism, peptic ulcer, gastro-intestinal haemorrhage, hyperglycaemia, increased intracranial pressure, headache, insomnia, fatigue, purpura, hirsutism, vertigo and leucopenia. Caution is recommended during prolonged use in children because of the possibility of growth suppression. Subcapsular cataracts may be formed on high dosage for long periods. Flushing of the face may occur. Necrotising angitis is a rare possibility. Ulcerative oesophagitis and acute pancreatitis have occurred during corticosteroid therapy and may be related to its administration.

The long-term administration of all anti-inflammatory steroids results in definite catabolic effects, as indicated by negative protein and calcium balance. This catabolic effect, coupled with anorexia, may produce weight loss, which is undesirable in some patients. A steroid myopathy with advanced muscle weakness may involve muscles of the thighs, pelvis and low back.

The effect of Leder cort on fluid and electrolyte balance differs from older corticosteroids in that it promotes mild sodium excretion. Patients with sodium retention and oedema, from underlying disease or from previous therapy with other corticosteroids, will frequently lose weight and show increased urinary output associated with sodium diuresis during the first three to seven days of therapy. This effect will not be seen in patients with decreased glomerular filtration.

Potassium balance is not affected under ordinary dosage circumstances, and potassium supplementation is not ordinarily necessary unless prolonged and/or high dosage is prescribed. Since hypertension and oedema are not commonly observed with Leder cort they should not be used as indications of overdosage.

Overdosage: No specific antidote. Symptomatic treatment with electrolyte supplements.

Pharmaceutical precautions The product should be stored at room temperature in either the original pack or in containers which prevent access of moisture.

Legal category POM.

Package quantities *Tablets 2 mg:* Bottles of 100 and 500.

Tablets 4 mg: Bottles of 30, 100 and 500.

Further information In order to discontinue the use of azo-dyes, pink Leder cort tablets 2 mg embossed 'LL4405' are being replaced by blue Leder cort tablets 2 mg embossed 'LLII'.

Product licence numbers

Leder cort Tablets 2 mg 0095/5006

Leder cort Tablets 4 mg 0095/5007

LEDERFEN* ▼

Presentation *300 mg capsules:* Dark blue capsules each containing 300 mg of fenbufen and printed 'Lederle 300 mg' on both the cap and body.

300 mg tablets: Light blue, film coated, capsule shaped tablets each containing 300 mg of fenbufen and engraved 'LL300'.

Uses Lederfen is a potent non-steroidal anti-inflammatory and analgesic agent indicated for the symptomatic treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis.

Dosage and administration *Adults:* 600 mg as a single daily dose or 900 mg daily in divided doses. Many patients can be adequately controlled with a daily dosage of two capsules or two tablets taken at night, whereas some may require an extra capsule or tablet in the morning.

It is unnecessary to modify the dosage of Lederfen in cases of mild to moderate renal impairment. Lederfen may therefore be used in elderly patients in whom renal impairment commonly occurs.

Children: Not recommended for administration to children under the age of 14.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to propionic acid anti-inflammatory drugs, or aspirin.

Precautions: As with other non-steroidal anti-inflammatory agents, Lederfen should be used with great caution in patients with a history or evidence of active peptic or intestinal ulceration, and only when considered essential in pregnant and nursing women.

Warnings and adverse effects: Lederfen is well tolerated by most patients and unlike other non-steroidal anti-inflammatory agents, is extremely unlikely to cause gastro-intestinal ulceration. However, adverse effects may include symptoms of gastro-intestinal intolerance such as nausea. Other reactions which have occurred infrequently include skin rash, dizziness, drowsiness and headache. Slight decreases in blood leucocytes, haemoglobin and haematocrit, as well as slight increases in prothrombin time and eosinophils, have occasionally been recorded. Transient elevations in values of liver function tests have occurred in some patients.

Drug interactions: When single doses of aspirin 900 mg and Lederfen 500 mg are administered together, serum concentrations of Lederfen and its metabolites are reduced by 10–20%. Concomitant use of aspirin may require adjustment of dosage of Lederfen.

Lederfen is strongly protein bound. Although no clinically significant interactions have been noted as yet, practitioners should be alert to this possibility.

Overdosage: There is no experience with overdosage, consequently the signs, symptoms and treatment have not been identified. There is no specific antidote.

Pharmaceutical precautions *Capsules:* keep lid tightly closed.

Legal category POM.

Package quantities Bottle of 100.

Further information Lederfen is extremely unlikely to cause gastro-intestinal bleeding or ulceration since it is present in the stomach as fenbufen which is not a gastric irritant. Following absorption, fenbufen is converted into active metabolites whose prolonged duration of action (half lives 10–17 hours) provides sustained anti-inflammatory and analgesic activity. Therefore in many patients, single oral doses given at night will provide adequate plasma levels to provide symptomatic relief of nocturnal pain and morning stiffness.

Product licence numbers

Lederfen Capsules 0095/0043
Lederfen Tablets 0095/0081

LEDERKYN*

Presentation Each peach-coloured tablet coded 'Lederle 3945' contains sulphamethoxypyridazine 0.5 g.

Uses Lederkyn is a sulphonamide indicated in infections caused by sulphonamide-susceptible organisms. Because of its slow excretion and long-lasting blood levels, Lederkyn is primarily recommended for use in urinary tract infections due to sulphonamide-sensitive organisms such as *E. Coli*, *Aerobacter aerogenes*, *paracolon bacillus*, *Streptococci*, *Staphylococci*, Gram-negative rods, diphtheroids and Gram-positive cocci. Some cases of urinary tract infection in which *Proteus* was present have responded to Lederkyn.

Recent reports indicate Lederkyn to be of considerable value in the treatment of dermatitis herpetiformis, acne vulgaris, in the prophylaxis of infection especially against streptococcal infections in rheumatic fever patients.

Dosage and administration *Adults and children:* It is recommended that the dosages given in the table are not exceeded. Therapy should continue until the patient is asymptomatic for 48–72 hours. Adequate fluid intake must be maintained during and for at least 24 to 48 hours after treatment.

Patients on sulphonamides may vary in their capacity to maintain therapeutically optimum blood levels and therefore routine blood-level determinations are advisable to establish optimal dosage.

In dermatitis herpetiformis dosage should be determined by disease response and doses of less than 0.5 g per day may be found to be satisfactory.

For prophylaxis of streptococcal infection in rheumatic fever a single weekly dose of 2.0–3.0 g (4–6 tablets) may be given depending on weight. Drowsiness is

sometimes observed at this dosage level, so it may be advisable to administer the drug at bedtime.

Contra-indications, warnings, etc

Contra-indications: Lederkyn is contra-indicated in premature and newly born infants – especially those with erythroblastosis. For this reason the drug should not be used at term in pregnancy or in lactating women who are breast feeding infants, and only during pregnancy if considered essential. Lederkyn is also contra-indicated in patients with a known hypersensitivity to sulphonamides.

Precautions: Crystalluria and haematuria rarely occur during treatment with Lederkyn. However the drug should be used with caution in patients with hepatic or renal dysfunction and their treatment monitored closely to avoid excessive accumulation. Adequate fluid intake must be maintained during and for at least 24–48 hours after treatment.

Headache and drug fever may be side-effects, as with other sulphonamides, and seem to appear usually in those patients who attain the higher blood levels. Relief may be obtained by reducing the dosage or stopping the drug. The appearance of a rash indicates the need for immediate withdrawal of the drug.

Proper clinical judgement and laboratory control, including periodic complete blood and platelet counts, should prevail for all patients on Lederkyn therapy.

Prolonged use of Lederkyn may lead to an overgrowth of non-susceptible or resistant organisms.

Side-effects: Minor cutaneous eruptions, nausea, headache and drug fever have been most frequently encountered. Abdominal pain, dizziness, drowsiness, tingling of the extremities, nervousness and malaise have occasionally been reported.

More severe reactions include erythema multiforme exudativum, urticaria, exfoliative dermatitis, toxic hepatitis, interstitial myocarditis, lupus erythematosus, aplastic anaemia, leucopenia, pancytopenia, Stevens-Johnson syndrome, thrombocytopenia, purpura, and haemolytic anaemia.

Drug interactions: Possible potentiation of the effects of folic acid antagonists, hypoglycaemics and oral anticoagulants.

Overdosage: No specific antidote. Rapid evacuation of stomach, and general supportive measures. Forcing of fluids and routine measures in the event of crystalluria.

Pharmaceutical precautions The product should be stored at room temperature in either the original pack or in containers which prevent access of moisture, and provide protection from light.

Legal category POM.

Package quantities Bottles of 24 and 100.

Further information Nil.

Product licence number 0095/5012.

LEDERMIX*

Presentation Ledermix combination kit consists of a package containing 4 units.

1. **Ledermix paste.** Each gram contains: Demeclocycline Calcium equivalent to Demeclocycline hydrochloride 30 mg. Triamcinolone acetonide 10 mg.

2. **Ledermix cement.** Each gram contains: Demeclocycline hydrochloride 20 mg. Triamcinolone acetonide

Dosage of Lederkyn

Dosage	Tablets	
	Initial dose first day	Daily maintenance dose
Adults†	2 (1 g)	1 (0.5 g)
Children: 1–3 years: Approx. weight 20 lb (9 kg)	½ (0.25 g)	¼ (0.125 g)
4–6 years: Approx. weight 40 lb (18 kg)	1 (0.5 g)	½ (0.25 g)
6–10 years: Approx. weight 60 lb (27 kg)	1½ (0.75 g)	¾ (0.375 g)

† Adults under 130 lb in weight may be maintained on ½ tablet (0.25 g). An initial dose of 4 tablets (2 g) may be given where prompt, high blood levels are indicated.

6.7 mg in combination with zinc oxide and calcium hydroxide.

3. **Hardener 'F' (fast setting time).** 85% w/w Eugenol USP in rectified turpentine oil.

4. **Hardener 'S' (slow setting time).** 85% w/w Eugenol USP and 10% w/w polyethylene glycol 4000 USP in rectified turpentine oil.

Uses Ledermix is a dental treatment which combines the antibiotic action of demeclocycline with the anti-inflammatory action of triamcinolone acetonide.

Ledermix is indicated in pulpitis, periodontitis, and hypersensitive dentine.

Dosage and administration *Adults and Children:*

Pulpitis: In all instances of exposed pulp and in acute pulpitis (except total purulent pulpitis) Ledermix Paste is applied with a small cotton pledget to the dentine adjacent to the pulp or to the exposed pulp. The cavity is then closed with a temporary filling such as zinc oxide-eugenol. Approximately 3 to 6 days later the vitality of the tooth is determined, the cavity is reopened, and the cotton pledget is removed. The dentine close to the pulp, or the wound in the pulp, is covered with Ledermix Cement prepared in the following manner: To one drop of the Hardener (no more) add sufficient Ledermix Cement powder to obtain a homogeneous mixture of cream-like consistency. This cement, which hardens rapidly, may be applied with an amalgam plugger or blunt probe.

In small cavities with small areas of pulp exposure, Ledermix Cement suffices as a base. In larger cavities or more extensive pulp exposure, it is advisable to use Ledermix Cement as a lining cement only and then to cover it with a layer of zinc oxyphosphate cement before inserting the permanent amalgam filling. In certain instances of hyperaemia and partial serous pulpitis with closed pulp cavity, the use of Ledermix Paste may be eliminated and Ledermix Cement (mixed with the Hardener) applied in the first treatment period. However, as a general rule, and particularly in acute pulpitis and in teeth where the pulp is exposed, the prepared Ledermix Cement should *NOT* be applied without previous treatment with Ledermix Paste.

Periodontitis: In primary acute periodontitis and acute exacerbations of chronic periodontitis, the canal may be prepared to the apex at the first sitting. After irrigation, the canal may be filled completely with Ledermix Paste and sealed. This treatment can be repeated if necessary on the follow-up visit about one week later, or the canal may be irrigated to remove the paste and further treatment carried out according to one of the generally accepted methods. If an alveolar abscess is present, drainage should be effected before beginning treatment with Ledermix.

Hypersensitive Dentine: In instances of hypersensitive dentine following cavity or crown preparations, Ledermix Cement plus Hardener may be used as a lining for deep cavities.

Preparation of the cement: Ledermix Cement belongs to the class of zinc oxide-eugenol dental cements. The setting time of all such cements is greatly affected by temperature and humidity conditions and by the technique of the individual operator. Vigorous and prolonged mixing, or spreading the mix thinly over the slab leads to accelerated setting whilst lowering the temperature of the mixing slab will prolong the setting time. Under any given set of conditions, however, the operator may

obtain a faster or slower setting of the paste by using the appropriate hardener. In general it will be found that the time required for the mixture to set, obtained by the use of Hardener 'S', will be approximately 3 to 4 times that obtained with Hardener 'F'.

Under conditions of high temperature and humidity, care should be taken to blend rapidly a small amount of Ledermix Cement powder (taking no more than 10 to 15 seconds) into 1 drop of Hardener with 2 or 3 strokes of the spatula. All of the resultant mix should then be taken up at once on the spatula blade.

Contra-indications, warnings, etc

Contra-indications: Ledermix is contra-indicated in instances of total purulent pulpitis.

Precautions: The suppression of the inflammatory process by the use of a corticosteroid may result in a temporary reduction of the resistance of the pulp to infection. Therefore, Ledermix Paste should not be in contact with the exposed pulp for too long. If the application of this water-soluble preparation is uncontrolled, or if the temporary filling fits loosely, the danger exists that the pulp may not survive. The tip of the Ledermix Paste tube should always be kept clean and tightly closed after use. Store in a cool place.

The Ledermix Cement Vial must be kept tightly closed after use.

If severe reactions or idiosyncrasies are encountered the filling should be removed and appropriate measures instituted.

Side-effects: Since Ledermix is only administered locally, and the various constituents are drained from the site in minute amounts over a long period of time, the possibility of systemic side-effects is remote. Local side reactions are limited to paradental effects.

Pharmaceutical precautions The product should be stored in a cool place in the original pack. Each container must be kept tightly closed.

Legal category POM.

Package quantities *Ledermix Combination Kit:* 2 g bottle of cement powder.

5.0 ml bottle with separate dropper of Hardener 'F' (fast setting time).

5.0 ml bottle with separate dropper of Hardener 'S' (slow setting time).

3 g tube of Ledermix Paste.

Ledermix Refill Kit No. II:

5 g Ledermix Paste.

Ledermix Refill Kit No. III:

3 g Ledermix Powder.

Ledermix Refill Kit No. IV:

5 ml bottle with separate dropper of Hardener 'F'.

Ledermix Refill Kit No. V:

5 ml bottle with separate dropper of Hardener 'S'.

Further information Nil.

Product licence number 0095/5014.

LEDERMYCIN*

Presentation *Capsules 150 mg:* Each two-piece dark red/pale red hard shell capsule printed Lederle 9282 contains 150 mg of demeclocycline hydrochloride.

Tablets 300 mg: Each red, film-coated tablet printed Lederle 9157 contains 300 mg of demeclocycline hydrochloride.

Syrup 75 mg/5 ml: Each 5 ml of rose-red suspension contains demeclocycline equivalent to demeclocycline hydrochloride 75 mg.

Drops Aqueous 60 mg/ml: Each ml yellow suspension contains demeclocycline equivalent to demeclocycline hydrochloride 60 mg or 3 mg per drop.

Uses

1. A broad-spectrum antibiotic indicated for the treatment of infective conditions due to demeclocycline-sensitive organisms. Typical indications include: Ear, nose and throat infection. Acute and chronic bronchitis. Pneumonia. Venereal diseases. Non-gonococcal urethritis. Gastro-intestinal infections. Urinary tract infections. Soft tissue infections. Acne. Pre- and post-operative prophylaxis of infection, and other infections caused by Ledermycin-sensitive organisms.

2. For the treatment of chronic hyponatraemia associated with the syndrome of inappropriate secretion of antidiuretic hormone (SIADH); where water restriction is ineffective.

Dosage and administration

1. *For antibiotic use: Adults (Capsules, Tablets, Syrup):* 600 mg daily in two or four divided doses. For primary atypical pneumonia the average daily dose is 900 mg in 3 divided doses for six days.

Children (Syrup and Drops) (also adults):

Dosage of Ledermycin			
Age	Weight (kg)	Total mg/day	Dosage
Syrup			
5-9 years	20-30	120-180	5 ml twice daily
	35-40	210-240	5 ml three times daily
9-15 years	45	270	5 ml four times daily
	(Adults)	600	10 ml four times daily
Drops Aqueous			
under 1 year	5	30	5 drops twice daily
1-5 years	10	60	5 drops four times daily
	15	90	8 drops four times daily
	20	120	10 drops four times daily

2. *For the treatment of chronic hyponatraemia due to SIADH. (Adults only):* Initially: 900-1,200 mg daily in divided doses. Maintenance dose: 600-900 mg daily in divided doses.

Ledermycin Drops Aqueous may be administered with small amounts of water or fruit juices. Ledermycin should be taken an hour before or two hours after meals and antibiotic therapy should be continued for one to three days after characteristic symptoms or fever have subsided. The incidence of rheumatic fever or glomerulonephritis following streptococcal infections suggests that therapy of a streptococcal infection should be continued for eight full days even though symptoms have subsided.

Ledermycin therapy in the treatment of chronic hyponatraemia due to SIADH should not be withdrawn without commencing other methods of control.

Contra-indications, warnings, etc

Contra-indications: A history of hypersensitivity to tetracyclines. Overt renal insufficiency. Systemic lupus erythematosus.

Warnings: Tetracyclines may cause a yellow to brown discoloration of the teeth in the developing foetus or child and therefore Ledermycin should only be administered if considered essential to pregnant women and young children under eight years of age. Ledermycin should be used with caution in patients with renal or hepatic dysfunction, or in conjunction with other potentially hepatotoxic drugs. Cross-resistance between tetracyclines may develop in micro-organisms and cross-sensitisation in patients. The treatment of chronic hyponatraemia may necessitate the administration of high doses of Ledermycin for prolonged periods, so increasing the potential for nephrotoxicity (manifested by rises in plasma urea and creatinine) and photo-allergic reactions.

Precautions: Absorption of Ledermycin is impaired by the concomitant administration of calcium, magnesium, iron and particularly aluminium salts commonly used as antacids. Tetracyclines depress plasma prothrombin activity therefore reduced dosages of concurrent anticoagulants may be required. Lower doses are indicated in cases of renal impairment to avoid excessive systemic accumulation, and if therapy is prolonged, serum level determinations are advisable.

Side-effects: Nausea, diarrhoea and dermatitis may occur, and, as with all antibiotics, overgrowth of resistant organisms may cause glossitis, stomatitis, vaginitis or staphylococcal enterocolitis. Ledermycin has the greatest potential of the tetracycline analogues for causing photo-allergic reactions in hypersensitive persons. Such patients should be warned to avoid direct exposure to natural or artificial sunlight and to discontinue therapy at the first sign of skin discomfort. Occurrences of enamel hypoplasia have been reported. Rarely, increased intracranial pressure with bulging fontanelles has been observed in infants which disappears rapidly upon cessation of treatment. Rare cases of anaphylactoid reactions have been reported.

Overdosage: No specific antidote. Gastric lavage plus oral administration of milk or antacids.

Pharmaceutical precautions Ledermycin Capsules and Tablets should be stored at room temperature and Ledermycin Syrup and Drops Aqueous in a cool place, in either the original pack or in containers which prevent access of light and moisture. Dilution of Ledermycin Syrup or Drops Aqueous is not recommended as it will affect the stability of the products.

Legal category POM.

Package quantities *Capsules 150 mg:* Bottles of 20 and 100.

Tablets 300 mg: Bottles of 20 and 100.

Syrup 75 mg/5 ml: Bottles of 100 ml and 500 ml.

Drops Aqueous 60 mg/ml: Bottles of 10 ml with calibrated dropper.

Further information Ledermycin Syrup contains 0.232 millimole of sodium per 5 ml. Ledermycin Drops contain 0.069 millimole of sodium per 1 ml.

Product licence numbers

Capsules 150 mg	0095/0052
Tablets 300 mg	0095/5044
Syrup 75 mg/ml	0095/5048
Drops Aqueous 60 mg/ml	0095/5047

LEDERPLEX*

Presentation Each 5 ml of dark orange liquid contains:

Thiamine hydrochloride (B_1) 2.0 mg
 Riboflavin (B_2) 2.0 mg
 Niacinamide 10.0 mg
 Pyridoxine hydrochloride (B_6) 0.2 mg
 Pantothenic acid (as Panthanol) 2.0 mg
 Choline 20.0 mg
 Inositol 10.0 mg
 Soluble liver fraction 470.0 mg
 Cyanocobalamin USP (B_{12}) 5 mcg
 Flavoured with natural orange.

Uses For supplemental administration where it is suspected that the diet is deficient in one or more of the B complex factors.

Dosage and administration *Adults:* 10 ml daily.

Children and infants: According to age as recommended by the physician. Unless acid formulae are being used, Lederplex Liquid should not be added to milk formulae for infants as the lactic acid used as a stabilising agent will cause the milk to curdle.

Contra-indications, warnings, etc Contra-indications, precautions, side-effects and overdosage do not apply.

Pharmaceutical precautions Lederplex Liquid should be stored at room temperature in either the original pack or in a container which prevents access of light and air.

Legal category GSL.

Package quantities Bottles of 100 ml.

Further information Lederplex Liquid contains 0.035 millimole of sodium per 5 ml.

Product licence number 0095/5064.

LEDERSPAN* INJECTION 20 mg/ml**LEDERSPAN* INJECTION 5 mg/ml**

Presentation *Suspension 20 mg/ml:* Vials containing a sterile suspension of 20 mg or 100 mg of micronised triamcinolone hexacetonide in 1 ml or 5 ml respectively of an aqueous vehicle with 0.9% benzyl alcohol as a preservative.

Suspension 5 mg/ml: Vials containing 25 mg of micronised triamcinolone hexacetonide in 5 ml of an aqueous vehicle with 0.9% benzyl alcohol as a preservative.

Uses Triamcinolone hexacetonide is a relatively insoluble corticosteroid (0.0003% at 25°C in water). It has a prolonged effect on tissue at the local injection site, the duration usually ranging from a few weeks to several months.

Lederspan 20 mg/ml (*for intra-articular and intra-synovial administration*) is indicated in the treatment of rheumatoid arthritis; osteoarthritis; traumatic arthritis; gouty arthritis; synovitis and bursitis; fibrositis, tendinitis, and epicondylitis; intermittent hydrarthrosis; and other

subacute or chronic diseases where glucocorticoids can be expected to be useful.

Lederspan 5 mg/ml (*for intralesional and sublesional administration*) is indicated in the treatment of cystic acne; alopecia areata, nummular and dyshidrotic eczema; granuloma annulare; keloids; lichen planus; discoid lupus erythematosus; localised neurodermatitis; prurigo nodularis; and psoriasis of the nails.

Dosage and administration *Adults and children:* For intra-articular and intrasynovial use, 2–30 mg (0.1–1.5 ml), depending on the size of the joint (or synovial space) to be injected, the degree of inflammation and the amount of fluid present. In general, large joints (such as knee, hips, shoulder), require 10–30 mg whereas small joints (such as interphalangeal, metacarpophalangeal) require 2–6 mg. When much synovial fluid is present, aspiration may be performed before administering Lederspan. Subsequent dosage and frequency of injection can best be judged by clinical response. Since Lederspan provides prolonged activity, injections into a single joint or synovial space more frequently than every three to four weeks are not recommended. Repeated intra-articular injections should be as infrequent as possible, consistent with adequate patient care.

For intralesional and sublesional use, the dosage is 0.5 mg or less per square inch of affected skin.

Strict asepsis is mandatory during administration. Topical ethyl chloride spray may be used locally before injection. Since micronised triamcinolone hexacetonide has been designed for ease of administration, a small-bore needle (including 25 or 26 gauge needles) may be used. The vial should be gently agitated to achieve uniform suspension before each use.

The optimum dilution (see under 'Pharmaceutical precautions') should be determined according to the nature of the lesion, its size, the depth of the injection, the volume needed, and the location of the lesion. In general, more superficial injections should be accomplished with more dilution. Certain conditions, such as keloids, require a less dilute suspension. Subsequent dose, dilution and frequency of injection should be determined on the basis of the clinical response. With the 20 mg/ml suspension, concentrations stronger than 1:4 should not be used intralesionally, since local subcutaneous atrophy may result.

Lederspan may be administered by Dermojet and the Porton Injector.

Contra-indications, warnings, etc

Contra-indications: Although active, latent or questionably healed tuberculosis, ocular herpes simplex and acute psychosis are generally considered to be absolute contra-indications to glucocorticoid therapy, the minimal systemic activity of triamcinolone hexacetonide after local injection might permit cautious use when indicated. The drug should not be used when there is history of hypersensitivity to any of the components of the formulation or when previous injections have produced local atrophy. Infected joints should not be injected with corticosteroids.

As with other glucocorticoid agents, relative contra-indications are active peptic ulcer, acute glomerulonephritis, myasthenia gravis, osteoporosis, fresh intestinal anastomoses, diverticulitis, thrombophlebitis, psychic disturbances, pregnancy, diabetes mellitus, hyperthyroidism, acute coronary artery disease, hypertension, limited cardiac reserve and local or systemic infections, including fungal and exanthematous diseases. The minimal systemic activity of this preparation, however,

reduces the risks involved in its use in the presence of these conditions.

Precautions and side-effects: As with all glucocorticoids, an exacerbation of symptoms or 'flare-up' may occur following intra-articular or intrasynovial injections. Local atrophy, burning, flushing, pain and swelling may occur. In addition, prolonged and repeated use in weight-bearing joints may result in further joint degeneration. This is probably related to premature use of still-diseased joints following relief of pain and other symptoms. Not more than two or three large joints should be treated simultaneously in the same patient.

In treating conditions such as tendinitis or tenosynovitis care should be taken that Lederspan is injected into the space between tendon sheath and tendon and not into the tendon itself.

Overdosage or excessive frequency of intralesional injections into the same site may produce local subcutaneous atrophy. If this occurs, recovery may be delayed for several months because of the prolonged action of the drug. Other local effects include abscess, erythema, pain, swelling and necrosis at the injection site.

Systemic effects are rare with Lederspan due to its slow release from the injection site. In addition to those common to all glucocorticoids, some effects particularly associated with triamcinolone therapy are anorexia, myopathy and depression of mood.

If severe reactions occur or an acute infection develops during therapy, use of the drug should be discontinued and appropriate measures taken.

Pharmaceutical precautions Lederspan should be stored at room temperature. Do not freeze.

It may be diluted with Water for Injections BP, Sodium Chloride Injection BP, Sodium Chloride and Dextrose Injection BP, Lignocaine Hydrochloride Injection BP, immediately prior to injection.

Fluids containing methyl or propyl hydroxybenzoates or phenol should be avoided since these tend to cause flocculation of the steroid.

Legal category POM.

Package quantities 20 mg/ml: Single vials containing 20 mg in 1 ml or 100 mg in 5 ml.

5 mg/ml: Single vials containing 25 mg in 5 ml.

Further information Nil.

Product licence numbers

Lederspan 20 mg/ml 0095/0008

Lederspan 5 mg/ml 0095/0009

LEUCOVORIN – see Calcium Leucovorin.

METHOTREXATE TABLETS METHOTREXATE INJECTION METHOTREXATE POWDER FOR INJECTION

Presentation *Tablets 2.5 mg:* Round, convex, scored, uncoated, yellow tablets embossed 'M1' and containing 2.5 mg of Methotrexate per tablet.

Tablets 10 mg: Round, convex, plain, uncoated, mottled, light orange tablets containing 10 mg of Methotrexate per tablet.

Injection: A clear, yellow, sterile, aqueous, isotonic solution containing Methotrexate Sodium equivalent to 2.5 mg, 5 mg, 25 mg, 50 mg or 250 mg of Methotrexate per ampoule together with sodium chloride and sodium

hydroxide to adjust the pH to approximately 8.5. This presentation does not contain parabens or any other preservatives.

Powder for Injection 50 mg: Vials containing a yellow, lyophilised powder of Methotrexate sodium equivalent to 50 mg of Methotrexate, methylparaben 3.2 mg, propylparaben 0.8 mg, sodium chloride and sodium hydroxide to adjust the pH of the solution (when reconstituted with 2 ml of water for injection) to approximately 8.4. *Because parabens preservative may cause neurotoxicity this presentation is unsuitable for intrathecal or intraventricular administration.*

Powder for Injection 500 mg and 1 g: Vials containing a yellow, lyophilised powder of Methotrexate sodium equivalent to 500 mg or 1 g of Methotrexate, which is reconstituted before use with 10 ml or 20 ml of water for injection respectively. This presentation does not contain parabens or any other preservatives.

Uses *Properties:* Methotrexate, a derivative of folic acid, belongs to the class of cytotoxic agents known as antimetabolites. It acts principally during the 'S' phase of cell division, by the competitive inhibition of the enzyme dihydrofolate reductase, thus preventing the reduction of dihydrofolate to tetrahydrofolate, a necessary step in the process of DNA synthesis and cellular replication.

Indications: The treatment of neoplastic disease. The treatment of severe cases of uncontrolled psoriasis, unresponsive to conventional therapy.

Dosage and administration *Adults and children:* Methotrexate may be given by oral, intramuscular, intravenous (bolus injection or infusion) intrathecal, intra-arterial and intraventricular routes of administration. Dosages are based on the patient's body weight or surface area except in the case of intrathecal or intraventricular administration when a maximum dose of 15 mg is recommended. Doses should be reduced in cases of haematological deficiency and hepatic or renal impairment. Larger doses (greater than 100 mg) are usually given by intravenous infusion over periods not exceeding 24 hours. Part of the dose may be given as an initial rapid intravenous injection.

All parenteral Methotrexate preparations are stable for at least 24 hours when diluted with the following infusion fluids:—Normal Sodium Chloride. Dextrose. Sodium Chloride and Dextrose. Compound Sodium Chloride (Ringers Injection). Compound Sodium Lactate (Lactated Ringers Injection). Dextran. Dextran in Sodium Chloride. Dextran in Dextrose.

Methotrexate has been used with beneficial effects in a wide variety of neoplastic diseases, alone and in combination with other cytotoxic agents, hormones, immunotherapy, radiotherapy or surgery. Dosage schedules therefore vary considerably, depending on the clinical use, particularly when intermittent high-dose regimes are followed by the administration of Calcium Leucovorin (calcium folinate) in order to rescue normal cells from toxic effects.

Dosage regimes for Calcium Leucovorin rescue are discussed under Further Information.

Examples of doses of Methotrexate that have been used for particular indications are given below.

Choriocarcinoma and other trophoblastic tumours: Non-metastatic gestational trophoblastic neoplasms have been treated successfully with 0.25–1 mg/kg up to a maximum of 60 mg intramuscularly every 48 hours for four doses, followed by Calcium Leucovorin rescue. This course of treatment is repeated at seven day intervals

until levels of urinary chorionic gonadotrophin hormone return to normal. Not less than four courses of treatment are usually necessary. Patients with complications, such as extensive metastases, may be treated with Methotrexate in combination with other cytotoxic drugs.

Methotrexate has also been used in similar doses for the treatment of hydatidiform mole and chorio-adenoma destruens.

Leukaemia in children: Remissions in acute lymphocytic leukaemia are usually best induced with a combination of corticosteroids and other cytotoxic agents.

Methotrexate 15 mg/m², given parenterally or orally once weekly, in combination with other drugs appears to be the treatment of choice for the maintenance of drug-induced remissions.

Meningeal leukaemia in children: The cerebro-spinal fluid (CSF) should be examined in all leukaemic patients in order to diagnose leukaemic invasion of the central nervous system. Doses up to 15 mg, intrathecally, at weekly intervals, until the CSF appears normal (usually 2–3 weeks), have been found useful for the treatment of meningeal leukaemia. It is now common practice because of the frequency of meningeal leukaemia to administer Methotrexate intrathecally, in similar doses, as prophylaxis in all cases of lymphocytic leukaemia.

Although intravenous doses of the order of 50 mg of Methotrexate do not appreciably penetrate the CSF, larger doses of the order of 500 mg/m² do produce cytotoxic levels of Methotrexate in the CSF. This type of therapy has been used in short courses, followed by administration of Calcium Leucovorin, as initial maintenance therapy to prevent leukaemic invasion of the central nervous system in children with poor prognosis lymphocytic leukaemia.

Lymphoma: Non-Hodgkin's lymphoma, e.g. childhood lymphosarcoma has recently been treated with 3–30 mg/kg (approximately 90–900 mg/m²) of Methotrexate given by intravenous injection and infusion followed by administration of Calcium Leucovorin with the higher doses. Some cases of Burkitt's lymphoma, when treated in the early stages with courses of 15 mg/m² daily for five days have shown prolonged remissions. Combination chemotherapy is also commonly used in all stages of the disease and a course of 15 mg/day of Methotrexate intrathecally for four days has been found useful for controlling episodes of invasion of the central nervous system.

Breast cancer: Methotrexate, in intravenous doses of 10–60 mg/m², is commonly included in cyclical combination regimes with other cytotoxic drugs in the treatment of advanced breast cancer. Similar regimes have also been used as adjuvant therapy in early cases following mastectomy and/or radiotherapy.

Osteogenic sarcoma: The use of Methotrexate alone and in cyclical combination regimes has recently been introduced as an adjuvant therapy to the primary treatment of osteogenic sarcoma by amputation with or without prosthetic bone replacement. This has involved the use of intravenous infusions of 20–300 mg/kg (approximately 600–9,000 mg/m²) of Methotrexate followed by Calcium Leucovorin rescue. Methotrexate has also been used as the sole treatment in metastatic cases of osteogenic sarcoma.

Bronchogenic carcinoma: Intravenous infusions of 20–100 mg/m² of Methotrexate have been included in cyclical combination regimes for the treatment of

advanced tumours. High doses with Calcium Leucovorin rescue have also been employed as the sole treatment.

Head and neck cancer: Intravenous infusions of 240–1,080 mg/m² with Calcium Leucovorin rescue have been used recently with encouraging results both as pre-operative adjuvant therapy and in the treatment of advanced tumours. Intra-arterial infusions of Methotrexate are indicated for certain head and neck cancers although this route of administration is not now used extensively.

Bladder carcinoma: Intravenous injections or infusions of Methotrexate in doses up to 100 mg every one to two weeks have been used in the treatment of bladder carcinoma with promising results, varying from only symptomatic relief to complete though unsustained regressions. Diuretics and hydration are employed in an attempt to reduce the excessive drug toxicity that has occurred in cases with renal impairment. The use of higher doses of Methotrexate with Calcium Leucovorin rescue is currently being evaluated.

Psoriasis: In cases of severe uncontrolled psoriasis, unresponsive to conventional therapy, 10–25 mg orally once a week and adjusted by the patient's response is recommended.

Particular attention should be given to the appearance of liver toxicity by carrying out liver function tests before starting Methotrexate treatment and repeating these at two to four month intervals during therapy. Treatment should not be instituted or should be discontinued if any abnormality of liver function tests, or liver biopsy, is present or develops during therapy.

Such abnormalities should return to normal within two weeks after which treatment may be recommenced at the discretion of the physician.

The use of Methotrexate may permit the return to conventional topical therapy which should be encouraged.

Contra-indications, warnings, etc

Contra-indications: Profound impairment of renal or hepatic function. Serious cases of anaemia, leucopenia, or thrombocytopenia. Pregnancy.

Warnings: Methotrexate should not normally be administered to patients who are pregnant or to mothers who are breast-feeding. Methotrexate has been shown to be teratogenic. Methotrexate should be used with extreme caution in patients with haematological depression, renal impairment, peptic ulcer, ulcerative colitis, ulcerative stomatitis, diarrhoea, debility and in extreme youth or old age.

Symptoms of gastro-intestinal toxicity, usually first manifested by stomatitis, indicates interruption of therapy otherwise haemorrhagic enteritis and death from intestinal perforation may occur.

Methotrexate affects spermatogenesis and oogenesis during the period of its administration which may result in decreased fertility. To date this effect appears to be reversible on discontinuing therapy. Conception should be avoided for at least six months after treatment with Methotrexate has ceased. Patients receiving Methotrexate and their partners should be advised appropriately.

Methotrexate has some immunosuppressive activity and therefore the immunological response to concurrent vaccination may be decreased. In addition, concomitant use of a live vaccine could cause a severe antigenic reaction.

Precautions: Methotrexate should only be used by clinicians who are familiar with the various characteristics of the drug and its established clinical usage. It is essential that the following laboratory tests are included as part of the clinical evaluation and monitoring of patients receiving Methotrexate: complete haematological analysis, urinalysis, renal function tests, liver function tests and, when high doses are administered, determination of plasma levels of Methotrexate. These tests should be performed prior to, during and after termination of each course of therapy.

Haemopoietic suppression caused by Methotrexate may occur abruptly and with apparently safe dosages. Any profound drop in white-cell or platelet counts indicates immediate withdrawal of the drug and appropriate supportive therapy.

It should be noted that intrathecal doses are transported into the cardiovascular system and may give rise to unexpected systemic toxicity, as can the use of Methotrexate in patients with renal dysfunction, ascites, or other effusions due to a longer serum half-life.

High doses may cause the precipitation of Methotrexate or its metabolites in the renal tubules. Alkalinisation of the urine to pH 6.5–7.0 by the oral or intravenous administration of sodium bicarbonate (5 × 625 mg tablets every three hours) or Diamox (500 mg orally four times a day) is recommended as a preventative measure.

Drug interactions: Methotrexate is extensively protein bound and may be displaced by certain drugs such as salicylates, sulphonamides, diuretics, hypoglycaemics, diphenylhydantoins, tetracyclines, chloramphenicol, p-aminobenzoic acid, and the acidic anti-inflammatory agents, so causing a potential for increased toxicity when used concurrently. Concomitant use of other drugs with nephrotoxic or hepatotoxic potential (including alcohol) should be avoided.

Side-effects: These occur as a result of cytotoxic activity on rapidly reproducing normal cells of the haemopoietic system, gastro-intestinal tract, and sometimes skin. Consequently common adverse reactions are bone-marrow depression, leucopenia, anaemia, thrombocytopenia, nausea, vomiting, diarrhoea and ulcerative stomatitis. Upon prolonged treatment erythematous rashes, hepatic cirrhosis, acute liver atrophy and genitourinary toxicity manifested by renal failure, severe nephropathy, defective oogenesis or spermatogenesis may occur.

Adverse effects upon the central nervous system that may occur following intrathecal or intraventricular administration are headache, drowsiness, blurred vision, transient paresis, ataxia, and rarely, dementia and major convulsions. Other reactions such as pneumonitis, osteoporotic effects and photosensitivity have been attributed to the use of Methotrexate.

Overdosage: Calcium Leucovorin is the antidote for neutralising the immediate toxic effects of Methotrexate on the haemopoietic system. It may be administered orally, intramuscularly, or by an intravenous bolus injection or infusion. In cases of accidental overdosage, a dose of Calcium Leucovorin equal to or higher than the offending dose of Methotrexate should be administered within one hour and further doses as required. Other supporting therapy such as a blood transfusion and renal dialysis may be required.

Pharmaceutical precautions Methotrexate Powder for Injection 50 mg should be reconstituted with 2 ml of water for injection before use. Reconstituted solutions

may be stored at room temperature for two weeks. However, if a precipitate forms, the solution should be discarded.

Methotrexate Powder for Injection 500 mg and 1 g should be reconstituted immediately before use with 10 ml or 20 ml of water for injection respectively. The appropriate dose of the resulting solution (50 mg/ml) is then diluted for administration by intravenous infusion over periods not exceeding 24 hours. Part of the dose may be given by an initial bolus intravenous injection. Reconstituted solutions do not contain any preservative and therefore any unused injection should be discarded.

All parenteral Methotrexate preparations are stable for at least 24 hours when diluted with the following infusion fluids:—Normal Sodium Chloride. Dextrose. Sodium Chloride and Dextrose. Compound Sodium Chloride (Ringers Injection). Compound Sodium Lactate (Lactated Ringers Injection). Dextrans. Dextrans in Sodium Chloride. Dextrans in Dextrose.

Methotrexate preparations should be protected from direct sunlight. Other drugs should not be mixed with Methotrexate in the same infusion container.

The labels of the various strengths of Methotrexate Injection are colour-coded: blue for 2.5 mg and 5 mg/ampoule (2.5 mg/ml) and red for 25 mg, 50 mg and 250 mg/ampoule (25 mg/ml).

Legal category POM.

Package quantities

Tablets 2.5 mg: Bottles of 100.

Tablets 10 mg: Bottles of 100.

Injection 2.5 mg/ampoule: Boxes of 10 by 1 ml ampoules.

Injection 5 mg/ampoule: Boxes of 5 by 2 ml ampoules.

Injection 25 mg/ampoule: Boxes of 1 by 1 ml ampoule.

Injection 50 mg/ampoule: Boxes of 1 by 2 ml ampoule.

Injection 250 mg/ampoule: Boxes of 1 by 10 ml ampoule.

Powder for Injection 50 mg/vial: Boxes of 1 vial.

Powder for Injection 500 mg or 1 g/vial: Boxes of 1 vial.

Further information Dosage regimes for Calcium Leucovorin rescue vary, depending upon the dose of Methotrexate administered. In general, up to 120 mg are usually given in divided doses, over 12–24 hours, by intramuscular injection, bolus intravenous injection or intravenous infusion in normal saline, followed by 12–15 mg intramuscularly, or 15 mg (1 tablet) orally, every six hours for the next 48 hours. Rescue therapy is usually started following a delay, of up to 24 hours, from the beginning of the Methotrexate infusion. One tablet (15 mg) of Calcium Leucovorin every six hours for 48–72 hours may be sufficient when lower doses (less than 100 mg) of Methotrexate have been given.

Calcium Leucovorin is available as an injection (3 mg/ml) in 1 ml ampoules, as a vial of powder for injection (30 mg) and as tablets (15 mg) in bottles of 10.

The clinical use of high doses of Methotrexate with Calcium Leucovorin rescue in the treatment of a wide variety of previously resistant tumours remains the subject of intense research. Further information on other formulations of Methotrexate, on results with particular cyclical regimes of combinations of cytotoxic drugs and any other aspects of cancer chemotherapy with Methotrexate is available on request.

Product licence numbers

Tablets 2.5 mg	0095/5079
Tablets 10 mg	0095/0060
Injection 2.5 mg and 5 mg/ampoule	0095/0015
Injection 25 mg, 50 mg, and 250 mg/ampoule	0095/0016
Powder for Injection 50 mg/vial	0095/5082
Powder for Injection 500 mg/vial	0095/0054
Powder for Injection 1 g/vial	0095/0055

MINOCIN®

Presentation *Tablets 100 mg:* Each orange, film-coated tablet, printed 'Lederle 5334' contains Minocycline hydrochloride equivalent to 100 mg Minocycline base.

Tablets 50 mg: Each plain beige film-coated tablet contains Minocycline hydrochloride equivalent to 50 mg Minocycline base.

Uses Minocycline is a broad spectrum antibiotic used for the treatment of infections caused by tetracycline-sensitive organisms. Some tetracycline-resistant strains of *Staphylococci* are also sensitive.

Typical indications include: Gonorrhoea. Non-gonococcal urethritis. Prostatitis. Acne. Acute and chronic bronchitis. Bronchiectasis. Lung abscess. Pneumonia. Ear nose and throat infections. Urinary tract infections. Salpingitis. Skin and soft tissue infections. Ophthalmological infections. Nocardiosis. Prophylactic treatment of asymptomatic meningococcal carriers. Pre- and post-operative prophylaxis of infection.

Dosage and administration *Adults:*

1. Routine antibiotic use: 200 mg initially followed by 200 mg daily in divided doses.
2. Acne: Initially 100–200 mg daily in single or divided doses. Average Maintenance Dose: 50 mg twice daily.
3. Gonorrhoea: In adult males, 300 mg as a single dose. Adult females may require more prolonged therapy.
4. Prophylaxis of asymptomatic meningococcal carriers: 100 mg b.i.d. for five days, usually followed by a course of rifampicin.

Children: Safety for use in children under 13 years of age has not been established.

Administration: Unlike earlier tetracyclines, absorption of Minocin is not significantly impaired by food or moderate amounts of milk. A normal course of treatment for acute bacterial infections is four days. In more severe infections, treatment should be continued for up to three days after characteristic symptoms of the infection have subsided. Because of the incidence of rheumatic fever or glomerulonephritis following streptococcal infection, therapy should be continued for 10 days even though symptoms have subsided.

Treatment of acne should be continued for a minimum of six weeks.

Contra-indications, warnings, etc

Contra-indications: Known hypersensitivity to tetracyclines. Systemic lupus erythematosus.

Warnings: Tetracyclines may cause a yellow to brown discoloration of the teeth and enamel hypoplasia in the developing foetus or child and therefore Minocin should only be administered if considered essential to pregnant or lactating women and to children under eight years of age.

Minocin should be used with caution in patients with

hepatic dysfunction and in conjunction with alcohol or other potentially hepatotoxic drugs. Cross-resistance between tetracyclines may develop in micro-organisms and cross-sensitisation in patients.

Precautions: Clinical studies have shown that there is no significant drug accumulation in patients with renal impairment when they are treated with Minocin in the recommended doses. In cases of extreme renal insufficiency, reduction of dosage and monitoring of renal function may be required.

Tetracyclines depress plasma prothrombin activity and reduced doses of concomitant anticoagulants may be necessary.

Absorption of Minocin is impaired by the concomitant administration of iron salts and by antacids containing calcium, magnesium and aluminium salts.

Side-effects: Gastro-intestinal disturbances may occur and as with all antibiotics overgrowth of resistant organisms may cause glossitis, stomatitis, vaginitis or staphylococcal enteritis. Photo-sensitivity and dermatological reactions are rare.

Lightheadedness, dizziness and vertigo have occurred with Minocin and patients should be warned about the possible hazards of driving or operating machinery during treatment.

Overdosage: No specific antidote. Gastric lavage plus appropriate supportive treatment.

Pharmaceutical precautions The product should be stored under normal room temperature conditions in the original pack or in containers which prevent access of moisture.

Legal category POM.

Package quantities *100 mg Tablets:* Bottles of 20 and 50.

50 mg Tablets: Bottles of 100.

Further information Nil.

Product licence numbers

100 mg Tablets	0095/0006
50 mg Tablets	0095/0062

MYAMBUTOL®

Presentation *Tablets 100 mg:* Each yellow, coated tablet contains 100 mg ethambutol hydrochloride.

Tablets 400 mg: Each grey, coated tablet contains 400 mg ethambutol hydrochloride.

Powder: Each bottle contains 50 g ethambutol hydrochloride.

Uses The primary treatment and re-treatment of tuberculosis and for prophylaxis in cases of inactive tuberculosis or large tuberculin-positive reaction. Myambutol should only be used in conjunction with other antituberculous drugs to which the patient's organisms are susceptible.

Dosage and administration The dosage of Myambutol must be adjusted according to the body weight of the patient.

Adults: For primary treatment and prophylaxis: Myambutol should be administered in a single daily oral dose of 15 mg/kg, concomitant drugs being used at their recommended dosage levels.

For re-treatment: For the first 60 days of treatment, Myambutol should be administered in a single daily oral

dose of 25 mg/kg. Thereafter the dosage should be reduced to 15 mg/kg, concomitant drugs being maintained at their recommended dosage levels.

Children: For primary treatment and re-treatment: For the first 60 days of treatment, a single daily oral dose of 25 mg/kg. Thereafter the dosage should be reduced to 15 mg/kg, concomitant drugs being maintained at their recommended dosage levels.

For prophylaxis: A single daily oral dose of 15 mg/kg, concomitant drugs being used at their recommended dosage levels.

Administration: In order to obtain maximum effect due to high serum levels, drug administration should be once daily. Absorption of Myambutol is not significantly altered by administration with food.

Paediatric doses can be given using an extemporaneously prepared syrup (see Further Information).

A table of dosages is given below.

Dosage of Myambutol
15 mg/kg (7 mg/lb) schedule:

Weight range	kg	Total daily dose (mg)			
Children	8	120			
	17	255			
	25	375			
	33	495			
Adults			Number of tablets		
lb	kg		100 mg	400 mg	
85-94.5	38-42.5	600	2	+	1
95-109.5	43-49.5	700	3	+	1
110-124.5	50-56.5	800			2
125-139.5	57-63.5	900	1	+	2
140-154.5	64-70.5	1,000	2	+	2
155-169.5	71-78.5	1,100	3	+	2
170-184.5	79-83.5	1,200			3
185-199.5	84-89.5	1,300	1	+	3
200-214.5	90-96.5	1,400	2	+	3
215 and over	97 and over	1,500	3	+	3

25 mg/kg (11 mg/lb) schedule:

Weight range		kg	Total daily dose (mg)	
Children		5	125	
		10	250	
		15	375	
		20	500	
		25	625	
		30	750	
		35	875	
Adults			Number of tablets	
	lb	kg	100 mg	400 mg
	85-92.5	38-41.5	1,000	2 + 2
	93-101.5	42-44.5	1,100	3 + 2
	102-109.5	45-49.5	1,200	3
	110-118.5	50-53.5	1,300	1 + 3
	119-128.5	54-57.5	1,400	2 + 3
	129-136.5	58-61.5	1,500	3 + 3
	137-146.5	62-66.5	1,600	4
	147-155.5	67-70.5	1,700	1 + 4
	156-164.5	71-74.5	1,800	2 + 4
	165-173.5	75-78.5	1,900	3 + 4
	174-182.5	79-82.5	2,000	5
	183-191.5	83-86.5	2,100	1 + 5
	192-199.5	87-90.5	2,200	2 + 5
	200-209.5	91-94.5	2,300	3 + 5
	210-218.5	95-98.5	2,400	6
	219 and over	99 and over	2,500	1 + 6

Contra-indications, warnings, etc

Contra-indications: Myambutol is contra-indicated in patients who are known to be hypersensitive to the drug. It is also contra-indicated in patients with known optic neuritis unless clinical judgement determines that it may be used.

Precautions: Patients with decreased renal function may need to have the dosage adjusted as determined by blood levels of Myambutol. Animal studies with Myambutol have not demonstrated any teratogenic potential and there have been several reports of the drug having been administered during pregnancy without untoward effect. Nevertheless, it is recommended that the possibility of such effects should be kept in mind when treating women of child-bearing age.

Because this drug has a unique effect on the eye, it is recommended that patients undergo a full ophthalmic examination before starting treatment. This should include visual acuity, colour vision, perimetry and ophthalmoscopy. Many physicians consider that routine ophthalmological examination for adults is not thereafter necessary, but patients should be informed of the importance of reporting any change in vision. However, routine ophthalmological examinations may be considered desirable when treating young children.

Side-effects: Myambutol may produce a unique type of visual impairment which is generally reversible and which appears to be due to optic neuritis and to be related to dose and duration of treatment. Less than 1% of patients undergoing treatment with the higher dose regimen of 25 mg/kg/day for two months, and 15 mg/kg/day thereafter, have exhibited decrease in visual acuity. The change may be unilateral or bilateral and hence both eyes must be tested individually. The effects are generally reversible when administration of the drug is discontinued promptly. In rare cases recovery may be delayed for up to one year or more and the effect may possibly be irreversible in these cases.

Recovery of visual acuity has usually occurred over a period of weeks to months after the drug was discontinued, and patients have then received Myambutol at lower dosages without toxicity. Test patients receiving Myambutol as sole therapy did not have gastro-intestinal disturbances (e.g. anorexia, nausea, vomiting, diarrhoea), transient impairment of liver function or allergic reactions, although these have been noted during multiple-drug antituberculous therapy in which Myambutol was employed. Numbness and paraesthesia of the extremities have been reported.

Overdosage: No specific antidote, but gastric lavage should be employed if necessary.

Pharmaceutical precautions Myambutol should be stored at room temperature in either the original pack or in containers which prevent access of moisture.

Legal category POM.

Package quantities Myambutol 100 mg: Bottles of 100 and 500.

Myambutol 400 mg: Bottles of 100 and 500.

Powder: Bottles of 50 g.

Further information Details of a formulation for ethambutol syrup suitable for paediatric use are available on request from the Medical Information Department. A mixture of ethambutol syrup and isoniazid elixir BPC should not be prepared as isoniazid is unstable in the presence of sugars.

Product licence numbers

Myambutol 100 mg 0095/0002

Myambutol 400 mg 0095/0003

Myambutol Powder 50 g 0095/5083

MYNAH*

Presentation *Mynah 200*: Each white tablet coded 'Lederle 5033' contains 200 mg ethambutol hydrochloride plus 100 mg isoniazid.

Mynah 250: Each yellow tablet coded 'Lederle 5133' contains 250 mg ethambutol hydrochloride plus 100 mg isoniazid.

Mynah 300: Each orange tablet coded 'Lederle 5137' contains 300 mg ethambutol hydrochloride plus 100 mg isoniazid.

Mynah 365: Each pink tablet coded 'Lederle 5134' contains 365 mg ethambutol hydrochloride plus 100 mg isoniazid.

Uses The primary treatment and re-treatment of tuberculosis and for prophylaxis in cases of inactive tuberculosis or large tuberculin-positive reaction.

Dosage and administration *Adults*: Dosage of Mynah is gauged according to the patient's body weight, which governs the included amount of ethambutol; the dosage of isoniazid is standardised at 100 mg per tablet.

For primary treatment and prophylaxis: Mynah should be administered in a single daily oral dose such that the patient receives 15 mg/kg of ethambutol plus 300 mg isoniazid, concomitant drugs being used at their recommended dosage levels.

For re-treatment: For the first 60 days of treatment Mynah should be administered in a single daily oral dose such that the patient receives 25 mg/kg of ethambutol plus 300 mg of isoniazid, concomitant drugs being used

at their recommended dosage levels. Thereafter proceed as in 'Primary treatment' above.

Children: The quantities and proportions of the component drugs make Mynah tablets unsuitable for most children. (See Further Information).

Administration: In order to obtain maximum effect due to high serum levels, drug administration should be once daily. As absorption of isoniazid but not ethambutol is significantly reduced by administration with food, it is recommended that Mynah be taken on an empty stomach.

Contra-indications, warnings, etc

Contra-indications: Mynah is contra-indicated in patients who are known to be hypersensitive to ethambutol or isoniazid. It is also contra-indicated in patients with known optic neuritis unless clinical judgement determines that it may be used. Although no absolute contra-indications to the administration of isoniazid have been reported, care should be exercised in the administration of Mynah to epileptic patients since it may induce convulsions, or in psychotic states characterised by mania and hypomania, or in the presence of impaired renal function.

Precautions: Patients with decreased renal function may need to have the dosage adjusted as determined by blood levels of ethambutol. Animal studies with ethambutol have not demonstrated any teratogenic potential and there have been several reports of isoniazid or ethambutol having been administered during pregnancy without untoward effect. Nevertheless, it is recommended that the possibility of such effects should be kept in mind when treating women of childbearing age.

Because ethambutol has a unique effect on the eye, it is recommended that patients undergo a full ophthalmic examination before starting treatment. This should include visual acuity, colour vision perimetry and

Dosage of Mynah:

Table 1 Mynah tablets weight/dose schedule 15 mg/kg (7 mg/lb)

Body weight		Ingredients		Daily dose
lb	kg	INH mg	Ethambutol mg	
77-98	35-44.5	300	600	3 tablets Mynah 200
99-120	45-54.5	300	750	3 tablets Mynah 250
121-142	55-64.5	300	900	3 tablets Mynah 300
143-175	65-79.5	300	1095	3 tablets Mynah 365

Table 2 Mynah tablets weight/dose schedule 25 mg/kg (11 mg/lb)

Body weight		Ingredients		Daily dose	
lb	kg	INH mg	Ethambutol mg	Mynah	Myambutol
Under 77	Under 35	300	750	3 × 250	
77-83	35-37.8	300	900	3 × 300	
83.5-107	37.9-47	300	1095	3 × 365	
108-125	48-55	300	1300	3 × 300 + 1 × 400 mg	
126-143	56-63	300	1495	3 × 365 + 1 × 400 mg	
144-161	64-71	300	1700	3 × 300 + 2 × 400 mg	
162-180	72-79	300	1895	3 × 365 + 2 × 400 mg	
181-198	80-87	300	2100	3 × 300 + 3 × 400 mg	
199-216	88-94	300	2295	3 × 365 + 3 × 400 mg	
217-234	95-103	300	2500	3 × 300 + 4 × 400 mg	

ophthalmoscopy. Many physicians consider that routine ophthalmological examination is not thereafter necessary, but patients should be informed of the importance of reporting any change in vision.

Side-effects: *For ethambutol:* Ethambutol may produce a unique type of visual impairment which is generally reversible and which appears to be due to optic neuritis and to be related to dose and duration of treatment. Less than 1% of patients undergoing treatment with the higher dose regimen of 25 mg/kg/day for two months and 15 mg/kg/day thereafter, have exhibited decrease in visual acuity. The change may be unilateral or bilateral and hence both eyes must be tested individually. The effects are generally reversible when administration of the drug is discontinued promptly. In rare cases recovery may be delayed for up to one year or more and the effect may possibly be irreversible in these cases.

Recovery of visual acuity has usually occurred over a period of weeks to months after the drug is discontinued, and patients have then received ethambutol at lower dosages without toxicity. Test patients receiving ethambutol as sole therapy did not have gastro-intestinal disturbances (e.g. anorexia, nausea, vomiting, diarrhoea), transient impairment of liver function or allergic reactions, although these have been noted during multiple-drug antituberculous therapy in which ethambutol was employed. Numbness and paraesthesia of the extremities has been reported.

For isoniazid: Side-effects are infrequently encountered and are rarely serious. Peripheral neuritis is most often observed, and correlation exists between the dosage level and this reaction. When the dosage is 3 mg/kg/day, the incidence is approximately 1%; at 10 mg/kg/day, it rises to 15% or higher. Pyridoxine (vitamin B₆) has been used successfully for prophylaxis and treatment of isoniazid-induced peripheral neuritis.

Severe and sometimes fatal hepatitis associated with isoniazid therapy may occur and may develop even after many months of treatment. The risk of developing hepatitis is age related and is increased with daily consumption of alcohol.

CNS effects (insomnia, headache, restlessness, mental confusion, toxic psychoses, increased reflexes, muscle twitching, paraesthesia) may be encountered. Optic neuritis and optic atrophy have been reported. Ophthalmological examinations should be carried out wherever visual complaints occur, since the optic lesions are likely to be reversible if isoniazid is discontinued promptly. Extremely high dosages have produced convulsions in apparently normal individuals.

Urinary disturbances in the male (prostatic obstruction syndrome), constipation and dryness of the mouth have been reported. Allergic reactions occur infrequently. Agranulocytosis and exfoliative dermatitis have occasionally been reported.

Overdosage: No specific antidote, but gastric lavage should be employed if necessary.

Pharmaceutical precautions Mynah Tablets should be stored at room temperature, in either the original pack or in containers which prevent access of moisture.

Legal category POM.

Package quantities *Mynah 200:* Bottles of 84.

Mynah 250: Bottles of 84.

Mynah 300: Bottles of 84.

Mynah 365: Bottles of 84.

Further information The quantities and proportions of the component drugs make Mynah tablets unsuitable for most children. Details of a formulation of ethambutol syrup suitable for paediatric use are available on request from the Medical Information Department. A mixture of ethambutol syrup and isoniazid elixir BPC should not be prepared as isoniazid is unstable in the presence of sugars.

Product licence numbers

Mynah 200 0095/0044

Mynah 250 0095/0045

Mynah 300 0095/0046

Mynah 365 0095/0047

PARFENAC*

Presentation Cream. Each gram contains 50 mg ofufexamac in an aqueous base consisting of cetyl alcohol, glycerin, sodium lauryl sulphate with methylparaben as a preservative.

Uses Parfenac is a synthetic, non-steroidal agent with potent anti-inflammatory effects upon topical application. It is intended for topical use in the treatment of acute and chronic dermatoses; eczematous dermatitis; atopic dermatitis (disseminated neurodermatitis); lichen simplex (circumscribed neurodermatitis); contact dermatitis; nummular dermatitis; radiodermatitis; anogenital dermatitis; pruritus ani and vulvae; psoriasis; haemorrhoids and anal fissures.

In addition to the treatment of radiodermatitis, the cream can be used as a preventative in patients receiving deep radiotherapy with the result that the symptoms of radiodermatitis may be diminished in severity and duration.

Parfenac Cream is also useful as an adjuvant in the treatment of rheumatic and traumatic conditions. When it is applied by iontophoresis or ultrasound apparatus, good results have been obtained in contusions, haematomas, sprains, tendinitis, epicondylitis, bursitis, periarthritis of the shoulder (adhesive capsulitis), fibromyositis (for example, lumbago); sciatica and osteoarthritis. Satisfactory results in these conditions can sometimes be obtained also when the cream is applied by massage. Parfenac (bufexamac) has been used successfully in the treatment of various eczematous conditions. Its value in the treatment of psoriasis has, however, not been firmly established.

Dosage and administration *Adults and children:* In dermatoses, Parfenac Cream should be applied in small quantities to the affected areas two or three times daily. The cream should be rubbed in gently and thoroughly until it disappears. Since the cream base is water washable no stains on clothing will remain after washing. The duration of treatment varies according to the condition and its course, and can be prolonged if necessary without risk of adverse effects. An occlusive non-permeable dressing may be used if indicated, with the frequency of dressing change being determined on an individual basis.

In traumatic and rheumatic conditions, Parfenac Cream may be applied as follows:

- by iontophoresis, usually for a period of 20 minutes.
- by means of ultrasound apparatus, usually for a period of five minutes, or
- by massage (as a substitute for the conventional dermassage), usually for a period of 10 minutes.

The frequency of such applications and the duration of therapy are determined by the physician. In certain cases, particularly in rheumatic conditions, it may be desirable to combine the topical therapy with appropriate systemic therapy. If infection is present, an appropriate anti-infective agent should be prescribed.

Contra-indications, warnings, etc Parfenac is contra-indicated in patients with a history of hypersensitivity to any of its components.

Local intolerance to Parfenac Cream, as manifested by burning and irritation, is rare, and is attributable to components of the cream vehicle. Bufexamac itself has not been found to have a sensitising potential. When occlusive non-permeable dressings are used, miliaria, folliculitis and pyoderma may develop beneath the occlusive material. If such reactions occur the use of Parfenac should be discontinued.

Pharmaceutical precautions The product should be stored in a cool place. It is not recommended that the product be diluted as this may affect its stability.

Legal category POM.

Package quantities Tubes of 15 g and 30 g.

Further information Nil

Product licence number 0095/0010

PIPRIL* INJECTION ▼

Presentation Vials containing 1 g or 2 g of piperacillin as piperacillin sodium.

Infusion bottles containing 4 g of piperacillin as piperacillin sodium.

Each gram of Pipril contains 1.98 mEq (45.5 mg) of sodium.

Uses Pipril is a broad spectrum bactericidal penicillin antibiotic indicated for the treatment of infections caused by sensitive organisms.

Pipril is highly active against the following clinically important bacteria:

Gram-Negative:

<i>Acinetobacter</i> species	<i>Neisseria gonorrhoeae</i>
<i>Citrobacter</i> species	<i>Neisseria meningitidis</i>
<i>Enterobacter</i> species	<i>Proteus</i> sp. (indole positive and negative)
<i>Escherichia coli</i>	<i>Providencia</i> species
<i>Haemophilus influenzae</i>	<i>Pseudomonas aeruginosa</i>
<i>Klebsiella pneumoniae</i>	and other species
and other species	<i>Serratia marcescens</i> and other species
	<i>Shigella</i> species

Anaerobes:

<i>Bacteroides fragilis</i>	<i>Fusobacterium</i> species
<i>Bacteroides</i> species	<i>Peptococcus</i> species
<i>Clostridium</i> species	<i>Peptostreptococcus</i> species
	<i>Veillonella</i> species

Gram-Positive:

<i>Enterococci</i>	<i>Streptococcus</i>
<i>Staphylococcus</i> species (non- β -lactamase-producing)	<i>(Diplococcus) pneumoniae</i>
	<i>Streptococcus pyogenes</i>
	Other <i>Streptococcus</i> species

Because of its broad spectrum of activity, Pipril is indicated for the treatment of the following systemic

and/or local infections in which one or more susceptible organisms have been detected or are suspected.

Systemic infections including bacterial septicaemia and endocarditis.

Urogenital tract infections including gonorrhoea.

Respiratory tract infections.

Ear, nose and throat and oral cavity infections.

Intra-abdominal infections including those of the biliary tract.

Gynaecological and obstetric infections.

Skin and soft tissue infections including infected wounds and burns.

Bone and joint infections.

Proven or suspected infections in patients with impaired or suppressed immunological status.

Pipril acts synergistically with aminoglycosides. Concurrent therapy with both drugs given in full therapeutic doses may be used in the treatment of life-threatening infections or in patients with impaired immune status. Pipril and aminoglycosides should not, however, be mixed in the same solution but administered separately.

Pipril may be used in combination with β -lactamase resistant penicillins in proven or suspected mixed infections involving β -lactamase producing *Staphylococcus aureus*.

Pipril may be administered (separately) with metronidazole in the treatment of mixed aerobic/anaerobic infections.

Cefoxitin should not be given with Pipril when *Pseudomonas* infections are suspected or confirmed as *in vitro* data have shown possible antagonism. However, Pipril may be administered concomitantly with other β -lactam antibiotics provided that an additive or synergistic antibacterial action is first ascertained through *in vitro* tests where appropriate.

Dosage and administration Pipril may be given by slow intravenous injection, by intravenous infusion or by intramuscular injection.

Intravenous Injection: Each gram of Pipril should be reconstituted with at least 5 ml of Water for Injection and given by slow intravenous injection over three to five minutes.

Intravenous Infusion: Each gram of Pipril should be reconstituted with at least 5 ml Water for Injection. The total dose should then be further diluted to at least 50 ml before infusion over 20-40 minutes. Suitable diluents are listed under Pharmaceutical Precautions.

Intramuscular Injection: Each gram of Pipril should be reconstituted with at least 2 ml of Water for Injection or 0.5% lignocaine. Administration should be by deep intramuscular injection. A single dose in adults should not exceed 2 g. A single dose in children should not exceed 0.5 g.

Adult dosage: Patients with normal renal function: Serious and complicated infections: 200-300 mg/kg/day. The usual dose is therefore 4 g every six or eight hours by IV administration. In life-threatening infections, particularly those caused by *Pseudomonas* and *Klebsiella* species a dosage of not less than 16 g/day is recommended.

Mild and uncomplicated infections: 100-150 mg/kg/day. The usual dose is therefore 2 g IV every six or eight hours; 4 g IV every twelve hours or 2 g IM every eight or twelve hours.

Acute gonorrhoea: a single dose of 2 g IM.

Patients with renal insufficiency: In adults with renal impairment, intravenous or intramuscular dosage should

be adjusted. Given below are the recommended maximum daily dosages of Pipril according to the degree of renal impairment as assessed by the physician.

<i>Renal function</i>	<i>Creatinine clearance (ml/min)</i>	<i>Maximum daily dosage (in divided doses)</i>	<i>Dose schedule</i>
Mild Impairment	40–80	16 grams	4 g q 6h
Moderate Impairment	20–40	12 grams	4 g q 8h
Severe Impairment	< 20	8 grams	4 g q 12h
Patients on Haemodialysis*		6 grams	2 g q 8 h

* Haemodialysis removes 30% to 50% of the drug in four hours; 1 g of Pipril should be administered following each dialysis period.

Duration of Therapy: Pipril treatment in acute infections should be continued for three to four days after the disappearance of clinical signs and symptoms of the disease. However, the duration of treatment should be determined by the physician on the basis of the clinical course of infection.

Paediatric dosage: Children: Two months to twelve years of age: 100–300 mg/kg daily in three or four divided doses.

Neonates and Infants: Under two months of age: 100–300 mg/kg daily in two equally divided doses.

Contra-indications, warnings, etc

Contra-indications: Penicillin hypersensitivity or severe cephalosporin hypersensitivity.

Precautions: Safety for use in pregnant or lactating women has not yet been established. Use with caution in patients with infectious mononucleosis.

Warnings and side-effects: Although not reported to date with piperacillin sodium, serious and occasionally fatal anaphylactic reactions have been reported in patients receiving other penicillins.

Side effects are uncommon and typical of other injectable penicillins.

Gastro-intestinal disturbances have been reported and transient leucopenia, neutropenia and/or eosinophilia can occur.

In vitro: Pipril can be inactivated by β -lactamases produced by some strains of gram-negative and gram-positive bacteria.

Pain after intramuscular injections (rarely accompanied by induration) has been observed infrequently. This can be minimised by reconstituting Pipril with 0.5% lignocaine.

Pharmaceutical precautions Pipril should be stored in a dry place at room temperature. Pipril should be freshly prepared prior to administration, any unused solution being discarded.

Pipril may be administered in all commonly used infusion fluids including:

- Dextran 6% in Sodium Chloride 0.9% Injection
- Dextrose 30% Injection
- Dextrose 5% in Sodium Chloride 0.9% Injection
- Dextrose 5% Injection containing supplemental 40 mEq Potassium Chloride
- Dextrose 5% in Sodium Chloride 0.9% Injection containing supplemental 40 mEq Potassium Chloride

Dextrose 5% in Sodium Chloride 0.9% Injection containing supplemental 40 mEq Potassium Chloride and 30 mEq Sodium Bicarbonate

Lactated Ringer's Injection

Lactated Ringer's Injection containing supplemental 40 mEq Potassium Chloride

Lactated Ringer's Injection containing supplemental 40 mEq Potassium Chloride and 30 mEq Sodium Bicarbonate

Mannitol 20% IV

Sodium Chloride 0.9% Injection containing supplemental 40 mEq Potassium Chloride

Pipril solutions are stable for at least 24 hours at room temperature or 48 hours at 4°C.

Because of chemical instability, Pipril should not be diluted with solutions containing only sodium bicarbonate.

Pipril should not be added to blood products or protein hydrolysates.

Pipril has also been shown to be compatible over 24 hours at room temperature when mixed with cephazolin sodium, flucloxacillin sodium, cefamandole nafate, or ceftiofur sodium in either Dextrose 5% and Saline 0.9% or Lactated Ringer's Injections.

Pipril should not be mixed in the same solution with aminoglycosides and should be administered separately from any other drugs unless compatibility is proven.

Legal category POM.

Package quantities Single vials or infusion bottles.

Further information Pipril shows a pronounced activity against many clinically significant organisms resistant to other penicillins (including the acylureido group), cephalosporins and aminoglycosides. Some ampicillin-resistant *Escherichia coli* and *Proteus* and carbenicillin-resistant *Citrobacter*, *Klebsiella*, *Pseudomonas*, *Proteus* and *Serratia* are sensitive to piperacillin. Many ticarcillin-resistant *Pseudomonas*, *Klebsiella* and *Serratia*; cephalothin-resistant *Enterobacteriaceae* and many strains of *Pseudomonas* resistant to amikacin, gentamicin or tobramycin are susceptible to Pipril.

Pipril is widely distributed following parenteral administration into human tissues and body fluids, particularly bile. Pipril penetrates into cerebrospinal fluid in the presence of meningitis. It is not absorbed when given orally. As with other penicillins, Pipril is rapidly excreted, unchanged, by glomerular filtration and tubular secretion achieving high urinary concentrations for up to 12 hours after dosing. The binding of piperacillin to human serum protein is low (16%).

Product licence number 0095/0073.

SILDERM*

Presentation Topical white cream. Each gram contains:

- Triamcinolone acetonide 1 mg
- Neomycin sulphate, equivalent to 3.5 mg neomycin base
- Undecylenic acid 25 mg
- with 0.16% methylparaben and 0.04% propylparaben as preservatives.

Uses Silderm is an anti-inflammatory, antibacterial and antifungal preparation which is indicated in the treatment of superficial bacterial and mycotic infections of the skin or its appendages, particularly infections due to dermatophytes (dermatophytosis), including tinea pedis (ath-

lete's foot) and other types of tinea; and many dermatoses which are actually or potentially complicated by bacterial infection, including acne, eczema, psoriasis, anogenital pruritus, intertrigo, lichen simplex chronicus (localised neurodermatitis), and various forms of dermatitis such as atopic, eczematoid, nummular and seborrhoeic.

Dosage and administration Small quantities of the cream should be applied to the affected areas three or four times a day.

Contra-indications, warnings, etc

Contra-indications: This preparation is contra-indicated in tuberculosis of the skin, viral exanthemas, herpes simplex, smallpox vaccination reactions, and in patients with a history of hypersensitivity to any of the components of the preparation. It should not be used in the eyes, or in ears with a perforation of the tympanic membrane.

Precautions: Use of an antibiotic may occasionally result in an overgrowth of non-susceptible organisms, while the presence of an anti-inflammatory steroid may encourage their spread. If superinfection does occur the drug should be stopped and appropriate therapy instituted.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in early pregnancy, i.e. in large amounts or for prolonged periods.

In infants, long-term continuous topical steroid therapy should be avoided. Adrenal suppression can occur even without occlusion.

Side-effects: Adverse local effects from triamcinolone acetonide are extremely rare, but neomycin has occasionally been responsible for localised skin sensitisation. The use of corticosteroids over large areas or for prolonged periods, especially under occlusive dressings, may result in systemic steroid absorption. However, serious systemic toxicity, such as peptic ulceration, osteoporosis and Cushing's syndrome, has not been reported with the topical use of triamcinolone acetonide. When occlusive non-permeable dressings are used, miliaria, folliculitis and pyoderma will sometimes develop beneath the occlusive material. Localised atrophy and striae have been reported with the use of steroids by the occlusive technique.

Pharmaceutical precautions The cream should be stored in a cool place in either the original pack or in containers with complete closure.

Dilution of Silderm Cream is not recommended.

Legal category POM.

Package quantities Tubes of 15 g and 30 g.

Further information Nil.

Product licence number 0095/0007.

THIOTEPA

Presentation Vials of dry, white, sterile powder, requiring refrigeration (2–8°C). Each vial contains:

Thiotepa	15 mg
Sodium chloride	80 mg
Sodium bicarbonate	50 mg

Uses Thiotepa (triethylenethiophosphoramide) is a polyfunctional alkylating agent used alone or in combination with other cytotoxic drugs, hormones, radiotherapy or surgery in the treatment of neoplastic diseases. It is believed to exert its cytotoxic effects by alkylation of DNA.

Dosage and administration Thiotepa (15 mg) should be reconstituted with 1.5 ml water for injection immediately prior to use. Occasionally on reconstitution a precipitate may form. In this event the solution should be discarded.

Thiotepa may be given by intravenous, intramuscular and intrathecal routes of injection; it may be given directly into pleural, pericardial or peritoneal cavities and as a bladder instillation.

Adults: For intramuscular injection, bladder and intracavitary instillations: Up to 60 mg in single or divided doses. Doses should be reduced in cases of leucopenia as indicated in Table 1. Single dose administration of 90 mg Thiotepa as a bladder instillation is described under 'Bladder Cancer'.

Table 1

WBC Count	Dose of Thiotepa Adults and Children over 12 years
6000	60 mg
5000–6000	45 mg
4500–5000	30 mg
4000–4500	20 mg
3500–4000	10 mg
3000–3500	5 mg
below 3000	omit dose

Intravenous injection: Half of the above adult doses.

Children under 12 years of age: Half of the above adult doses.

Intrathecal injection: Up to a maximum of 10 mg.

It is essential that a full WBC count should be performed 12–24 hours before each dose of Thiotepa.

Dosage schedules of Thiotepa vary widely according to the route of administration and the indication.

Examples of dosage schedules used according to specific tumour types are given below:

Breast cancer: Patients with advanced breast cancer have been treated with Thiotepa, as part of a combination regime, given intramuscularly in divided doses of 15–30 mg three times weekly for two weeks; this representing one course of treatment. An interval of six to eight weeks is recommended between courses to allow bone marrow recovery.

An alternative schedule employs Thiotepa as part of a combination regime, given as an initial priming dose of 15 mg intramuscularly each day for four days. This may be followed in three weeks by maintenance doses of 15 mg i.m. every 14–21 days.

Bladder cancer: Instillations of Thiotepa have been used to treat multiple superficial tumours of the bladder, resulting in a complete clinical response in about one third of patients. Patients are dehydrated for 8–12 hours prior to treatment. Up to 60 mg Thiotepa dissolved in 60 ml sterile water is instilled into the bladder by catheter once a week for four weeks. During removal of the catheter following instillation, Thiotepa injection is continued to ensure bathing of the prostatic and pendulous urethra. The solution should be retained for up to two hours and the patient should be frequently

repositioned to ensure maximum contact with the urothelium.

Patients are generally cystoscoped two weeks after a course of four instillations. If a response is observed a second course of four Thiotepea instillations may be given, generally at reduced dosage, e.g. 15–60 mg, with intervals of one to two weeks between instillations.

Instillations of Thiotepea have been used prophylactically as an adjunct to surgical resection of superficial tumours of the bladder, resulting in a marked decrease in the recurrence rate. It is recommended that there should be a minimum interval of one week between tumour resection and the commencement of prophylactic instillations of Thiotepea. 30–60 mg Thiotepea dissolved in 60 ml sterile water is instilled into the bladder for two hours and repeated at intervals of one to two weeks for a total of 4–8 instillations. This initial course may be followed by instillations of Thiotepea, 30–60 mg every four to six weeks for one year or longer.

Single dose Thiotepea instillations have been used prophylactically as an adjunct to surgical resection in the treatment of superficial tumours of the bladder. 90 mg Thiotepea dissolved in 100 ml sterile water is instilled into the bladder with the patient in the left lateral position. After 15 minutes the patient is transferred to the right lateral position and after a further 15 minutes the bladder is emptied. It is felt that such single dose administration decreases the incidence of systemic toxicity by decreasing the extent of systemic absorption of the drug.

Note: Patients who have had previous radiotherapy to the bladder are at increased risk of drug toxicity.

Malignant meningeal disease: Intrathecal injections of Thiotepea have been used to treat carcinomatous, lymphomatous and leukaemic meningeal disease. Thiotepea, at a concentration of 1 mg/ml in sterile water, is administered by intrathecal injection, in doses up to 10 mg, on alternate days, until there is a complete disappearance of abnormal mononuclear cells from the cerebrospinal fluid (CSF). It is recommended that intrathecal injections be given on alternate days for no more than four injections. However, if a CSF specimen taken before the third Thiotepea dose indicates stable or progressive disease, treatment with Thiotepea should be stopped and therapy changed. As with other routes of administration of Thiotepea each dose should be preceded by a full WBC count.

Patients who achieve a complete remission may receive maintenance Thiotepea consisting of two intrathecal doses spaced one week apart, and reducing to one dose per month thereafter.

Ovarian cancer: Ovarian cancer has been treated with Thiotepea as a single agent or as part of a combination regime in a variety of schedules. For example, 15 mg Thiotepea IV or IM may be given daily for four days initially and then continued with single doses administered at weekly or two weekly intervals.

Intracavitary instillation of Thiotepea: Instillations of Thiotepea have been used to treat malignant pleural effusions and abdominal ascites. The procedure recommended is first to aspirate as much fluid as possible and then to instil the dose of Thiotepea, 10–30 mg in 20–60 ml sterile water. This may be repeated at weekly or two weekly intervals.

Prevention of recurrence of Pterygium: A 1:2,000 solution of Thiotepea in sterile Ringer's solution (i.e. 15 mg powder in 30 ml Ringer's) applied topically as eye drops at three hourly intervals daily for up to six

weeks after surgical removal of the pterygium, is effective in reducing the recurrence rate following surgery.

Condyloma Acuminata: Thiotepea applied topically or instilled intraurethrally in a gel has been successfully used to eradicate condyloma acuminata. The drug may be administered by first reconstituting 60 mg Thiotepea with 5 ml sterile water. This is diluted to 15 ml using a sterile mixture of water and lubricating jelly made to a consistency viscous enough to remain in the urethra and fluid enough to allow easy injection. This therapy may be repeated at weekly intervals.

Contra-indications, warnings, etc Thiotepea administration is contra-indicated in patients with a WBC count below 3,000 and/or a platelet count below 100,000. Thiotepea should not normally be administered to patients who are pregnant or to mothers who are breast feeding. In addition, the drug has been shown to interfere with spermatogenesis and ovarian function.

Precautions: Thiotepea should only be used by clinicians who are familiar with the various characteristics of cytotoxic drugs and their clinical toxicity. WBC and platelet counts are recommended 12–24 hours before each dose of Thiotepea regardless of route of administration, except when used topically as eye drops or in the treatment of condyloma acuminata. Dosage should be reduced as indicated above in the presence of a compromised bone marrow as manifested by a reduced WBC count.

Side-effects: The most serious side-effect is upon the blood forming elements and is a direct consequence of the cytotoxic action of the drug. In addition, Thiotepea may occasionally cause vomiting, headache and anorexia. Alopecia has been reported as a rare complication of therapy with Thiotepea. Local irritation, comparable to a mild radiation cystitis, may follow bladder instillations of Thiotepea, while haemorrhagic cystitis is rare.

Overdosage: There is no specific antidote. Gastric lavage, forced fluids and general supportive measures are recommended. Blood counts should be carried out to estimate damage to the haematopoietic system and blood transfusions should be given as required.

Pharmaceutical precautions Thiotepea must be stored in a refrigerator (2–8°C). The occurrence of a precipitate on reconstitution (with 1.5 ml of water for injection) indicates that polymerisation has occurred with the formation of less active constituents and the injection must be discarded.

Reconstituted solutions may be stored in a refrigerator (2–8°C) for up to five days.

Thiotepea may be mixed in the same syringe with Procaine Hydrochloride 2% or with adrenaline 1 in 1,000 or with both.

Legal category POM.

Package quantities Boxes of one vial.

Further information Thiotepea contains 1.97 millimoles of sodium per vial.

Product licence number 0095/5060.

TUBERCULIN, OLD, TINE TEST* (ROSENTHAL)

Presentation Each Tuberculin Tine Test unit consists of a stainless steel disc with four tines or prongs attached to a plastic handle. The tines have been dipped in Old Tuberculin, stabilised and dried. The entire unit has been

sterilised. The reactivity of the Tuberculin Tine Test[®] is comparable to the intermediate strength Mantoux test (5 T.U. or 0.0001 mg PPD).

Uses Tuberculin Tine Test is an intradermal test for the detection of tuberculin sensitivity, and is used for screening for tuberculosis. Tuberculin testing may be done during the first year of life. Frequency of repeated tuberculin tests depends on risk of exposure of the child and on the prevalence of tuberculosis in the population group; tuberculin testing may be repeated at intervals of a year or less.

Dosage and administration *Adults and children:* *Site:* for accurate, standardised tuberculin testing, the volar surface of the mid-forearm is the preferred site. The skin must be clean and dry. It may be cleansed with alcohol, acetone, ether, or soap and water. On other skin areas reactions are less reliable, and quantitatively do not bear the same significance to the standardised test. Hairy areas and areas without adequate subcutaneous tissue, such as concavities over a tendon or bone, should be avoided.

Method of application: Remove the Tuberculin Tine Test unit by levering or snapping the handle from the base of the container. Grasp the patient's arm firmly with one hand, stretching the skin of the forearm tightly, and apply the disc with the other hand. Hold for one second and withdraw. Sufficient pressure should be exerted to produce four visible puncture sites and a circular depression of the skin from the plastic base. The Tine Test should *never* be re-used. Local care of the skin site is not necessary.

Reading the reaction: Tests should be read at 48–72 hours. Induration is the only criterion. It is important to measure it exactly, by examining under adequate light and by thoroughly palpating the area. Identification of the application site is usually easy because of the distinct four-point pattern. A reaction of 2 mm or more of palpable induration around one or more puncture sites is clinically comparable to a zone of induration of 5 mm or more by the intermediate strength PPD (0.0001 mg PPD) Mantoux test. Recently, the interpretation of tuberculin test reactions as recommended by the National Tuberculosis and Respiratory Disease Association has been revised. Their recommendations for interpretation of the tine test are as follows:

5 mm or more of induration Positive Reaction.

The significance of the test and the management of the individual is the same as that for one who reacts with 10 mm or more of induration to the standard Mantoux test.

2 mm through 4 mm of induration Doubtful Reaction.

Even though such reactions may be due to M. tuberculosis, a significant proportion of them may not be confirmed by a positive standard Mantoux test. Therefore, a Mantoux test should be done on all individuals in this group, and management should be based on Mantoux reactions.

Less than 2 mm of induration Negative Reaction.

There is no need for retesting unless the individual is in contact with a case of tuberculosis or there is suggestive clinical evidence of the disease.

Contra-indications, warnings, etc

Contra-indications: None.

Precautions: Tuberculin testing should be done with caution in persons with active tuberculosis. However, activation of quiescent lesions is rare.

Although clinical allergy to acacia is very rare, Tine Test contains some acacia as a stabiliser and should be used with caution in patients with known allergy to this component.

Reactivity to the test may be suppressed in patients who are receiving corticosteroids or immunosuppressive agents, or those who have recently been vaccinated with live virus vaccine such as measles.

With a *large* positive reaction to the Tine Test, further diagnostic procedures must be considered. These may include X-ray of the chest, microbiological examinations of sputa and other specimens and confirmation of the positive Tine Test using the Mantoux method. Anti-tuberculous therapy should not be instituted solely on the basis of a single positive Tine Test.

Side-effects: Vesiculation, ulceration, or necrosis may occur at the test site in highly sensitive persons. Pain, pruritus and discomfort at the test site may be relieved by cold packs or by a topical glucocorticoid ointment or cream. Transient bleeding may be observed at a puncture site and is of no significance.

Overdosage: Does not apply.

Pharmaceutical precautions Tuberculin Tine Test should be stored at room temperature in the original pack. DO NOT REFRIGERATE.

Legal category POM.

Package quantities Container of 25 tests.

Further information Nil.

Product licence number 0095/5002.

VARIDASE[®] TOPICAL

Presentation Each vial of dry, sterile powder which requires storage under refrigeration (2–8°C) contains: Streptokinase 100,000 units and Streptodornase 25,000 units with thiomersal 2 mg as preservative.

Uses Streptokinase acts indirectly upon a substrate of fibrin or fibrinogen by activating a fibrinolytic enzyme in human serum. Upon application of streptokinase in situ, the activation of this fibrinolytic system brings about rapid dissolution of blood clots and the fibrinous portion of exudates. Streptodornase liquefies the viscous nucleoprotein of dead cells or pus. Thus the action of the enzymes results in the liquefaction of the two main viscous substances resulting from inflammatory or infectious processes thereby facilitating cleansing and de-sloughing of wounds.

Varidase Topical has no effect on living cells.

Indications: Varidase Topical is indicated wherever clotted blood, fibrinous or purulent accumulations are undesirably present, following trauma or infectious processes which have led to ulceration or abscess formation.

It is indicated in the treatment of suppurative surface lesions such as ulcers, pressure sores, amputation stumps, diabetic gangrene, radiation necrosis, infected wounds, and surgical incisions. It is also indicated in the treatment of burns and may be used prior to skin grafting.

Varidase Topical can be used to dissolve clots in the bladder or in urinary catheters.

Dosage and administration

Adults and children: *Directions for use in the cleansing of necrotic and infected wounds, Reconstitution:* The contents of each vial should be gently mixed with 20 ml

of sterile physiological saline. Care should be taken to control the rate of addition of saline to the vial to avoid frothing. Avoid vigorous shaking which can denature the enzymes. The resulting clear solution can then be withdrawn into a syringe.

Reconstituted solutions are stable for two weeks at room temperature.

Standard methods of application: Pre-soak gauze with Varidase Topical solution then apply to the wound.

Following application a semi-occlusive dressing is necessary to prevent drying-out of the wound, e.g. a polythene film taped on two sides.

Alternatively the wound may be packed with dry gauze which is then soaked with Varidase Topical solution and dressed with a semi-occlusive dressing.

Alternative method of application: Where wounds are covered by a thick dry slough or eschar it is usually necessary to cross hatch the slough into approximately 3–5 mm squares and to a sufficient depth to allow the access of the enzymes to the underlying fibrous and purulent material. Alternatively, Varidase Topical may be injected under the eschar, taking care that the solution enters only the cavity beneath and that the volume is not sufficient to cause pain through increased pressure. Injection of Varidase Topical in this way often results in the eschar becoming detached thus facilitating its mechanical removal.

Special technique of application: Varidase Topical may be applied in jelly form. This can be prepared by dissolving the contents of one vial in 5 ml of sterile water and mixing the resulting solution thoroughly but gently, with 15 ml of inert jelly, such as K-Y^R or carboxymethylcellulose (CMC) jelly. This method can be particularly useful in cases of burns where dressings are not employed.

Frequency of application: Varidase Topical treatment should be repeated once or twice a day. Care should be taken to irrigate the lesion thoroughly with physiological saline and remove loosened material prior to the next application.

Duration of treatment: Treatment should be continued until healthy granulations are present and re-epithelialisation has begun, usually within one to two weeks, although it can be administered until wound healing is complete.

Contra-indications, warnings, etc

Contra-indications: Active haemorrhage.

Precautions: Varidase Topical is intended for local use only. It should not be used intramuscularly or intravenously.

In order to avoid cross-infection the contents of one vial of Varidase Topical and a separate sterile syringe and needle should be used for each individual patient.

Side-effects: Allergic reactions to the topical application of Varidase Topical are infrequent and may be minimised by careful and frequent removal of exudate followed by thorough irrigation using physiological saline prior to retreatment with Varidase Topical.

Pharmaceutical precautions Varidase Topical must be stored in a refrigerator (2–8°C) and should be reconstituted in 20 ml of sterile physiological saline or if unavailable Water for Injection. If the reconstituting fluid has a high calcium content, the solution becomes opalescent, but this does not affect the potency of the enzymes.

Reconstituted solutions may be stored for two weeks at room temperature.

The preparation is buffered to physiological pH. The enzymes of Varidase Topical can be denatured by the concomitant use of other preparations of an acidic or alkaline pH. Varidase Topical is compatible with tetracyclines and other antibiotics such as penicillin and streptomycin.

Legal category POM.

Package quantities Boxes of 1 vial.

Further information Information on the intracavitary use of Varidase Topical in the treatment of, for example, haemothorax or thoracic empyema is available on request to the Medical Information Department.

Product licence number 0095/5038.

VARIDASE* TABLETS

Presentation *Oral Tablets:* Each peach-coloured tablet contains 10,000 units of Streptokinase and at least 2,500 units of Streptodornase. Each tablet is printed 'Lederle 2209'.

Uses Varidase Tablets have a generalised anti-inflammatory effect thereby relieving the symptoms of inflammation; pain; swelling; tenderness; erythema and resolution of the discoloration caused by extravasated blood. Varidase Tablets are therefore indicated for the management of oedema associated with infection or trauma in such conditions as acute and chronic thrombophlebitis; cellulitis; abscesses; sinusitis; haematoma; contusions; chronic bronchiectasis and chronic bronchitis; arteriosclerotic, varicose and stasis ulcers; sprains and fractures.

They are also indicated for the control of oedema and resorption of local haemorrhage into tissue in certain dental conditions such as extractions involving local surgical trauma, pericoronitis, and wherever the inflammatory process is involved.

The use of Varidase in these conditions should be considered as an adjunct to the usual appropriate therapeutic measures including surgical procedures. In the presence of infection; simultaneous administration of an appropriate antibiotic is recommended.

Dosage and administration *Adults and children:* The usual dose is 1 tablet (10,000 units of Streptokinase) four times daily. In acute situations, more frequent dosage on the first day may be advisable. Usually treatment is continued for four to six days.

Contra-indications, warnings, etc

Contra-indications: Varidase Oral Tablets are contra-indicated in patients with reduced plasminogen or fibrinogen. They do not act upon fibrous tissues, mucoproteins or collagen, and therefore are less effective if extensive scarring or organisation of exudate or blood clots has occurred.

Precautions: Where infection is present or suspected, the simultaneous administration of a broad-spectrum antibiotic is recommended. Allergic reactions have not been reported in trials over an extended period. Patients with a history of collagen diseases should be treated with caution. Varidase should be administered with caution when the possibility exists that a defect in blood coagulation or depression of liver function may prolong coagulation.

Side-effects: Side-effects are not common and usually

minor and all have responded promptly to discontinuation of the medication. There have been no serious side-effects. Allergic manifestations have been reported on rare occasions consisting primarily of urticaria and rashes.

Overdosage: No specific antidote. Transfusion, in case of haemorrhage.

Pharmaceutical precautions The product should be stored in a cool dry place in either the original pack or in containers which prevent the access of light and moisture.

Legal category POM.

Package quantities Bottles of 12.

Further information Varidase Oral Tablets contain 0.014 millimole of sodium per tablet.

Product licence number 0095/5072.

VINBLASTINE INJECTION BP 10 mg

Presentation A combination package consisting of (i) one vial of lyophilised powder consisting of 10 mg of Vinblastine sulphate for reconstitution before use with (ii) one ampoule of Diluting Solution, i.e. 10 ml of sodium chloride injection 0.9% with 2% benzyl alcohol as an antimicrobial preservative.

Uses The treatment of neoplastic disease.

Dosage and administration

Adults and Children: The dosage of Vinblastine must always be adjusted individually because of individual variations in the degree of leucopenia. Vinblastine is administered intravenously at intervals no more frequently than once a week, and has been used alone and in combination or sequence with other cytotoxic agents, radiotherapy or surgery in a wide variety of neoplastic diseases e.g. lymphomas including Hodgkin's disease, breast cancer unresponsive to appropriate endocrine, surgical, and hormonal therapy, testicular cancer, Methotrexate-resistant choriocarcinoma, reticulum cell sarcoma, mycosis fungoides, neuroblastoma and histiocytosis X (Letterer-Siwe disease).

Initial dosage is calculated by body weight or body surface area and varies according to the disease. However, in general, 0.1–0.2 mg/kg is given. Rarely, up to 0.5 mg/kg may be necessary. It is important to monitor the patients white blood cell count before each dose and the dose can be increased by increments of 0.05 mg/kg each week until an objective response is obtained or a nadir in the white cell count of approximately 3,000 cells/mm³ is observed. A dose one increment smaller than this can then be administered at weekly or longer intervals for maintenance. It should be emphasised that, even if seven days have elapsed, the next dose of Vinblastine should not be given until the white cell count has returned to at least 4,000 cells/mm³.

Administration: Vinblastine is irritant, particularly to the eyes and skin and it is recommended that goggles and gloves are worn during reconstitution and administration of the product. Following reconstitution, the calculated dose of Vinblastine is withdrawn from the vial and should only be injected either directly into a vein or into the tubing of a fast running intravenous infusion of Sodium Chloride Injection 0.9%.

When reconstituted with the Diluting Solution provided, Vinblastine Injection may be stored in a refrigerator for 30 days without significant loss of potency.

Severe local pain and tissue damage will occur if Vinblastine injection extravasates during intravenous administration. The injection should be discontinued immediately and any remaining portion of the dose should then be introduced into another vein. Local injection of hyaluronidase and the application of moderate heat to the area of leakage help to disperse the drug and are thought to minimise discomfort and the possibility of cellulitis.

Care must be taken to avoid contamination of the eye with concentrations of Vinblastine used clinically. If accidental contamination occurs, severe irritation (or if the drug was delivered under pressure, even corneal ulceration) may result. The eye should be washed with water thoroughly and immediately.

Contra-indications, warnings, etc

Contra-indications: Vinblastine should not normally be administered to patients who are pregnant or to mothers who are breast-feeding. Leucopenia. Concurrent untreated infection. Intrathecal administration. Use in elderly cachectic patients.

Precautions: Vinblastine should be administered under the direction of a specialist oncology service having the facilities for regular monitoring of clinical, biochemical and haematological effects during and after administration.

The use of small amounts of Vinblastine daily for long periods is not advised. Little or no added therapeutic benefit compared with intermittent dosing has been demonstrated and convulsions, severe and permanent central nervous system damage and even death have occurred. If leucopenia with less than 2,000 white blood cells/mm³ occurs following a dose of Vinblastine, the patient should be watched carefully for evidence of infection until the white blood cell count has returned to a safe level.

When cachexia or ulcerated areas of the skin surface are present, there may be a more profound leucopenic response to the drug. Its use should be avoided in older persons suffering from either of these conditions. In patients with malignant-cell infiltration of the bone marrow, the leucocyte and platelet counts have sometimes fallen precipitously after moderate doses of Vinblastine. Further use of the drug in such patients is inadvisable.

Vinblastine has been shown to be teratogenic. However, only limited information is available concerning the effect of Vinblastine on spermatogenesis. Although no abnormalities of the human foetus have been reported thus far, animal studies with Vinblastine would suggest that teratogenic effects may occur. Patients receiving Vinblastine and their partners should be advised to avoid conception.

There is a possibility that Vinblastine may exert a carcinogenic effect with long-term therapy, although to date no positive evidence is available.

Side-effects: Clinically, leucopenia is an expected effect of Vinblastine and the level of the leucocyte count is an important guide of treatment. Following therapy with Vinblastine, the nadir in the white blood cell count may be expected to occur five to ten days after the last day of drug administration, with complete recovery within another seven to fourteen days.

The effect of Vinblastine upon the thrombocyte count

and/or red blood cell count is usually insignificant when other treatment does not complicate the picture.

Nausea and vomiting are common but are usually readily controlled by anti-emetic agents.

Stomatitis, constipation, diarrhoea, ileus, anorexia, abdominal pain, rectal bleeding, pharyngitis, bleeding from an old peptic ulcer and, rarely, haemorrhagic enterocolitis have also been observed.

Alopecia is uncommon and is frequently not total. Regrowth may occur during maintenance treatment.

Neurological side-effects such as numbness, paraesthesiae, peripheral neuritis, mental depression, loss of deep tendon reflexes, headache or convulsions can occur but are much less common than with Vincristine.

Other adverse reactions that have been reported are malaise, weakness, dizziness, pain in the tumour site and vesiculation of the skin.

Toxicity is increased in patients with obstructive jaundice.

Pharmaceutical precautions Vinblastine should be stored in a refrigerator (2–8°C). Injections reconstituted with the Diluting Solution provided contain an antimicrobial preservative and may be kept in a refrigerator for 30 days without significant loss of potency. Goggles and gloves should be worn during reconstitution and administration of Vinblastine.

Legal category POM.

Package quantities Combination package consisting of one vial of Vinblastine 10 mg and one ampoule of Diluting Solution.

Further information Nil.

Product licence number 0095/0067.

VINCRIStINE INJECTION BP, 1 mg, 2 mg, 5 mg

Presentation A combination package consisting of (i) one vial of lyophilised powder consisting of 1 mg, 2 mg or 5 mg of Vincristine sulphate with 10 mg, 20 mg or 50 mg of lactose respectively, for reconstitution before use with (ii) one ampoule of Diluting Solution, i.e. 10 ml of sodium chloride injection 0.9% with 2% benzyl alcohol as an antimicrobial preservative.

Uses The treatment of neoplastic disease.

Dosage and administration

Adults and Children: The dosage must always be adjusted individually because of the narrow range between therapeutic and toxic levels and individual variations in response. Extreme care must be used in calculating and administering doses of Vincristine since overdosage may have a very serious or fatal outcome.

Vincristine is administered intravenously, usually at weekly or longer intervals and has been used alone and in combination or sequence with other cytotoxic agents, radiotherapy and/or surgery in a wide variety of neoplastic diseases, e.g. acute leukaemias, malignant lymphomas including Hodgkin's disease, sarcomas, neuroblastoma, Wilms's tumour and rhabdomyosarcoma. Vincristine may also be considered in the treatment of breast cancer, bronchial carcinoma, and gastro-intestinal cancer. Initial dosage is calculated by body surface area or body weight and varies according to the disease. However, in general, 1.0–2.0 mg/m² is given with a normal maximum weekly adult dose of 2 mg.

In children, remissions from acute leukaemia have been induced with weekly doses of 0.05–0.15 mg/kg of body weight.

In acute leukaemia of children the following incremental approach to dosage may be employed:

First dose: 0.05 mg/kg

Second dose: 0.075 mg/kg

Third dose: 0.1 mg/kg

and Fourth dose: 0.125 mg/kg up to a maximum of 0.15 mg/kg.

There is no need to advance the dosage beyond that level which produces therapeutic benefit. After remission has been obtained, the dosage may be reduced in some cases to a maintenance level of 0.05 to 0.075 mg/kg/week.

In adult leukaemia the suggested dosage is 0.025–0.075 mg/kg of body weight per weekly dose.

For malignancies other than leukaemia, a suggested dosage for Vincristine is 0.025 mg/kg/week intravenously until some beneficial effect is seen. Thereafter much smaller weekly doses in the range of 0.005–0.01 mg/kg may be employed for maintenance therapy for so long as an anti-tumour effect can be maintained.

Administration: Vincristine is irritant, particularly to the eyes and skin, and it is recommended that goggles and gloves are worn during reconstitution and administration of the product. Following reconstitution, the calculated dose of Vincristine is withdrawn from the vial and should only be injected either directly into a vein or into the tubing of a fast running intravenous infusion of Sodium Chloride Injection 0.9%.

When reconstituted with the Diluting Solution provided, Vincristine Injection may be stored in a refrigerator for 14 days without significant loss of potency.

Severe local pain and tissue damage will occur if Vincristine injection extravasates during intravenous administration. The injection should be discontinued immediately and any remaining portion of the dose should then be introduced into another vein. Local injection of hyaluronidase and the application of moderate heat to the area of leakage help to disperse the drug and are thought to minimise discomfort and the possibility of cellulitis.

Care must be taken to avoid contamination of the eye with concentrations of Vincristine used clinically. If accidental contamination occurs, severe irritation (or if the drug was delivered under pressure, even corneal ulceration) may result. The eye should be washed with water thoroughly and immediately.

Contra-indications, warnings, etc

Contra-indications: Vincristine should not normally be administered to patients who are pregnant or to mothers who are breast-feeding.

Intrathecal administration.

Use in the presence of untreated infection.

Precautions: Vincristine should only be administered under the direction of a specialist oncology service having the facilities for regular monitoring of clinical, biochemical and haematological effects during and after administration.

Effective Vincristine therapy does not normally result in leucopenia. Neuromuscular rather than bone-marrow toxicity is usually the dose-limiting factor. However, because of the possibility of leucopenia both physician and patient should remain alert for signs of any complicating infection. Although pre-existing leucopenia does not necessarily contra-indicate the adminis-

tration of Vincristine the appearance of leucopenia during treatment warrants careful consideration before giving the next dose. Similarly, Vincristine should only be used with caution in patients with malignant infiltration of bone marrow.

Acute uric acid nephropathy has occurred following Vincristine treatment.

Vincristine has been shown to be teratogenic. However, no data are available concerning the effect of Vincristine on spermatogenesis. Patients receiving Vincristine and their partners should be advised to avoid conception.

Routine use of laxatives and enemas is recommended to ensure regular bowel function.

If central nervous system leukaemia is diagnosed, additional therapy, such as intrathecal Methotrexate, may be required, since Vincristine does not appear to cross the blood-brain barrier in adequate amounts. There is a possibility that Vincristine may exert a carcinogenic effect with long-term therapy, although to date no positive evidence is available.

Side-effects: In general, adverse reactions are reversible and are related to dosage. The most common side-effect is some degree of alopecia.

The main toxicity of Vincristine is neuropathy which may take any form but usually presents as a sensory motor peripheral neuropathy with paraesthesia, loss of tendon reflexes, muscle wasting and muscular weakness.

Frequently, there appears to be a sequence in the development of neuromuscular side-effects, in that initially sensory impairment and paraesthesia develop followed later by neuritic pain and motor difficulties. With single weekly doses, neuritic pain and difficulty in walking are usually of short duration (i.e. less than seven days). Other side-effects, such as sensory loss, paraesthesia, slapping gait, loss of deep tendon reflexes, and muscle wasting do not reverse so rapidly but persist for at least as long as treatment is continued. In most instances, these side-effects have disappeared by about the sixth week after discontinuing treatment, but in some patients neuromuscular difficulties may persist for prolonged periods.

No reports have yet been made of any agent that can reverse the neuromuscular manifestations of Vincristine. Discontinuation of treatment should be considered if neuromuscular effects continue to be a problem.

Vincristine commonly causes constipation which usually responds well to measures such as enemas and laxatives. Constipation may take the form of upper colon impaction and the rectum may be found to be empty on physical examination. Colicky abdominal pain, coupled with an empty rectum, may mislead the physician. A flat film of the abdomen is useful in demonstrating this condition. A routine prophylactic regimen against constipation is recommended for all patients receiving Vincristine.

Convulsions, frequently with hypertension, have been reported in a few patients receiving Vincristine.

Rare occurrences of the syndrome of inappropriate secretion of antidiuretic hormone have also been observed. With fluid deprivation, improvement occurs in the hyponatraemia and in the renal loss of sodium.

Other reported adverse reactions include abdominal cramps, ataxia, foot drop, weight loss, fever, cranial nerve manifestations, paraesthesiae and numbness of the digits, polyuria, dysuria, oral ulceration, headache, vomiting and diarrhoea.

Vincristine does not appear to have any constant or significant effect upon the platelets or the red blood cells. If thrombocytopenia is present when treatment with Vincristine is begun, it may actually improve before the appearance of marrow remission.

Pharmaceutical precautions Vincristine should be stored in a refrigerator (2–8°C). Injections, reconstituted with the Diluting Solution provided, contain an antimicrobial preservative and may be kept in a refrigerator for 14 days without significant loss of potency. Goggles and gloves should be worn during reconstitution and administration of Vincristine.

Legal category POM.

Package quantities Combination packages consisting of one vial of Vincristine 1 mg, 2 mg or 5 mg and one ampoule of Diluting Solution.

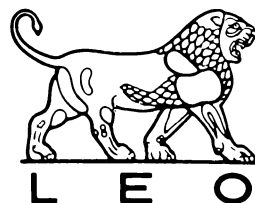
Further information Nil.

Product licence numbers

Vincristine Injection BP 1 mg and 2 mg	0095/0065
Vincristine Injection BP 5 mg	0095/0066

**Trade Mark*

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Bucks. HP17 9RR



BURINEX* TABLETS
BURINEX* INJECTION

Presentation *Tablets 1 mg:* Each tablet contains 1 mg bumetanide – a yellow, flat, circular, uncoated tablet marked with a score line and '1 mg' on one face.

Tablets 5 mg: Each tablet contains 5 mg bumetanide – a white, flat, circular, uncoated, bevelled-edge tablet, marked with a score line and '5 mg' on one face.

Injection: A solution containing 0.5 mg bumetanide per ml in amber glass ampoules of 2 ml, 4 ml and 10 ml, each ampoule containing 1 mg, 2 mg and 5 mg bumetanide respectively.

Uses *Mode of action:* Burinex (bumetanide) is a potent high ceiling diuretic with a rapid onset and a short duration of action. After oral administration of 1 mg Burinex, diuresis begins within 30 minutes with a peak effect between one and two hours. The diuretic effect is virtually complete in three hours after a 1 mg dose.

After intravenous injection, diuresis usually starts within a few minutes and ceases in about two hours.

Burinex has been shown to exert its major effect in the ascending limb of the loop of Henle, but it may also have an additional action in the proximal tubule.

Burinex is chemically distinct from other diuretics. In contrast to frusemide and the thiazides, which are derived from sulphanilamide, Burinex is a derivative of metanilamide.

Pharmacological and clinical studies have shown that 1 mg Burinex produces a diuretic response similar to that of 40–60 mg frusemide.

Burinex is well absorbed when given orally, as shown by the almost equal diuretic response after oral and parenteral administration. Investigations in healthy volunteers as well as in patients, have revealed that Burinex is excreted in the urine. Extrarenal elimination also occurs.

Indications: Burinex is indicated whenever diuretic therapy is required in the treatment of oedema, e.g. that associated with congestive heart failure, cirrhosis of the liver and renal disease including the nephrotic syndrome.

In oedema of cardiac or renal origin where high doses of a potent, short acting diuretic are required, Burinex 5 mg tablets may be used.

For those oedematous conditions where a prompt diuresis is required, Burinex Injection may be used, e.g. acute pulmonary oedema, acute and chronic renal failure, salicylate or barbiturate poisoning. Burinex Injection can be given intravenously or intramuscularly to those patients who are unable to take Burinex tablets or who fail to respond satisfactorily to oral therapy.

Dosage and administration *Oral dosage:* **Burinex 1 mg tablets:** Most patients require a daily dose of 1 mg which can be given as a single morning or early evening dose. Depending on the patient's response, a second

dose can be given six to eight hours later. In refractory cases, the dose can be increased until a satisfactory diuretic response is obtained.

Burinex 5 mg tablets: The dose should be carefully titrated in each patient according to the patient's response and the required therapeutic activity. As a general rule, dosage should be started at 5 mg daily, and then increased by 5 mg increments every 12–24 hours until the required response is obtained or side-effects appear. Consideration should be given to a twice daily dosage, rather than once daily. Direct substitution of Burinex for frusemide in a 1:40 ratio at high doses should be avoided. Treatment should be initiated at a lower equivalent dose and gradually increased in 5 mg increments.

Parenteral dosage: *Pulmonary oedema:* Initially 1–2 mg by intravenous injection. This can be repeated, if necessary, 20 minutes later.

In those conditions in which an infusion is appropriate, 2–5 mg may be given in 500 ml infusion fluid over 30–60 minutes. (See pharmaceutical precautions.)

In salicylate or barbiturate poisoning, initially 2 mg should be given intravenously, then 1 mg every four hours to a total of 7 mg in 24 hours. The usual procedure for alkaline diuresis should be followed.

When intramuscular administration is considered appropriate, a dose of 1 mg should be given initially and the dose then adjusted according to diuretic response.

Contra-indications, warnings, etc

Contra-indications: Although Burinex can be used to induce diuresis in renal insufficiency, any marked increase in blood urea or the development of oliguria or anuria during treatment of severe progressing renal disease are indications for stopping treatment with Burinex.

Burinex is contra-indicated in hepatic coma and care should be taken in states of severe electrolyte depletion.

As with other diuretics, Burinex should not be administered concurrently with lithium salts. Diuretics can reduce lithium clearance resulting in high serum levels of lithium.

Precautions: Excessively rapid mobilisation of oedema particularly in elderly patients, may give rise to sudden changes in cardiovascular pressure-flow relationships with circulatory collapse. This should be borne in mind when Burinex is given intravenously to susceptible subjects and during treatment with Burinex 5 mg tablets, special care should be taken to monitor fluid balance. Electrolyte disturbances may occur, particularly in those patients taking low-salt diet. Regular checks of serum electrolytes, in particular sodium, potassium, chloride and bicarbonate should be performed and replacement therapy instituted where indicated.

Like other diuretics, Burinex shows a tendency to increase the excretion of potassium which can lead to an

increase in the sensitivity of the myocardium to the toxic effects of digitalis. Thus the dose may need adjustment when given in conjunction with cardiac glycosides.

Burinex may potentiate the effects of antihypertensive drugs. Therefore, the dose of the latter may need adjustment when Burinex is used to treat oedema in hypertensive patients.

As with other diuretics, Burinex may cause an increase in blood uric acid. Periodic checks on urine and blood glucose should be made in diabetics and patients suspected of latent diabetes.

Patients with chronic renal failure on high doses of Burinex should remain under constant hospital supervision.

Pregnancy: Although tests in four animal species have shown no teratogenic effects, the ordinary precaution of avoiding use of Burinex in the first trimester of pregnancy should at present be observed.

Adverse Reactions: Reported reactions include skin rashes and muscular cramps in the legs, abdominal discomfort, thrombocytopenia and gynaecomastia.

High Dose Therapy: In patients with severe chronic renal failure given high doses of Burinex, there have been reports of severe, generalised, musculoskeletal pain sometimes associated with muscle spasm, occurring one to two hours after administration and lasting up to 12 hours. The lowest reported dose causing this type of adverse reaction was 5 mg by intravenous injection and the highest was 75 mg orally in a single dose. Occasionally, analgesic medication has been required to treat the pain. All patients recovered fully and there was no deterioration in their renal function.

The cause of this pain is uncertain but it may be a result of varying electrolyte gradients at the cell membrane level.

Experience suggests that the incidence of such reactions is reduced by initiating treatment at 5–10 mg daily and titrating upwards using a twice daily dosage regimen at doses of 20 mg per day or more.

Overdosage: General measures should be taken to restore blood volume, maintain blood pressure and correct electrolyte disturbance.

Pharmaceutical precautions Burinex is presented in amber glass containers to protect against deterioration due to exposure to light.

When an intravenous infusion is required, Burinex Injection may be added to Dextrose Injection BP, Sodium Chloride Injection BP or Sodium, Chloride and Dextrose Injection BP.

When 25 mg bumetanide (as Burinex Injection) was added to 1 litre of these infusion fluids, no evidence of precipitation was observed over a period of 72 hours. Higher concentrations of Burinex in these infusion fluids may cause precipitation. It is good practice to inspect all infusion fluids containing Burinex from time to time. Should cloudiness appear, the infusion should be discarded.

Legal category POM.

Package quantities 1 mg Tablets: Bottles of 100 and 1,000.

5 mg tablets: Bottles of 100.

Injection: Packs of 5 × 2 ml, 5 × 4 ml and 5 × 10 ml.

Further information Burinex is also available as Burinex K tablets, each containing 0.5 mg bumetanide and 573 mg potassium chloride in a slow release core.

Product licence numbers

Burinex 1 mg	0043/0021
Burinex 5 mg	0043/0043
Burinex Injection	0043/0060

BURINEX* K

Presentation White, ovoid, unmarked tablets each containing 0.5 mg bumetanide (Burinex) and 573 mg Potassium chloride BP (7.7 mmol potassium in a slow release wax core).

Uses Mode of Action: Burinex K combines the very potent high-ceiling diuretic bumetanide, with a slow-release potassium chloride supplement. Bumetanide has a rapid onset and a short duration of action. As with most diuretics, long-term therapy may be associated with potassium depletion.

The potassium supplement in Burinex K should help to maintain normal levels of potassium, especially in those patients whose dietary intake of potassium is inadequate.

The formulation of Burinex K presents the following advantages. The diuretic is coated around the tablet, from which it is rapidly released. The diuretic and saluretic effects begin within 30 minutes after oral administration, peak at one to two hours, and are largely complete within three hours. In contrast, the potassium chloride, which is included in an inert wax core, is released only slowly over a period of six hours after oral ingestion. This slow-release minimises the risk of gastrointestinal intolerance as well as that of ulceration and stenosis resulting from localised high concentrations of potassium salts in the small bowel.

Indications: Burinex K is indicated for the treatment of oedema where a potassium supplement is necessary. Low serum potassium levels are, for example, known to increase the toxic effects of the cardiac glycosides; Burinex K may therefore be of particular value in those patients being treated with digitalis.

Dosage and administration For initial therapy, most patients will be treated with Burinex 1 mg tablets alone. The dose required will be adjusted to the patient's response, but is likely to vary between 0.5 and 2 mg ($\frac{1}{2}$ –2 tablets of Burinex). For maintenance therapy Burinex K is more convenient than Burinex. In many patients, 2 tablets daily (1.0 mg Burinex and 15.4 mmol potassium) which may be given as a single morning or early evening dose should prove adequate.

For some patients, however, this maintenance dose may be inadequate. Larger doses should preferably be given in divided doses. If a daily dosage of more than 4 tablets of Burinex K is required, then Burinex itself should be substituted and potassium chloride given separately, in divided doses, as a slow-release preparation (such as Leo K).

Burinex K tablets must be swallowed whole and never chewed.

Contra-indications, warnings, etc

Contra-indications: Burinex K should not be used with potassium-sparing diuretics (e.g. spironolactone, triamterene or amiloride) or in patients with renal insufficiency.

As with other diuretics, Burinex K should not be administered concurrently with lithium salts. Diuretics can reduce lithium clearance resulting in high serum levels of lithium.

Precautions: The 15.4 mmol of potassium included in the usual dose of Burinex K (2 tablets daily) should help to prevent hypokalaemia in many patients. Certain patients, however – as, for example, those with hepatic ascites or those on a very low potassium diet – may require considerably more potassium than this. Periodic checks should therefore be made on the serum potassium level in patients on long-term therapy.

The diuretic in Burinex K may potentiate the effect of antihypertensive drugs, increase blood uric acid and (though rarely) affect carbohydrate metabolism.

Non-specific small bowel lesions characterised by stenosis and possibly accompanied by ulceration have been associated with the oral administration of tablets and capsules containing potassium salts. Symptoms and signs which indicate ulceration or obstruction of the small bowel in patients taking tablets or capsules containing potassium salts are indications for stopping treatment with such preparations immediately.

Adverse reactions: Reported reactions include skin rashes and muscular cramps in the legs, abdominal discomfort, thrombocytopenia and gynaecomastia.

Pregnancy: Although tests in four animal species have shown no teratogenic effects, the ordinary precaution of avoiding use of Burinex in the first trimester of pregnancy should at present be observed.

Overdosage: General methods should be taken to restore blood volume and maintain blood pressure.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Packs of 100, 500 and 1,000 tablets.

Further information Nil.

Product licence number 0043/0027B.

FUCIDIN* TABLETS FUCIDIN* SUSPENSION FUCIDIN* FOR INTRAVENOUS INFUSION

Presentation *Fucidin Tablets:* Each white, ovoid enteric-coated tablet contains 250 mg Sodium Fusidate BP.

Fucidin Suspension: Each 5 ml of pale orange, banana-flavoured aqueous suspension contains 250 mg fusidic acid (therapeutically equivalent to 175 mg Sodium Fusidate BP).

Fucidin for Intravenous Infusion: A pack of 2 vials. One vial contains Diethanolamine Fusidate BPC 1968, 580 mg (equivalent to 500 mg sodium fusidate) as a dry powder. The second vial contains 50 ml sterile phosphate-citrate buffer solution (pH 7.4–7.6).

Sodium fusidate is the sodium salt of fusidic acid.

Uses *Mode of Action:* Fucidin and its salts are potent antistaphylococcal agents with unusual ability to penetrate tissue. Bactericidal levels have been assayed in bone and necrotic tissue. Blood levels are cumulative, reaching concentrations of 50–100 mcg/ml after oral administration of 1.5 g daily for three to four days. Concentrations of 0.03–0.12 mcg/ml inhibit nearly all strains of *Staphylococcus aureus*.

Fucidin is excreted mainly in the bile, little or none being excreted in the urine.

Indications: Fucidin is indicated in the treatment of all staphylococcal infections such as: osteomyelitis; pneu-

monia; septicaemia; wound infections; endocarditis; superinfected cystic fibrosis; cutaneous infections.

Fucidin should be administered intravenously whenever oral therapy is inappropriate which includes cases where absorption from the gastro-intestinal tract is unpredictable.

Dosage and administration *For Fucidin tablets:*

Adults: Standard dose: 500 mg three times daily. In severe or fulminating infections, this dosage may be doubled or appropriate combined therapy may be used.

For Fucidin Suspension: Adult dose: 15 ml three times daily.

Children: 0–1 year: 1 ml/kg body weight daily divided into 3 equal doses.

1–5 years: 5 ml three times daily.

5–12 years: 10 ml three times daily.

Intravenous therapy: Adults weighing more than 50 kg: 580 mg diethanolamine fusidate three times daily.

Children and adults weighing less than 50 kg: 6 to 7 mg diethanolamine fusidate per kg body weight, three times daily.

Recommended procedure: Dissolve 580 mg diethanolamine fusidate powder (1 vial) in the 50 ml buffer provided.

1. For adults weighing more than 50 kg: Add the fusidate/buffer solution to 500 ml of infusion fluid and infuse slowly over a period of not less than six hours.

2. For children and adults weighing less than 50 kg: Each dose corresponds to approximately 0.6 ml of the fusidate/buffer solution per kg body weight. This volume should be further diluted, at least tenfold, with the appropriate infusion fluid, and infused slowly over a period of not less than six hours.

Since Fucidin is excreted in the bile, no dosage modifications are needed in renal impairment.

The dosage in patients undergoing haemodialysis needs no adjustment as Fucidin is not significantly dialysed.

Contra-indications, warnings, etc *Intravenous Fucidin: Contra-indications:* Fucidin should not be infused with amino-acid solutions or in whole blood. Due to local tissue injury, Fucidin should not be administered intramuscularly or subcutaneously.

Precautions: Caution should be exercised with other antibiotics which have similar biliary excretion pathways, e.g. lincomycin and rifampicin.

Periodic liver function tests should be carried out when high oral doses are used, when the drug is given for prolonged periods and in patients with liver dysfunction.

Pregnancy: Fucidin is detected in breast milk and it can cross the placenta.

Intravenous Fucidin: In most cases Sodium Chloride Injection is used as an infusion fluid. It has also been given in plasma and occasionally in 5% dextrose, 40% dextrose, 20% fructose, and Sodium Chloride and Dextrose Injection. Opalescence may be encountered with more acidic samples of dextrose, when the solution should be discarded. Infusion should be made into a wide bore vein with a good blood flow.

Adverse reactions: In some patients given Fucidin, a reversible jaundice has been reported, most frequently in patients receiving intravenous Fucidin in high dosage, or where the drug has been infused too rapidly or at too high a concentration in the infusion fluid. In some

instances, instituting oral therapy may be beneficial. If the jaundice persists, Fucidin should be withdrawn, following which the serum bilirubin will invariably return to normal.

Overdosage: There has been no experience of overdosage with Fucidin. Treatment should be restricted to symptomatic and supportive measures. Dialysis is of no benefit, since the drug is not significantly dialysed.

Pharmaceutical precautions *Fucidin tablets:* Nil.

Fucidin Suspension: Protect from direct sunlight and heat. The Suspension should be shaken before use and dilution is not recommended.

Fucidin Infusion: Fucidin powder is stable for 3 years. Once brought into solution, it should be used within 24 hours.

Legal category POM.

Package quantities *Tablets:* Bottles of 100.

Suspension: Bottles of 50 ml.

Infusion: Pack containing a single pair of vials.

Further information Fucidin should be administered intravenously into a wide bore vein with a good blood flow. Excessive doses may cause venospasm, thrombophlebitis and haemolysis of erythrocytes.

Both oral and intravenous Fucidin have been given in combination with other antibiotics e.g. Cloxacillin, flucloxacillin, ampicillin, methicillin and erythromycin.

Product licence numbers

Tablets: 0043/5000

Suspension: 0043/5014

Infusion: 0043/5003

FUCIDIN* OINTMENT FUCIDIN* GEL FUCIDIN* CAVIJECT FUCIDIN* INTERTULLE FUCIDIN* CREAM

Presentation *Fucidin Ointment* contains Sodium Fusidate BP 2% in an ointment base.

Fucidin Gel contains fusidic acid 2% in a water-miscible base.

Fucidin Caviject is a sterile, single-dose preparation containing fusidic acid 2% in a water-miscible base (Fucidin gel), fitted with an elongated flexible nozzle.

Fucidin Intertulle: Sterile gauze squares each impregnated with Sodium Fusidate BP 2% (Fucidin Ointment) in an ointment base and enclosed between two leaves of sterile parchment in a sealed foil pack.

Fucidin Cream contains Fusidic acid 2% in a cream base.

Uses *Mode of Action:* Sodium fusidate is the sodium salt of fusidic acid.

1 g Fucidin Ointment contains 20,000 mcg of Sodium Fusidate BP and 1 g Fucidin Gel or Fucidin Cream contains approx. 20,000 mcg fusidic acid.

Fucidin is a potent topical antibacterial agent. Fusidic acid and its salts show fat and water solubility and strong surface activity and exhibit unusual ability to penetrate intact skin. Concentrations of 0.03–0.12 mcg/ml inhibit nearly all strains of *Staphylococcus aureus*. Local concentrations with topical Fucidin are also effective against *Streptococci*, *Corynebacteria*, *Neisseria* and certain *Clostridia*.

Indications: Indicated, either alone or in combination

with systemic therapy, in the treatment of skin infections caused by Gram-positive organisms, particularly the *Staphylococcus*, e.g. abscesses, boils, carbuncles, impetigo, eczema, varicose ulcers, skin grafts, wounds, burns.

Dosage and administration *Fucidin Gel, Fucidin Ointment and Fucidin Cream: Adults and children:* Uncovered lesions – apply gently, three or four times daily. Covered lesions – less frequent applications may be adequate.

Fucidin Caviject: The abscess should be incised and carefully curetted. The cavity is filled by injecting Fucidin Caviject and a dressing applied. The caviject container should be used once only and then discarded.

Fucidin Intertulle: Usually, once a day application but frequency of application will vary with clinical circumstances.

Contra-indications, warnings, etc

Contra-indications: Infection caused by non-susceptible organisms, in particular, *Pseudomonas aeruginosa*.

Precautions: The sodium salt of fusidic acid has been shown to cause conjunctival irritation. The Ointment and Intertulle should not be used in or near the eye.

Fusidic acid does not appear to cause conjunctival irritation in experimental animals. Caution should, however, still be exercised when using Fucidin Gel, Caviject or Cream near the eye.

Adverse reactions: Hypersensitivity may occur.

Overdosage: Not applicable.

Pharmaceutical precautions *Fucidin Ointment:* Nil.
Fucidin Gel and Caviject: Store in a cool place but do not freeze.

Fucidin Intertulle and Cream: Store in a cool place.

Legal category POM.

Package quantities *Ointment and Gel:* Tubes of 10 g and 25 g.

Caviject: Tubes of 7 g.

Intertulle: Box of 10 foil packs, each containing one tulle piece (10 cm × 10 cm).

Cream: Tubes of 10 g.

Further information The gel base is non-staining and contains no lanolin or other fatty constituents.

The cream base is a vanishing base and contains no lanolin.

Product licence numbers

Ointment 0043/5005

Gel and Caviject 0043/5018

Intertulle 0043/5007

Cream 0043/0065

FUCIDIN H* OINTMENT FUCIDIN H* GEL

Presentation Fucidin H Ointment contains Sodium Fusidate BP 2% and Hydrocortisone Acetate BP 1% in an ointment base.

Fucidin H Gel contains fusidic acid 2% and Hydrocortisone Acetate BP 1% in a water-miscible gel base.

Sodium fusidate is the sodium salt of fusidic acid.

Uses *Mode of Action:* Fucidin H Ointment and Fucidin H Gel combine the potent topical antibacterial action of fusidic acid with the anti-inflammatory and antipruritic

effects of hydrocortisone. Concentrations of 0.03–0.12 mcg per ml inhibit nearly all strains of *Staphylococcus aureus*. Topical Fucidin is also effective against *Streptococci*, *Corynebacteria*, *Neisseria* and certain *Clostridia*.

Indications: It is indicated in inflammatory dermatoses, including dermatitis; seborrhoeic dermatitis; allergic, infantile and infected eczema and infected acne, where bacterial infection is present or likely to occur.

Dosage and administration *Adults and children:* Uncovered lesions – apply gently, three or four times daily. Covered lesions – less frequent applications may be adequate.

Contra-indications, warnings, etc

Contra-indications: As with other topical corticosteroid preparations, Fucidin H Gel and Fucidin H Ointment are contra-indicated in tuberculous, viral and fungal skin infections.

Precautions: Fucidin H Ointment should not be used in or near the eye, as sodium fusidate causes conjunctival irritation.

Fusidic acid does not appear to cause conjunctival irritation in experimental animals. Caution should still be exercised, however, when Fucidin H Gel is used near the eye.

Pregnancy: Topical administration of any corticosteroid to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

In infants, long-term continuous topical therapy with corticosteroids should be avoided. Adrenal suppression can occur even without occlusion.

Adverse reactions: Hypersensitivity may occur.

Overdosage: Not applicable.

Pharmaceutical precautions *Fucidin H Gel:* Store in a cool place but do not freeze.

Fucidin H Ointment: Nil.

Legal category POM.

Package quantities In tubes of 10 g and 25 g.

Further information The gel base is non-staining and contains no lanolin or other fatty constituents.

Product licence numbers

Fucidin H Gel 0043/0024

Fucidin H Ointment 0043/5012

HEPARIN (MUCOUS) INJECTION BP

Presentation Heparin (Mucous) Injection BP 1,000 units per ml: each ml contains 1,000 units sodium heparin. (Presented in 5 ml ampoules without preservative, and 5 ml vials with preservative.)

Heparin (Mucous) Injection BP 5,000 units per ml: each ml contains 5,000 units sodium heparin.

Heparin (Mucous) Injection BP 25,000 units per ml: each ml contains 25,000 units sodium heparin.

Uses *Mode of Action:* Heparin is a naturally occurring anticoagulant which prevents the coagulation of blood *in-vivo* and *in-vitro*. It potentiates the inhibition of several activated coagulation factors, including thrombin and factor X.

The anticoagulant properties of heparin are valuable for the prophylaxis and management of intravascular clotting and embolism. It is also used in extra-corporeal circulation, i.e. heart-lung and renal dialysis machines and blood transfusions.

In addition to the anticoagulant properties heparin also has some lipaemia-clearing effect which may be utilised in the treatment of fat embolism.

Indications: Treatment of thrombo-embolic disorders such as: Deep vein thrombosis, Thrombophlebitis, Pulmonary embolism, Fat embolism.

Dosage and administration Heparin is usually administered by intravenous injection or subcutaneously. Although the intramuscular route can be used, it is not recommended because of the high incidence of haematoma.

The increase in clotting time provided by heparin becomes apparent immediately after administration and lasts for four to six hours after intravenous injection and for about eight hours after subcutaneous injection.

Dosage: Intravenous administration: 5,000–10,000 units every four hours either by bolus injection or continuous infusion in Sodium Chloride Injection or Dextrose Injection. However, the dose should be monitored with coagulation tests, and varied according to individual response.

Subcutaneous administration: 5,000 units every eight hours.

The treatment period varies from 7–10 days in peri-operative prophylaxis to as much as six weeks in the treatment of established thrombosis.

Contra-indications, warnings, etc

Contra-indications: Haemorrhagic disorders and patients with an actual or potential bleeding site e.g. peptic ulcer.

Precautions: Heparin therapy should be given with caution to patients about to undergo surgery, and those with impaired renal or hepatic function.

Overdosage: The effect of heparin can be reversed immediately by intravenous administration of a 1% protamine sulphate solution. The quantity of protamine required for neutralisation falls rapidly with the lapse of time after the administration of heparin and can be accurately determined by titration of the patient's plasma, containing heparin, with protamine. If given within 15 minutes of the heparin injection 10 mg of protamine will neutralise 1,000 units of heparin, while 30 minutes after the heparin injection, only 5 mg of protamine per 1,000 units of heparin is needed. It is important to avoid overdosage of protamine sulphate because protamine itself has anticoagulant properties. A single dose of protamine sulphate should never exceed 50 mg. Intravenous injection of protamine may cause a sudden fall in blood pressure, bradycardia, dyspnoea and transitory flushing, but these may be avoided or diminished by slow and careful administration.

Pharmaceutical precautions Store below 25°C. Admixture of heparin with solutions of other medicinal products may result in precipitation or loss of potency.

Legal category POM.

Package quantities *Heparin 1,000 units per ml:* 5 ml ampoules (without preservative), 5 ml vials (with preservative); Packs of 5.

Heparin 5,000 units per ml: 5 ml; Packs of 5 vials.

Heparin 25,000 units per ml: 5 ml; 1 vial.

Further information *Preservative used:* 1,000 units (with preservative) and 5,000 units: 0.5% Chlorbutol. 25,000 Units: 0.4% Chlorbutol.

Available for low dose prophylactic use: Minihep: Single dose ampoules containing 5,000 units sodium heparin in 0.2 ml and

Minihep calcium: Single dose ampoules containing 5,000 units calcium heparin in 0.2 ml.

Menstruation and pregnancy are not contra-indications to heparin therapy. Heparin does not cross the placenta or appear in breast milk.

Product licence numbers

1,000 units (with preservative)	0043/0041
1,000 units (without preservative)	0043/0085
5,000 units	0043/0038
25,000 units	0043/0039

HEP-RINSE*

Presentation Heparin flush solution, each ml contains 100 units heparin sodium (mucous) injection BP with 0.5% chlorbutol as preservative.

Uses Heparin is an anticoagulant which prevents the formation of thrombin by accelerating the neutralisation of activated Factor X by naturally occurring inhibitors.

Indications: This strength of heparin is used as a 'heparin flush' every four hours, or as necessary, to keep intravenous lines patent. It is not recommended that this low-dose heparin be used therapeutically.

Dosage and administration For routine use, 2 ml containing 200 units of heparin sodium should be administered into the catheter/cannula every four to eight hours.

Contra-indications, warnings, etc When used as recommended the low dose of heparin reaching the blood should have no systemic effects.

Pharmaceutical precautions Store below 25°C.

Hep-Rinse is compatible with normal saline. Admixture with other drugs may cause inactivation of either the heparin solution or the drugs.

Legal category POM.

Package quantities Packs of 10 × 2 ml ampoules.

Further information Nil.

Product licence number 0043/0057.

LEO* K TABLETS

Presentation Potassium Chloride BP 600 mg (8 mmol potassium in a slow-release wax core). White film-coated, ovoid tablets with no superficial markings.

Uses *Mode of Action:* Potassium depletion can occur insidiously, as the symptoms often resemble those of the underlying condition and may be easily overlooked. It is difficult to assess potassium depletion from serum potassium levels because there is no correlation between intracellular and extracellular potassium concentrations.

Intake of dietary potassium may not be adequate to restore normal levels in patients who already have low cellular potassium. These patients require potassium supplements.

Because of the risk of localised high concentrations of potassium salts in the small bowel, the potassium of Leo

K is included in an inert wax core, from which it is released slowly over at least six hours.

Indications: As a potassium supplement, to reduce the risk of potassium depletion which may be associated with prolonged use of diuretics, and corticosteroids; congestive heart failure; primary or secondary aldosteronism; renal tubular acidosis; malabsorption syndrome, ulcerative colitis, liver cirrhosis and other conditions where potassium loss may be severe.

Dosage and administration 3-5 tablets daily in divided doses (24-40 mmol potassium) are often adequate. A smaller dose may be adequate in those patients with a more satisfactory dietary intake of potassium, but some patients, particularly those with hepatic or renal insufficiency, may require considerably more potassium chloride.

Contra-indications, warnings, etc *Precautions:* To avoid hyperkalaemia, a potassium supplement should be used with great caution in renal insufficiency or with the potassium-sparing diuretics like spironolactone, triamterene or amiloride. Some patients may develop potassium depletion despite the use of potassium supplements. This is a particular danger to digitalised patients or those with hepatic ascites.

Non-specific small bowel lesions, characterised by stenosis and possibly accompanied by ulceration have been associated with the oral administration of tablets and capsules containing potassium salts. Symptoms and signs which might indicate ulceration or obstruction of the small bowel in patients taking tablets or capsules containing potassium salts are indications for stopping treatment with such a preparation immediately.

Overdosage: Symptoms of overdosage include asthenia, hypotension, mental confusion, paraesthesia, and cardiac arrhythmias.

Characteristic ECG changes also occur. Hyperkalaemia should be treated with an intravenous infusion of sodium bicarbonate or by intravenous injection of calcium chloride or calcium gluconate (10-20 ml of a 1% solution).

Pharmaceutical precautions Nil.

Legal category GSL.

Package quantities Packs of 100 and 1,000 tablets.

Further information Nil.

Product licence number 0043/5006.

MINIHEP*

MINIHEP* CALCIUM

MINIHEP* DARTS*

MINIHEP* CALCIUM DARTS*

Presentation *Minihep:* Heparin (Mucous) Injection BP. Single dose ampoules containing Sodium Heparin 5,000 units in 0.2 ml (Preservative: 0.4% chlorbutol).

Minihep calcium: Calcium Heparin Injection (Mucous). Single dose ampoules containing Calcium Heparin 5,000 units in 0.2 ml (no preservative).

Minihep DARTS: Heparin (Mucous) Injection BP. Single dose DARTS, automatic injector system, containing Sodium Heparin 5,000 units in 0.2 ml (no preservative).

Minihep Calcium DARTS: Calcium Heparin (Mucous) Injection. Single dose DARTS, automatic injector system,

containing Calcium Heparin 5,000 units in 0.2 ml (no preservative).

Uses Mode of Action: Heparin is an anticoagulant which, even in low doses, prevents the formation of thrombin by accelerating the neutralisation of activated coagulation factors by naturally occurring inhibitors.

Indications: Prophylaxis against deep vein thrombosis and thromboembolic events in susceptible patients.

Dosage and administration Administration is by subcutaneous injection.

Patients undergoing surgery: 5,000 units in 0.2 ml should be given two to six hours pre-operatively and every eight hours post-operatively for 10–14 days, or until ambulation, whichever is the longer.

Other patients: 5,000 units in 0.2 ml should be given every 8–12 hours.

Contra-indications, warnings, etc Low doses of heparin, administered as recommended above, do not cause alterations in clotting times in most patients, but occasionally local haematomata may occur at injection sites.

Patients with haemorrhagic disorders may experience bleeding, especially from surgical wounds. The relative risks and benefits of heparin administration in these patients should be assessed carefully. Oral anticoagulants or drugs which interfere with platelet function e.g. aspirin and dextran solutions, should be administered with caution.

Overdosage: If bleeding should occur, the effect of heparin can be reversed immediately by intravenous administration of a 1% protamine sulphate solution. The dose of protamine sulphate required for neutralisation should be determined accurately by titrating with the patient's plasma.

Pharmaceutical precautions Store below 25°C. Admixture of heparin with solutions of other medicinal products may result in precipitation or loss of potency.

Legal category POM.

Package quantities *Minihep and Minihep Calcium:* 15 ampoules of 0.2 ml. *Minihep DARTS and Minihep Calcium DARTS:* 50 DARTS of 0.2 ml

Further information Menstruation and pregnancy are not contra-indications to heparin therapy. Heparin does not cross the placenta or appear in breast milk.

Heparin (Mucous) Injection BP is also available in strengths of 1,000 units per ml (with and without preservative), 5,000 units per ml and 25,000 units per ml.

Product licence numbers

Minihep	0043/0049
Minihep Calcium	0043/0051
Minihep DARTS	0043/0080
Minihep Calcium DARTS	0043/0082

ONE-ALPHA* CAPSULES

ONE-ALPHA* DROPS

DILUENT FOR ONE-ALPHA* DROPS

Presentation *One-Alpha Capsules:* Each capsule contains either 1 mcg (brown) or 0.25 mcg (white) Alfalcidol (1 α -hydroxyvitamin D₃).

One-Alpha drops: A clear or slightly opalescent, colourless solution.

One ml of solution contains 5 mcg Alfalcidol, corresponding to 0.25 mcg per drop

Diluent for One-Alpha Drops: A clear or slightly opalescent, colourless solution.

Uses Alfalcidol (1 α -OHD₃) is converted rapidly in the liver to 1,25-dihydroxyvitamin D₃ (1,25-(OH)₂D₃), the metabolite through which vitamin D is considered to express most of its effects on calcium and phosphorus metabolism. Impaired endogenous production of 1,25-(OH)₂D₃ by the kidney appears to contribute to the disturbances in mineral metabolism found in several disorders including renal bone disease, hypoparathyroidism and pseudodeficiency rickets. These disorders, termed 'vitamin D-resistant' since they usually require high doses of vitamin D for their correction, respond to small 'physiological' doses of 1 α -OHD₃.

Because 1 α -OHD₃ is metabolised rapidly to 1,25-(OH)₂D₃, the clinical effects of these agents are very similar. Patients taking barbiturates or other anticonvulsant drugs may need higher doses of 1 α -OHD₃ than otherwise, due possibly to interference with the hepatic conversion of 1 α -OHD₃ to 1,25-(OH)₂D₃ or to target-organ resistance to the actions of 1,25-(OH)₂D₃.

In treating 'vitamin D-resistant' disorders with vitamin D itself, the delay in achieving a response and the high doses required make dosage adjustments difficult. Unpredictable hypercalcaemia, once induced, may take several weeks or months to reverse. The major advantage of 1 α -OHD₃ resides in the rapidity with which it increases calcium absorption and plasma calcium, and the speed with which these effects can be reversed after stopping treatment, thus allowing dose requirements to be rapidly titrated. Should inadvertent hypercalcaemia occur, it can be reversed within days of stopping treatment.

Indications: One-Alpha drops should be administered whenever the patient is incapable of swallowing the capsules. One-Alpha is indicated in Renal bone disease, Hypoparathyroidism, Hyperparathyroidism (with bone disease), Hypophosphataemic vitamin D-resistant and Pseudo-deficiency (D-dependent) rickets and osteomalacia, Nutritional and Malabsorptive rickets and osteomalacia and Neonatal hypocalcaemia.

Dosage and administration To obtain accurate dosage of the One-Alpha drops the bottle should be held in a vertical position upside down. If the drops do not flow immediately, the bottle should be tapped gently.

If dilution is required the Diluent for One-Alpha drops should be used. The dilution should be performed in the Diluent bottle and then dispensed in this bottle.

Initial dose for all indications: *Adults:* 1 mcg daily.

Children over 20 kg bodyweight: 1 mcg daily.

Children under 20 kg bodyweight: 0.05 mcg/kg/day.

For neonates and premature infants: See neonatal hypocalcaemia.

It is important to adjust dosage thereafter according to the biochemical responses and to avoid hypercalcaemia. Indices of response include levels of plasma calcium, alkaline phosphatase, parathyroid hormone, urinary calcium excretion as well as radiographic and histological investigations. Patients with marked bone disease (other than those with renal failure) may tolerate a higher dose without developing hypercalcaemia. However, failure of the plasma calcium to rise promptly in osteomalacic patients does not necessarily mean that a higher dose is required since calcium from increased intestinal calcium absorption may be incorporated into demineralised bone. Most patients respond eventually to doses between 1–3 mcg daily.

The dose requirements generally decrease in bone disorders at a time when there is biochemical or radiographic evidence of bone healing, and in hypoparathyroid patients after normal plasma calcium levels have been attained. Maintenance doses are generally in the range 0.25–1 mcg daily.

Renal bone disease: Most patients with osteitis fibrosa and osteomalacia show a rapid symptomatic, and a gradual biochemical, radiographic and histological improvement. In these, the only unwanted effect of 1α -OHD₃ appears to be hypercalcaemia which is more likely when there is evidence of bone healing.

Patients with relatively high initial plasma calcium levels may have autonomous hyperparathyroidism which is often unresponsive to 1α -OHD₃; other therapeutic measures may be indicated.

Before and during treatment with 1α -OHD₃, phosphate-binding agents should be considered to prevent hyperphosphataemia, which, especially when associated with hypercalcaemia, is known to increase the risk of metastatic calcification. Because prolonged hypercalcaemia may aggravate the decline in renal function, it is particularly important to make frequent plasma calcium estimations in patients with chronic renal failure.

Early hypercalcaemia is more likely in patients with autonomous hyperparathyroidism, those with histologically 'pure' osteomalacia related possibly to phosphate depletion or aluminium intoxication, and those dialysed against a high dialysate calcium concentration.

Hypoparathyroidism: In contrast to the response to vitamin D, low plasma calcium levels are restored to normal relatively quickly with 1α -OHD₃. Severe hypocalcaemia (e.g. after extensive neck surgery) is corrected and symptoms abolished even more rapidly with higher doses of 1α -OHD₃ (e.g. 3–5 mcg) and calcium supplements. Normocalcaemia may be maintained with smaller doses within a relatively narrow dose range.

Hyperparathyroidism: Following parathyroidectomy, patients with primary or tertiary hyperparathyroidism and bone disease often require large doses of vitamin D and intravenous calcium to avoid severe hypocalcaemia. Preliminary studies suggest that pre-operative treatment with 1α -OHD₃ for two to three weeks alleviates bone pain and myopathy when present without aggravating pre-operative hypercalcaemia. Continued post-operative treatment decreases post-operative hypocalcaemia and should be continued until the plasma alkaline phosphatase levels falls to normal or hypercalcaemia occurs.

Hypophosphataemic vitamin D-resistant rickets and osteomalacia is characterised by hypophosphataemia due to defective renal tubular reabsorption and intestinal absorption of phosphorus. Neither large doses of vitamin D nor phosphate supplements are entirely satisfactory, the latter tending to produce hypocalcaemia and hyperparathyroidism. Treatment of children and adults with 1α -OHD₃ rapidly relieves myopathy when present, increases calcium and phosphorus retention and promotes bone healing. Phosphate supplements may also be required in some patients.

Pseudo-deficiency (D-dependent) rickets requires large doses of vitamin D, probably because of an inherited defect in the production of $1.25\text{-(OH)}_2\text{D}_3$. In contrast, effective doses of 1α -OHD₃ are similar to those required to heal nutritional vitamin D deficiency rickets.

Nutritional and malabsorptive rickets and osteomalacia: Nutritional rickets and osteomalacia can be rapidly cured

with 'physiological' doses of 1α -OHD₃. Limited experience suggests that patients with malabsorptive osteomalacia, responding only to large doses of vitamin D given parenterally, respond to small oral doses of 1α -OHD₃.

Neonatal hypocalcaemia: The normal starting dose of 1α -OHD₃ is 0.05–0.1 mcg/kg/day. Adjustment of the dose thereafter is by careful titration (but in severe cases doses up to 2 mcg/kg/day may be required). Whilst ionised serum calcium levels may provide a guide to response, measurement of plasma alkaline phosphatase activity may be more useful. Levels of plasma alkaline phosphatase may be markedly raised in the pre-term low birthweight infant. Whilst levels of 5 times the normal adult laboratory value may be useful in this group alkaline phosphatase levels above 7½ times the adult range indicate active disease. A dose of 1α -OHD₃ of 0.1 mcg/kg/day has proved effective as prophylaxis against early neonatal hypocalcaemia in premature neonates.

Contra-indications, warnings, etc Precautions and side-effects: If hypercalcaemia is induced by 1α -OHD₃, it can be rapidly corrected by stopping treatment. Throughout treatment, regular plasma calcium determinations are essential. Indeed, 1α -OHD₃ should only be used by those with facilities to monitor plasma calcium and other appropriate biochemical parameters on a regular basis. If hypercalcaemia occurs, 1α -OHD₃ should be stopped until the plasma calcium returns to normal (in about one week) and then restarted at half the dose.

The risk of hypercalcaemia depends on such factors as the degree of any mineralisation defect, renal function, and the dose of 1α -OHD₃ used. Thus hypercalcaemia is less likely in osteomalacia and more likely in renal failure.

Hypercalcaemia will occur when there is biochemical evidence of bone healing (e.g. a return towards normal in the level of plasma alkaline phosphatase) and the dose of 1α -OHD₃ is not reduced appropriately. Prolonged hypercalcaemia should be avoided, particularly in chronic renal failure.

Frequency of monitoring: Plasma calcium levels should be measured at weekly to monthly intervals depending on the progress of the patient. Frequent estimations are necessary in the early stages of treatment (particularly when the plasma calcium is already relatively high) and later when there is evidence of bone healing. Plasma calcium levels should also be estimated regularly during the initial treatment of disorders without significant bone involvement, e.g. hypoparathyroidism.

Patients concurrently taking barbiturates and other anticonvulsant drugs may require larger doses of 1α -OHD₃ to produce the desired effect.

Pregnancy: 1α -OHD₃ should only be used during pregnancy or lactation if considered essential by the physician.

Overdosage: Hypercalcaemia is treated by stopping 1α -OHD₃. Severe hypercalcaemia may be treated additionally with a 'loop' diuretic and intravenous fluids, or with corticosteroids.

Pharmaceutical precautions *One Alpha capsules:* Protect from direct sunlight. *One Alpha drops and diluted drops:* Protect from direct sunlight and store in a cool place (below 15°C).

Legal category

One-Alpha Capsules and Drops: POM
Diluent for One-Alpha Drops: GSL

Package quantities *Capsules:* Bottles of 100 capsules. *Drops:* Amber glass bottle of 10 ml.
Diluent: Packs of 10 amber glass bottles of 100 ml.

Further information Nil.

Product licence numbers

Capsules 1 mcg	0043/0050
Capsules 0.25 mcg	0043/0052
Drops	0043/0071
Diluent	0043/0083

PRESTIM* TABLETS

Presentation White, flat, petal-shaped tablets engraved with 132 on the scored face and with an Assyrian lion on the reverse. Each tablet contains timolol maleate 10 mg and Bendrofluazide BP 2.5 mg.

Uses *Mode of Action:* Bendrofluazide, a thiazide diuretic, has an established action in the treatment of hypertension.

Timolol maleate is a beta-adrenergic receptor blocking agent with marked hypotensive activity lasting up to 24 hours.

It has been shown that the combination of a beta-blocking agent with a thiazide diuretic gives an enhanced antihypertensive effect. This means that a relatively lower dose of the beta-blocker is required.

Indications: For the treatment of mild to moderate hypertension.

Dosage and administration The recommended dosage range is from 1 to 4 tablets daily. Most patients are controlled on 1 or 2 tablets, taken in a single dose in the morning or in two divided doses, morning and evening.

If blood pressure control is not achieved on 4 tablets daily, consideration should be given to titrating timolol and bendrofluazide separately or adding another agent with hypotensive activity.

Contra-indications, warnings, etc

Contra-indications: Anuria. Prestim should not be used in patients with renal failure or with a history of hypersensitivity to the thiazides.

Uncontrolled heart failure, bradycardia, cardiogenic shock, hay fever, obstructive lung disease, patients receiving adrenergic augmenting drugs (monoamine oxidase inhibitors and tricyclic antidepressants).

Anaesthesia with agents that produce myocardial depression, such as chloroform and ether.

Pregnancy.

As with other diuretics, Prestim should not be administered concurrently with lithium salts. Diuretics can reduce lithium clearance resulting in high serum levels of lithium.

Precautions: The continued depression of sympathetic drive through beta blockade may lead to cardiac failure, and, if it occurs, digitalisation should be considered.

Caution should be exercised in patients with diabetes mellitus, spontaneous hypoglycaemia, impaired renal or hepatic function and in patients receiving catecholamine depleting drugs, such as reserpine or guanethidine.

Adverse Reactions: Side-effects associated with beta blockade, e.g. gastro-intestinal symptoms, dizziness, insomnia, sedation, depression, weakness, dyspnoea, bradycardia, heart block, bronchospasm and heart failure.

Thiazide diuretics may cause excessive depletion of

fluid and electrolytes during prolonged or intense use. Symptoms are muscle pain or fatigue, thirst and oliguria. With thiazide diuretics hypokalaemia is more severe in patients already depleted of potassium, as in renal or hepatic insufficiency. Coma may be precipitated in hepatic cirrhosis.

The thiazides may induce hyperglycaemia and glycosuria in diabetic and other susceptible patients. The thiazides increase blood urea, which is most pronounced in patients with renal disease and pre-existing retention of nitrogen. Hyperuricaemia sometimes can occur.

Reports of other adverse reactions to the thiazides include skin rashes with associated photosensitivity, necrotising vasculitis, acute pancreatitis, blood dyscrasias and aggravation of pre-existing myopia.

Warning: There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuance of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with the beta-blocker should be gradual.

Overdosage: The most common signs of overdosage are bradycardia, hypotension, bronchospasm and acute cardiac failure. Suggested treatments are as follows:

Severe bradycardia: I.V. atropine sulphate 0.25–2 mg. If bradycardia persists, I.V. isoprenaline 25 mcg may be given.

Severe hypotension: I.V. noradrenaline or adrenaline.

Bronchospasm: Isoprenaline hydrochloride, orciprenaline or salbutamol.

Acute cardiac failure: digitalis, diuretics and oxygen. In refractory cases I.V. aminophylline and I.V. glucagon 0.5–1 mg have been reported useful.

General measures should be taken to restore blood volume, maintain blood pressure and correct electrolyte imbalance.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Glass bottles of 100 tablets.

Further information Both constituents cross the placenta and appear in breast milk.

Product licence number 0043/0047.

**SELEXID* TABLETS ▼
SELEXID* SUSPENSION ▼**

Presentation *Tablets:* Each tablet contains 200 mg pivmecillinam hydrochloride – a white film-coated tablet with convex surfaces, an Assyrian lion printed on one side and the number 137 on the other.

Suspension: Unit-dose foil sachets, each containing 100 mg of pivmecillinam as white granules.

Uses Selexid is an orally active antibiotic. Chemically it is the pivaloyloxymethyl ester of the amidinopenicillanic acid, mecillinam. On oral administration, it is well absorbed and subsequently hydrolysed in the body to mecillinam, the active antibacterial agent, by non-specific esterases present in blood, gastro-intestinal mucosa and other tissues. Peak serum levels of mecillinam averaging 5 mcg/ml are reached after one hour

following a dose of 10 mg/kg body weight in children and 400 mg in adults.

The serum half-life is 1.2 hours. The protein binding amounts to 5–10%. Approximately 50% of the administered dose is excreted as mecillinam in the urine within the first six hours. Mecillinam is partly excreted with the bile giving rise to biliary concentrations about three times the serum levels. Concurrent administration of probenecid delays the renal excretion of mecillinam, producing more sustained serum levels. The absorption of Selexid is practically unaffected by taking the tablets or suspension with food.

Selexid is highly active against most Enterobacteriaceae, including *E. coli*, *Klebsiella*, *Proteus*, *Enterobacter*, *Serratia*, *Salmonella*, *Shigella*, and *Yersinia*.

Selexid is less active against gram-positive bacteria, and organisms such as *Pseudomonas aeruginosa* and *Streptococcus faecalis* are practically resistant to mecillinam.

Whilst Selexid, like the penicillins and cephalosporins, interferes with the biosynthesis of the bacterial cell wall, the target of the inhibition is different. This different mode of action is probably responsible for the synergistic action which has been found, both *in-vitro* and *in-vivo*, between Selexid and various penicillins and cephalosporins.

Indications: Selexid is indicated in the treatment of infections due to mecillinam sensitive organisms, including.

- (a) Urinary tract infections.
- (b) Salmonellosis.

Preliminary experience in a small number of patients suggests Selexid may be a useful alternative antibiotic in the treatment of acute typhoid fever, and in some carriers of salmonellae when antibiotic treatment is considered essential.

Dosage and administration Both the tablets and suspension should be preferably taken with or immediately after a meal, or with bland fluids such as water or milk.

Suspension: Mix the contents of the sachet in a little water (5–10 ml) and stir before taking. The suspension should be taken immediately.

Dosage for adults and children weighing more than 40 kg:

Urinary tract infections:

1. Uncomplicated cystitis: 200 mg (1 tablet or 2 sachets) three to four times daily.
2. Chronic or recurrent bacteriuria: 400 mg (2 tablets or 4 sachets) three to four times daily.

Salmonellosis:

1. Enteric fever: 1.2–2.4 g daily for 14 days.
2. Salmonella carriers: 1.2–2.4 g daily for 2–4 weeks.

Dosage for children weighing less than 40 kg:

Urinary tract infections: 20–40 mg/kg body weight, daily, in three to four divided doses.

Salmonellosis: 30–60 mg/kg body weight, daily, in three to four divided doses.

Contra-indications, warnings, etc

Contra-indications: Penicillin and cephalosporin hypersensitivity.

Precautions: During long term usage, it is advisable to carry out routine liver and kidney function tests.

As with other antibiotics which are excreted mainly by the kidneys, raised blood levels of mecillinam may occur

if repeated doses are given to patients with impaired renal function.

Pregnancy: Although tests in two animal species have shown no teratogenic effects, in keeping with current practice, use during the first trimester of pregnancy should be avoided. The drug, as mecillinam, crosses the placenta.

Adverse Reactions: Anaphylactic reactions, though not yet reported, may occur. Upper gastro-intestinal disturbances such as nausea, vomiting and indigestion have occurred, more frequently when a dose has been given on an empty stomach. Other side effects reported are diarrhoea and urticarial rash.

Overdosage: There has been no experience of overdosage with Selexid. However, excessive doses are likely to induce nausea, vomiting and gastritis. Treatment should be restricted to symptomatic and supportive measures.

Pharmaceutical precautions Store in a cool, dry place.

Legal category POM.

Package quantities *Tablets:* Bottles of 10 and 100 tablets.

Suspension: Boxes of 20 sachets.

Further information Nil.

Product licence numbers

Tablets 0043/0048

Suspension 0043/0053

SELEXIDIN* INJECTION ▼

Presentation Each vial contains either 200 mg or 400 mg mecillinam, a white crystalline powder.

Uses Selexidin is the amidino-penicillanic acid, mecillinam. It may be administered by both intravenous and intramuscular injection.

Peak serum levels averaging 6 mcg/ml and 12 mcg/ml are obtained following intramuscular doses of 200 mg and 400 mg respectively. Intravenous injection produces initially very high concentrations, which rapidly decline as the compound is excreted. The serum half life is 1.2 hours, and the protein binding amounts to 5–10%. Approximately 50–60% of the dose may be recovered in the urine within the first six hours. Mecillinam is partly excreted with the bile giving rise to biliary concentrations about three times the serum level. Concurrent administration of probenecid delays the renal excretion of mecillinam.

Selexidin is highly active against most Enterobacteriaceae, including *E. coli*, *Klebsiella*, *Proteus*, *Enterobacter*, *Serratia*, *Salmonella*, *Shigella* and *Yersinia*.

Selexidin is less active against gram-positive bacteria and organisms such as *Pseudomonas aeruginosa* and *Streptococcus faecalis* are practically resistant to mecillinam.

Whilst Selexidin, like the penicillins and cephalosporins, interferes with the biosynthesis of the bacterial cell wall, the target of the inhibition is different. This different mode of action is probably responsible for the synergistic action which has been found, both *in-vivo* and *in-vitro*, between Selexidin and various penicillins and cephalosporins.

Indications: Selexidin injection is indicated in the treatment of serious infections due to mecillinam-sensi-

tive organisms, and in those patients where oral therapy, with Selexidin, is considered inappropriate.

Dosage and administration Selexidin should be dissolved in Water for Injections and administered either intramuscularly or by slow intravenous injection (three to four minutes) in the following concentrations:

Intravenous: Dissolve the mecillinam, in sterile water, as a 10% w/v solution, e.g. 400 mg in 4 ml.

Intramuscular: Dissolve 200 mg in 1 ml sterile water. Dissolve 400, 600 or 800 mg in 2 ml sterile water.

Alternatively, mecillinam, following dissolution in Water for Injections BP, may be added to either Sodium Chloride Injection or 5% dextrose and infused over 15–30 minutes. Such solutions should be made immediately before use and not stored. It is not recommended to store aqueous solutions of mecillinam. Mecillinam should not be added to infusion fluids containing other antibiotics.

Dosage: Adults and children.

1. *Urinary tract infections:* 5 mg/kg body weight every six to eight hours.

2. *Severe gram-negative infections due to susceptible organisms:* 10 mg/kg body weight every six hours.

3. *Enteric fever:* 12.5–15.0 mg/kg body weight every six hours. (Probenecid may also be administered.)

In some instances, for example where there was reason to expect a synergistic interaction, mecillinam has been given in combination with a broad-spectrum penicillin or cephalosporin. When combination therapy has been employed, normal dosages of both compounds were given.

Contra-indications, warnings, etc

Contra-indications: Penicillin and cephalosporin hypersensitivity.

Precautions: During long-term usage, it is advisable to carry out routine liver and kidney function tests.

As with other antibiotics which are excreted mainly by the kidneys, raised blood levels of mecillinam may occur if repeated doses are given to patients with impaired renal function.

Pregnancy: Although tests in two animal species have shown no teratogenic effects, in keeping with current practice, use during the first trimester of pregnancy should be avoided. The drug, as mecillinam, crosses the placenta.

Adverse reactions: Reported side-effects include urticarial rash, and suspected drug fever in a few patients with enteric fever. Anaphylactic reactions, though not yet reported, may occur. Preliminary experience indicates that intramuscular injections of mecillinam are well tolerated.

Overdosage: There has been no experience of overdosage with Selexidin. Treatment should be restricted to symptomatic and supportive measures.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Boxes of 10 vials.

Further information Nil.

Product licence numbers

0043/0054 (200 mg)

0043/0055 (400 mg)

TREOSULFAN* CAPSULES TREOSULFAN* INJECTION

Presentation *Capsules:* White, opaque capsules each containing 250 mg L-threitol 1,4-dimethane sulfonate.

Injection: Infusion bottles containing 5 g L-threitol 1,4-dimethane sulfonate, a white crystalline powder.

Uses Treosulfan is a bifunctional alkylating agent which has been shown to possess anti-neoplastic activity in the animal tumour screen and in clinical trials. The activity of Treosulfan is due to the formation of epoxide compounds *in vivo*.

Indications: For the treatment of all types of ovarian cancer, either supplementary to surgery or palliatively. Some uncontrolled studies have suggested activity in a wider range of neoplasms.

Because of a lack of cross-resistance reported between Treosulfan and other cytotoxic agents Treosulfan may be useful in any neoplasm refractive to conventional therapy.

Treosulfan has been used in combination regimens in conjunction with vincristine, methotrexate, 5-FU and procarbazine.

Dosage and administration *Capsules:* 1 g daily, given in four divided doses for four weeks followed by four weeks off therapy. This cycle should be repeated with the dose being adjusted, if necessary, according to the effect on the bone marrow. The capsules should be swallowed whole and not allowed to disintegrate within the mouth.

Injection: 5–15 g I.V. every 1–3 weeks depending on blood count and concurrent chemotherapy. Single injections of up to 15 g have been given with no serious adverse effects. Doses up to 3 g have been given intraperitoneally. Doses of 5 g Treosulfan may be given as a bolus injection. Larger doses should be administered as an IV infusion at a rate of 5 g every 5–10 minutes. The contents of each infusion bottle should be dissolved in 100 mls Water for Injection, a transfer needle may be used for this purpose. The resulting solution should be used immediately and any contents not used at once should be discarded.

Treatment should not be given if the white blood cell count is less than 3,000/mcl or the thrombocyte count less than 100,000/mcl. A repeat blood count should be made after a weeks interval, when treatment may be restarted if haematological parameters are satisfactory. Lower doses of Treosulfan should be used if other cytotoxic drugs or radiotherapy are being given concurrently. Treatment is initiated as soon as possible after diagnosis.

Contra-indications, warnings, etc *Warning:* This product should not normally be administered to patients who are pregnant or to mothers who are breast-feeding.

Adverse reactions: As with other alkylating agents, Treosulfan has a depressive effect on the bone marrow. Reduction in white blood cell and thrombocyte counts occur during treatment and minimal levels may not occur until two or three weeks after discontinuing treatment. These counts usually return to normal within four weeks of cessation of therapy.

Patients showing marked bone marrow depression in the first course of treatment often respond similarly during subsequent courses. In all cases blood cell counts should be monitored regularly. Other adverse reactions include gastro-intestinal complaints such as nausea,

vomiting, and abdominal pain, mild allergic reactions in the form of exanthema, and skin pigmentation. Alopecia may occur. Stomatitis may occur if the patients chew the capsule. Parenteral therapy has shown no local or systemic side effects apart from the expected bone marrow depression.

Overdosage: Although there is no experience of acute overdosage with Treosulfan, nausea, vomiting and gastritis may occur. Excessive prolonged high doses may lead to an irreversible depression of bone marrow. The drug should be withdrawn, a blood transfusion given and general supportive measures given.

Pharmaceutical precautions Once brought into solution, the injection should be used immediately.

Legal category POM.

Package quantities *Capsules:* Amber glass bottles of 100 capsules. *Injection:* Boxes of 5 × 100 ml infusion bottles, each containing 5 g Treosulfan, complete with 5 transfer needles and 5 plastic bottle holders.

Further information All centres using Treosulfan have reported noteworthy improvements in the general condition of patients responding to treatment, particularly in regard to reduction or disappearance of ascites. Treosulfan is remarkably well tolerated, allowing many patients to become fully ambulatory and return to their normal day to day work.

Product licence numbers

Capsules 0043/0040

Injection 0043/0072

UROKINASE*

Presentation Single ampoules of Urokinase as a sterile, white lyophilised powder. Ampoules of 5,000, 25,000 and 100,000 Ploug units (1 Ploug unit is equivalent to 1.49 international units and is approximately equivalent to 1.43 CTA units) (see Further information section).

Uses Urokinase is an enzyme prepared from the urine of adult males.

It activates the process of fibrinolysis as described below. Its prime advantage over other activators is that, being of human origin, it is free from antigenic properties in man and free from inherent toxicity.

Mode of Action: Digestion of a fibrin thrombus is brought about by the proteolytic enzyme, plasmin. This is normally present in the blood as an inactive precursor plasminogen and conversion of this substance to plasmin is provoked physiologically by plasminogen-activator. Urokinase activates plasminogen directly, in contrast to Streptokinase which appears to act indirectly on a proactivator in the plasma to form activator.

Indications: Urokinase can be used locally in the treatment of the following conditions: secondary hyphaemia, vitreous haemorrhage, and for the unblocking of clotted arteriovenous shunts and intravenous cannulae.

Urokinase (labelled with technetium) may also be used to detect and localise deep vein thrombosis.

Other indications: Urokinase has been used experimentally in pulmonary embolism, deep vein thrombosis, coronary thrombosis, intra-uterine transfusion, menin-

gitis and ventriculitis. It should in theory also be of value in the treatment of retinal vessel thrombosis, peripheral arterial thrombosis and cerebral vascular occlusion, but little clinical evidence is available.

Dosage and administration *Hypaema:* The following technique is generally used: 5,000 units of Urokinase are dissolved in 2 ml of sterile saline. An anterior chamber or lachrymal irrigator is inserted through a 3 mm incision, made just within the temporal limbus. The irrigator tip is turned towards the inner surface of the cornea, avoiding the pupillary space, and the chamber is irrigated with Urokinase solution using minimum pressure. The clot begins to loosen and may float free, small fragments being either sucked up by the syringe or forced out through the incision.

If a 5,000 unit dose proves ineffective, the dose may be increased to 10,000 or 25,000 units.

Vitreous haemorrhage: 5–25,000 units of Urokinase dissolved in 0.2–1.5 ml of sterile water. The most usual dosage used is 25,000 units dissolved in 0.3 ml sterile water.

Clotted arterio-venous shunts: Generally, 5–25,000 units of Urokinase in 5 ml of saline have been instilled into the affected limb of the shunt, which is then clamped off for two to four hours.

In one study, a concentration of 5,000 units per ml was used, up to a total local dose of 25,000–50,000 units. In some refractory cases, using this dosage, continued improvement has been noted after 6 consecutive doses over a period of three days.

To establish or maintain a state of systemic fibrinolysis, very much larger quantities of Urokinase are used. To detect deep vein thrombosis Urokinase is radio-labelled with technetium.

Contra-indications, warnings, etc

Contra-indications: Any evidence of bleeding constitutes a contra-indication to fibrinolytic therapy, except in 'closed' situations. Post-operative therapy with high doses of Urokinase is generally inadvisable within 48–72 hours.

High dose Urokinase therapy carries the risk of inducing haemorrhage, particularly cerebral haemorrhage, in patients with severe hypertension.

Pregnancy: Contra-indicated during pregnancy and suspected pregnancy.

Precautions: Previous preparations contained a small degree of thromboplastic activity, but the present formulation has been purified to the standard required by the Committee on Thrombolytic Agents (CTA) in America.

Use with caution in patients who have had active cardiopulmonary resuscitation with multiple intravascular and intracardiac punctures, and in patients with known gastro-intestinal lesions.

Adverse Reactions: Large doses of 0.5–1 million units have been infused intravenously without untoward effects. Repeated application to the anterior chamber of the eye has not produced any evidence of irritation. Nor have there been any reports of antigenicity associated with its use.

Overdosage: Infusion of Urokinase should be stopped if bleeding occurs. Administration of compatible whole blood may be necessary for patients treated with large doses of Urokinase. Epsilon aminocaproic acid (EACA), Trasylol (aprotinin for injection) and fibrinogen should also be readily available.

Pharmaceutical precautions Lyophilised Urokinase is extremely stable. It should be stored at 4°C and can be kept for at least five years at this temperature. Aqueous solutions at 4°C retain their activity for three to four days and have a high degree of stability over a wide pH range.

Legal category POM.

Package quantities Single ampoules: 5,000, 25,000 and 100,000 Ploug units.

Further information The activity of Urokinase is expressed in arbitrary Ploug units. There is a difference between the American and British dosage standards. In the US, activity is expressed as an arbitrary unit determined by the Committee on Thrombolytic Agents (CTA). One CTA unit is approximately equivalent to 0.7 Ploug units. More recently, an International Reference preparation has been established: 1 Ploug unit is equal to 1.49 international units.

Product licence numbers

5,000 Ploug units	0043/5011
25,000 Ploug units	0043/5024
100,000 Ploug units	0043/5023

VARIOTIN* OINTMENT

Presentation Each gram of Variotin Ointment contains pecilocin 3,000 units.

A unit is the minimum amount of pecilocin in 1 ml required to inhibit the growth of *Penicillin chrysogenum* Q-176 in Czapek Dox agar medium.

Uses *Mode of Action:* Variotin is an antifungal antibiotic produced by *Paecilomyces varioti* Bainier var. *antibioticus*. *In-vitro* studies have shown that Variotin is active against the common dermatophytes, including species of *Trichophyton*, *Epidermophyton* and *Microsporon*, as well as *Blastomyces* and *Cryptococcus*.

Variotin is an effective topical antibiotic for the treatment of ringworm of the skin. Prolonged courses of Variotin have proved effective even in persistent infections caused by *Trichophyton rubrum*. The action of Variotin is not affected by sebum or pH changes on the skin.

Indications: *Tinea pedis* (athlete's foot), *tinea cruris*, *tinea corporis* and other ringworm infections of the skin, nails and scalp.

Dosage and administration *Adults and Children:*

Uncovered dry lesions: The ointment should be rubbed into the skin thoroughly two or three times daily.

Covered moist lesions: Less frequent applications may be adequate. Initially the lesions should be cleansed and dried. Blisters should be broken with a sterilised needle or small scissors. The ointment should be applied fairly thickly on gauze. Clinical improvement is usually seen after one or two weeks therapy. Treatment should be continued for some time, however, in an attempt to eliminate fungi from the deeper layers of the skin and prevent recurrence of the infection, especially in *T. rubrum* infections. Care should also be taken to avoid re-infection from clothing which may have been contaminated by the infecting fungus.

Contra-indications, warnings, etc

Contra-indications: Lesions which are not clearly caused by fungi, e.g. eczematous lesions. Variotin is not effective in *Candida albicans* infections. As with other specific antifungal therapy, Variotin Ointment should not be used initially if the lesion is intensely inflamed.

Precaution: Variotin is not effective alone in fungal infections complicated by infection with pyogenic bacteria. In such infections, simultaneous treatment with an antibacterial agent is advisable.

Adverse reactions: Hypersensitivity may occur.

Overdosage: Not applicable.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities Available in tubes of 10 g.

Further information Nil.

Product licence number 0043/5020.

* *Trade Mark*

Eli Lilly & Company Limited

Kingsclere Road
Basingstoke
Hants RG21 2XA



AMESEC*

Presentation Capsules (blue and orange, coded Lilly 3066) each containing:

Aminophylline PhEur	130 mg
Ephedrine Hydrochloride PhEur	25 mg

Uses Prevention and symptomatic treatment of asthma.

Dosage and administration *Adults:* One of the capsules taken one to three times daily. Relief may be expected in about 30 minutes and the full effect within an hour.

The most satisfactory results are obtained when Amesec is given continuously for several months.

Contra-indications, warnings, etc

Contra-indication: Hypersensitivity to either of the constituents.

Warning: *Usage in pregnancy:* The safety of this product for use during pregnancy or for the nursing mother has not been established.

Precautions: Use with caution in patients who are overstimulated by ephedrine or other sympathomimetic agents, and in the presence of cardiac disease, hypertension or hyperthyroidism.

Side-effects: These are unlikely with the recommended dosage. Occasionally a patient who is hypersensitive to CNS stimulants may become hyperactive and emotionally upset, and may complain of insomnia, nervousness, nausea or vomiting. Tachycardia and extrasystoles may be produced.

Overdosage: Symptoms include nervousness, emotional disturbances, insomnia, nausea, vomiting, tachycardia and extrasystoles.

Treatment: General management should consist of symptomatic and supportive therapy, including gastric lavage, administration of intravenous fluids and maintenance of blood pressure, body temperature and adequate respiratory exchange.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Capsules: Bottles of 100 and 500.

Further information Nil.

Product licence number 0006/5064.

AMYTAL*

Presentation Tablets (white, coded T40) containing 15 mg Amobarbital BP.

Tablets (white, coded T56) containing 30 mg Amobarbital BP.

Tablets (white, coded T37) containing 50 mg Amobarbital BP.

Tablets (white, coded T32) containing 100 mg Amobarbital BP.

Tablets (white, scored, coded U13) containing 200 mg Amobarbital BP.

Uses Amytal can be used for the relief of anxiety and tension. Larger doses may be employed as a hypnotic.

Dosage and administration Doses must be individualised for each patient.

Sedation: 15–50 mg two to four times daily. Dosage may be adjusted to relieve tension and anxiety without significant loss of mental acuity.

Hypnosis: 100–200 mg. Occasionally a larger dose may be necessary.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to amobarbital. Patients with a history of porphyria should not receive barbiturates in any form. Barbiturates may stimulate the enzymes responsible for metabolising many other drugs; in particular they should not be administered concurrently with coumarin-type anticoagulants. They may also affect the metabolism of endogenous steroids. Barbiturates should not be administered in the presence of uncontrolled pain, because excitement may be produced.

Warning: May be habit-forming.

Precautions: Amytal should be used with caution in patients with decreased liver function, since a prolongation of effect may occur. The central nervous system depressant effect of amobarbital may be additive with that of other CNS depressants, including alcohol.

Except in emergencies, barbiturates should not be given to persons who are known to be, or are likely to become, dependent on sedative or hypnotic drugs. The repeated prescribing of any barbiturate drug for the same patient calls for careful consideration by the physician.

Amytal is not recommended for routine control of epilepsy.

Usage in pregnancy: The safety of Amytal for use during pregnancy or for the nursing mother has not been established.

Adverse reactions: Hypersensitivity reactions may occur in some patients, especially in those with asthma, urticaria or angioneurotic oedema. Idiosyncrasy, manifested as excitement, hangover or pain, has been reported rarely.

Overdosage: Symptoms include respiratory depression, depression of superficial and deep reflexes, constriction of the pupils to a slight degree (although in severe poisoning they may dilate), decreased urine formation, hypothermia and coma.

Treatment: General management should consist of symptomatic and supportive therapy, including gastric lavage, administration of intravenous fluids, and maintenance of blood pressure, body temperature and adequate respiratory exchange. Haemodialysis will in-

crease the rate of removal of barbiturates from the body fluids.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Tablets 15 mg: Bottles of 500.
Tablets 30 mg: Bottles of 500.
Tablets 50 mg: Bottles of 500.
Tablets 100 mg: Bottles of 100 and 500.
Tablets 200 mg: Bottles of 100.

Further information Nil.

Product licence numbers

Tablets 15 mg 0006/5057
Tablets 30 mg 0006/5058
Tablets 50 mg 0006/5059
Tablets 100 mg 0006/5060
Tablets 200 mg 0006/5061

AVENTYL*

Presentation Capsules (yellow and white, coded H17) each containing Nortriptyline Hydrochloride BP equivalent to 10 mg nortriptyline.

Capsules (yellow and white, coded H19) each containing Nortriptyline Hydrochloride BP equivalent to 25 mg nortriptyline.

Liquid (colourless) containing Nortriptyline Hydrochloride BP, equivalent to 10 mg nortriptyline per 5 ml.

Uses Aventyl is indicated for the relief of symptoms of depression. It may also be used for the treatment of some cases of nocturnal enuresis.

Dosage and administration For oral administration.

Adults: The usual adult dose is 20–40 mg daily in divided doses, increasing to 100 mg daily where necessary. The usual maintenance dose is 30–75 mg/day.

The elderly: Initial dosage should be 10 mg three times a day. This may be increased with caution under close supervision. Half the normal maintenance dose may be sufficient to produce a satisfactory clinical response.

Children: (for nocturnal enuresis only).

Age (years)	Weight		Dose (mg)
	kg	lbs	
6–7	20–25	44–55	10
8–11	25–35	55–77	10–20
> 11	35–54	77–119	25–35

The dose should be administered thirty minutes before bedtime.

The maximum period of treatment should not exceed three months. A further course of treatment should not be started until a full physical examination, including an ECG, has been made.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to nortriptyline. Recent myocardial infarction, any degree of heart block or other cardiac arrhythmias. Severe liver disease. Mania. Nortriptyline is contra-indicated for the nursing mother and for children under the age of six years.

Warnings: As improvement may not occur during the initial weeks of therapy, patients, especially those posing a high suicidal risk, should be closely monitored during this period.

Withdrawal symptoms, including insomnia, irritability and excessive perspiration may occur on abrupt cessation of therapy.

The use of nortriptyline in schizophrenic patients may result in an exacerbation of the psychosis or may activate latent schizophrenic symptoms. If administered to over-active or agitated patients, increased anxiety and agitation may occur. In manic-depressive patients, nortriptyline may cause symptoms of the manic phase to emerge.

Cross sensitivity between nortriptyline and other tricyclic antidepressants is a possibility.

Patients with cardiovascular disease should be given nortriptyline only under close supervision because of the tendency of the drug to produce sinus tachycardia and to prolong the conduction time. Myocardial infarction, arrhythmia and strokes have occurred. Great care is required if nortriptyline is administered to hyperthyroid patients or to those receiving thyroid medication, since cardiac arrhythmias may develop.

Nortriptyline may impair the mental and/or physical abilities required for the performance of hazardous tasks, such as operating machinery or driving a car; therefore the patient should be warned accordingly.

Drug interactions: Under no circumstances should nortriptyline be given concurrently with, or within two weeks of cessation of, therapy with monoamine oxidase inhibitors. Hyperpyretic crises, severe convulsions and fatalities have occurred when similar tricyclic antidepressants were used in such combinations.

Nortriptyline should not be given with sympathomimetic agents such as adrenaline, ephedrine, isoprenaline, noradrenaline, phenylephrine and phenylpropanolamine.

Nortriptyline may decrease the antihypertensive effect of guanethidine, debrisoquine, bethanidine and possibly clonidine. Concurrent administration of reserpine has been shown to produce a 'stimulating' effect in some depressed patients. It would be advisable to review all antihypertensive therapy during treatment with tricyclic antidepressants.

Barbiturates may increase the rate of metabolism of nortriptyline.

Usage in pregnancy: The safety of nortriptyline for use during pregnancy has not been established, nor is there evidence from animal studies that it is free from hazard; therefore the drug should not be administered to pregnant patients or women of childbearing age unless the potential benefits clearly outweigh any potential risk.

Precautions: The elderly are particularly liable to experience adverse reactions, especially agitation, confusion and postural hypotension.

Behavioural changes may occur in children receiving therapy for nocturnal enuresis.

If possible, the use of nortriptyline should be avoided in patients with narrow angle glaucoma, symptoms suggestive of prostatic hypertrophy or a history of epilepsy.

When it is essential, nortriptyline may be administered with electro-convulsive therapy, although the hazards may be increased.

Anaesthetics given during tricyclic antidepressant therapy may increase the risk of arrhythmias and hypotension. If surgery is necessary, the drug should be discontinued, if possible, for several days prior to the procedure, or the anaesthetist should be informed if the patient is still receiving therapy.

Tricyclic antidepressants may potentiate the CNS depressant effect of alcohol.

Both elevation and lowering of blood sugar levels have been reported.

Side-effects: Cardiac arrhythmias and severe hypotension are likely to occur with high dosage, or in patients with pre-existing heart disease taking normal dosage.

Other common side-effects include drowsiness, sweating, postural hypotension, tremor and skin rashes.

The following are seen occasionally: dizziness, confusion, restlessness, weakness, impotence and blurred vision. Side-effects rarely noted are epigastric distress, nausea and vomiting, dysgeusia, excessive weight gain, excessive weight loss, fatigue, insomnia, headache, paraesthesiae and pruritus.

The following adverse effects, although not necessarily all reported with nortriptyline, have occurred with other tricyclic antidepressants: atropine-like side-effects including dry mouth, disturbances of accommodation, tachycardia, constipation and hesitancy of micturition are common early in treatment, but usually lessen.

Serious adverse effects are rare; the following have been reported: depression of the bone marrow including agranulocytosis, cholestatic jaundice, hypomania, convulsions and peripheral neuropathy.

Adverse effects such as withdrawal symptoms, respiratory depression and agitation have been reported in neonates whose mothers had taken tricyclic antidepressants during the last trimester of pregnancy.

Overdose: Toxic overdosage may result in confusion, restlessness, agitation, vomiting, hyperpyrexia, muscle rigidity, hyperactive reflexes, tachycardia, cardiac arrhythmias, ECG evidence of impaired conduction, shock, congestive heart failure, severe hypotension, stupor, coma and CNS stimulation with convulsions followed by respiratory depression. Deaths have occurred following overdosage with drugs of this class.

Treatment of overdose: No specific antidote is known. General supportive measures are indicated, with gastric lavage. Activated charcoal absorbs tricyclic antidepressants very effectively. Respiratory assistance is apparently the most effective measure when indicated. The use of CNS depressants may worsen the prognosis.

Intramuscular paraldehyde or diazepam provides anticonvulsant activity with less respiratory depression than the barbiturates.

The use of digitalis and/or pyridostigmine may be considered in the event of serious cardiovascular abnormalities or cardiac failure.

The value of dialysis has not been established.

Pharmaceutical precautions Keep containers tightly closed and protect from light. Store below 25°C.

Legal category POM.

Package quantities

Capsules 10 mg: Bottles of 100 and 500.

Capsules 25 mg: Bottles of 100 and 500.

Liquid 10 mg/5 ml: Bottles of 120 ml and 500 ml.

Further information Nil.

Product licence numbers

Capsules 10 mg 0006/5054

Capsules 25 mg 0006/5055

Liquid 10 mg/5 ml 0006/5053

BRIETAL® Sodium

Presentation Brietal Sodium (methohexitone sodium), in crystalline form, is supplied as follows:

100 mg (with anhydrous sodium carbonate 6 mg) in 10 ml rubber-stoppered vials.

500 mg (with anhydrous sodium carbonate 30 mg) in 50 ml rubber-stoppered vials.

2.5 g (with anhydrous sodium carbonate 150 mg) in 17.5 ml rubber-stoppered vials.

2.5 g (with anhydrous sodium carbonate 150 mg) in 250 ml rubber-stoppered vials.

5 g (with anhydrous sodium carbonate 300 mg) in 35 ml rubber-stoppered vials.

Uses Brietal Sodium is used as an intravenous anaesthetic agent for short surgical procedures, for the induction of anaesthesia, and in conjunction with other agents for more prolonged anaesthesia.

Dosage and administration Pre-anaesthetic medication is generally advisable. Brietal Sodium may be used with any recognised pre-anaesthetic medications, but the phenothiazines are less satisfactory than the combination of an opiate and a belladonna derivative.

Brietal Sodium is administered intravenously, usually in a 1% solution (10 mg per ml).

Adults: As an initial guide a rate of 1 ml of a 1% solution (10 mg) in five seconds may be used – although a faster rate than this is preferred by some anaesthetists. The dose usually ranges between 5 and 12 ml (50–120 mg), but it must be adjusted to the needs of the individual patient. The induction dose maintains unconsciousness for about five to seven minutes.

Children: The dose should be adjusted for age and/or weight.

Maintenance: Brietal Sodium is best used simply as an induction agent. If further injection for maintenance is needed the dose must be individualised; but, as a guide, 2–4 ml of a 1% solution every four to seven minutes may be used. Constant drip infusion of a 0.1% or 0.2% solution may also be used for maintenance and the rate adjusted to the needs as indicated by presenting signs and surgical requirements. As a guide, one drop per second may be used. At this dilution the preferred solvents are 5% Dextrose Intravenous Infusion BP or Sodium Chloride Intravenous Infusion BP, to avoid undue hypotonicity.

Preparation of solutions: The recommended diluent for Brietal Sodium is Water for Injections PhEur. Solutions may also be prepared in Sodium Chloride Intravenous Infusion BP or 5% Dextrose Intravenous Infusion BP, but such solutions are not stable for more than twenty-four hours. Brietal Sodium is not compatible with Compound Sodium Lactate Intravenous Infusion BP.

For a 1% solution (10 mg per ml) vial contents should be diluted as follows:

100 mg: add 10 ml diluent.

500 mg: add 50 ml diluent.

2.5 g/17.5 ml: transfer contents of vial to 250 ml diluent in a suitable sterile container.

2.5 g/250 ml: add 250 ml diluent.

5 g: transfer contents of vial to 500 ml diluent in a suitable sterile container.

For continuous drip anaesthesia, a 0.1% solution can be prepared by dissolving 500 mg of Brietal Sodium in 500 ml of diluent; alternatively one volume of the 1% solution can be added to nine volumes of diluent.

A 0.2% solution can be prepared by adding 500 mg of Brietal Sodium to 250 ml of diluent; alternatively one volume of the 1% solution can be added to four volumes of diluent. Solutions in Water for Injections PhEur may be stored and used as long as they remain clear and

colourless. However, a single-dose vial (100 mg) is available, where this is preferred or specified.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to barbiturates. When general anaesthesia is contra-indicated, Brietal Sodium should not be used. Patients with a history of porphyria should not receive barbiturates in any form. Barbiturates may stimulate the enzymes responsible for metabolising many other drugs; in particular they should not be administered concurrently with coumarin-type anticoagulants. They may also affect the metabolism of endogenous steroids.

Warnings: May be habit-forming.

Usage in pregnancy: The safety of methohexitone sodium for use during pregnancy has not been established. Brietal Sodium should not be used in the pregnant patient unless in the opinion of the clinician, the expected benefit outweighs the possible risk.

Precautions: Brietal Sodium should be administered only by persons who are experienced in anaesthesia and who have appropriate equipment on hand for the prevention and treatment of anaesthetic emergencies. The dosage must be adjusted to each patient as response is variable and respiratory depression, apnoea or hypotension may occur. It is essential that a free airway be maintained at all times. As with any potent anaesthetic agent, pulmonary ventilation should be maintained if prolonged apnoea occurs. Repeated or continuous injection may cause cumulative effects resulting in respiratory and circulatory depression.

The patient's stomach should be empty. The usual pre-anaesthetic medications may be administered for the production of sedation and inhibition of secretions. If increased muscular relaxation is required for the performance of certain surgical procedures, it may be accomplished by the concomitant use of Brietal Sodium and skeletal muscle relaxants.

Extravasation of the solution may cause tissue reaction. Should it occur, moist heat may be applied to the infiltrated area. Special care should be taken to avoid accidental intra-arterial injection. Caution should be exercised in debilitated patients or in those with impaired function of respiratory, circulatory, renal, hepatic or endocrine systems. Methohexitone sodium should be used with extreme caution in patients in status asthmaticus.

The central nervous system depressant effect of methohexitone sodium may be additive with that of other CNS depressants, including alcohol.

Side-effects: During the induction, especially if it is too rapid, transitory apnoea may occur. This is easily treated

by maintaining pulmonary ventilation for a short time until spontaneous respiration is resumed.

Too rapid induction, inadequate dosage, or insufficient or unsuitable pre-anaesthetic medication may result in skeletal muscle activity, laryngospasm, cough, sneezing or hiccups.

Pain at the site of injection and a burning sensation along the course of the vein have occasionally been reported.

Other reported side-effects include: circulatory or respiratory depression; injury to nerves adjacent to injection site, headache, salivation, nausea, emesis, thrombophlebitis, bronchospasm and emergence delirium have been reported on rare occasions.

Acute allergic reactions, such as rash, erythema, urticaria, pruritus, rhinitis, dyspnoea, hypotension, restlessness, anxiety, abdominal pain and peripheral vascular collapse, have been reported with the use of Brietal Sodium.

Pharmaceutical precautions Owing to differences in pH, solutions of Brietal Sodium should not be mixed with acid solutions such as atropine sulphate, tubocurarine and succinylcholine chloride. However, in response to many requests from anaesthetists, the following chart is provided. This gives information obtained from compatibility studies in which a 1% solution of Brietal Sodium was mixed with therapeutic amounts of agents having a low (acid) pH.

Do not use solvents containing bacteriostats as these may cause precipitation.

Solutions of Brietal Sodium should not be stored in contact with rubber stoppers or parts of disposable syringes that have been treated with silicone as, under these conditions, they are incompatible.

Brietal Sodium is stable in Water for Injections PhEur at room temperature (15°–25°C) for at least six weeks. Solutions may be stored and used as long as they remain clear and colourless.

Vials of Brietal Sodium may be stored at room temperature (15°–25°C).

Legal category POM.

Package quantities 100 mg in 10 ml vial: Pack of 10 vials (No. 704).

500 mg in 50 ml vial: Single vials (No. 660).

2.5 g in 17.5 ml vial: Single vials (No. 663).

2.5 g in 250 ml vial: Single vials (No. 664).

5 g in 35 ml vial: Single vials (No. 659).

Further information Nil.

Active ingredient	Potency mg/ml	Volume used	Physical change			
			Immediate	15 min	30 min	1 h
BRIETAL Sodium	10	10 ml	CONTROL			
Atropine sulphate	0.4	1 ml	None	Haze		
Atropine sulphate	0.6	1 ml	None	Ppt.	Ppt.	
Succinylcholine chloride	0.5	4 ml	None	None	Haze	
Succinylcholine chloride	1	4 ml	None	None	Haze	
Dimethyltubocurarine iodide	0.5	4 ml	None	None	Ppt.	
Dimethyltubocurarine iodide	1	4 ml	None	None	Ppt.	
Scopolamine hydrobromide	0.5	1 ml	None	None	None	Haze
Tubocurarine chloride	3	4 ml	None	Haze		

Product licence numbers

100 mg	0006/5050
500 mg	0006/5051
2.5 g/17.5 ml	0006/5049
2.5 g/250 ml	0006/5049
5 g	0006/5049

CINOBAC* ▼

Presentation Capsules (green and orange, coded 3056) containing 500 mg cinoxacin.

Uses Cinoxacin is indicated for acute, recurrent and chronic upper and lower urinary tract infections (including cystitis, pyelonephritis or pyelitis and asymptomatic bacteriuria) caused by susceptible micro-organisms.

A single dose of 500 mg taken at bedtime has been shown to be effective as preventive therapy in reducing the number of episodes of infection in patients subject to recurrent urinary tract infections.

Cinoxacin is active against most strains of the following organisms: *Citrobacter* spp., *Enterobacter* spp. (including *Ent. aerogenes*, *Ent. cloacae* and *Ent. hafniae*), *Escherichia coli*, *Klebsiella* spp., *Proteus mirabilis*, *Morganella morganii*, *Pr. vulgaris*.

Cinoxacin is also active against approximately 50 per cent of strains of *Pr. rettgeri*, *Providencia* and *Serratia* species.

Dosage and administration The usual adult dose is 1 g daily administered orally as 500 mg b.d. for seven to fourteen days.

For prophylactic use, a single dose of 500 mg daily, taken at bedtime.

Not recommended for use in children.

Contra-indications, warnings, etc

Contra-indications: Cinoxacin is contra-indicated in patients with a history of hypersensitivity to cinoxacin.

Warnings – Use in pregnancy – cinoxacin should not be administered during pregnancy or to the nursing mother, since safety has not been established.

Usage in children – cinoxacin is recommended only for use in adults.

Precautions: Since cinoxacin is eliminated primarily by the kidney, it should be used with caution in patients with reduced renal function. Administration of cinoxacin is not recommended for patients with severely impaired renal function.

Adverse reactions: Gastro-intestinal – nausea, anorexia, vomiting, abdominal cramps and diarrhoea have been reported.

Hypersensitivity – rash, itching, urticaria and peripheral and oral oedema have occurred.

Other adverse reactions possibly related to cinoxacin include dizziness, headache, insomnia, tingling sensation, perineal burning, photophobia and tinnitus.

Transient changes in AST (SGOT), ALT (SGPT), blood urea, ALP, and creatinine clearance have been observed occasionally.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Capsules 500 mg: Blister pack of 14.

Further information Store at room temperature (15°–25°C).

Product licence number 0006/0124

COLOGEL*

Presentation An aromatised solution each 100 ml containing 9 g of methylcellulose in a lemon-flavoured, lemon-coloured vehicle, with alcohol 5%.

Uses Cologel is a liquid bulk laxative, which does not irritate the intestinal mucosa or interfere with the absorption of foods or vitamins. It is indicated for the treatment of chronic or acute constipation.

Dosage and administration For oral administration.

Adults: 5–15 ml (1–3 teaspoonsfuls) with a full glass of water three times daily after meals.

Maintenance dosage: 5–15 ml with a full glass of water once daily. In severe cases, up to 30 ml with a full glass of water may be administered once daily.

Children: The dosage should be scaled down in proportion to size.

Contra-indications, warnings, etc Cologel should not be given to children who are dehydrated. Intestinal obstruction has been reported after the administration of bulk laxatives, therefore it is essential that an adequate quantity of water be taken with each dose.

Pharmaceutical precautions Exposure to high temperatures may cause this product to gel. If this occurs, place in a refrigerator. Cologel should not be frozen.

Legal category GSL.

Package quantities Bottles of 500 ml.

Further information Nil.

Product licence number 0006/5047.

CO-PYRONIL*

Presentation Co-Pyronil is available as capsules (green and yellow, coded Lilly 3043). Each capsule contains: pyrrobutamine phosphate 15 mg, cyclopentamine hydrochloride 12.5 mg

Uses Co-Pyronil combines the long-lasting anti-histamine effect of pyrrobutamine phosphate and the sympathomimetic action of cyclopentamine hydrochloride. It gives prompt relief which lasts up to 12 hours.

It is indicated for the treatment of hay fever, allergic rhinitis, skin allergies, ocular allergies, gastro-intestinal allergies and headaches associated with generalised allergic response.

Dosage and administration

Adults: One capsule two or three times daily.

Children: Reduced dosage may be given at the physician's discretion. Co-Pyronil is administered orally.

Contra-indications, warnings, etc

Contra-indications: Co-Pyronil should not be used in patients allergic to antihistamines or to cyclopentamine.

Warnings: The central nervous system depressant effect of pyrrobutamine may be additive with that of other CNS depressants, including alcohol, and the patient should be so advised.

Co-Pyronil may cause drowsiness and modify patients' mental and physical reactions in the performance of potentially hazardous tasks (e.g. in driving ability, operation of machinery, etc.) to a varying extent, depending on dosage and individual susceptibility. If

drowsiness occurs, it may be lessened by halving the dose, then gradually increasing it to a therapeutic level.

Usage in pregnancy: The safety of Co-Pyronil for use during pregnancy has not been established.

Precautions: Co-Pyronil should be used with caution in the presence of hypertension, cardiovascular renal disease, hyperthyroidism or diabetes. In the presence of prostatism the administration of sympathomimetic drugs may cause urinary retention. In rare instances, sympathomimetic overstimulation may be noted after the use of vasoconstrictors.

Overdosage: CNS depression or stimulation.

Symptoms – CNS depression, followed by stimulation and later by depression. Stimulation of the central nervous system may progress to the point of convulsions, especially in children. Death results from respiratory arrest.

Treatment – No specific therapy. For general management, mechanical support of respiration is safer and more effective than the use of respiratory stimulants. Convulsions may be treated with CNS depressants (short-acting barbiturates) in amounts just adequate to control convulsive seizures.

Over-sedation should be avoided.

Pharmaceutical precautions Keep containers tightly closed and store below 25°C.

Legal category P.

Package quantities Bottles of 100 capsules.

Further information Nil.

Product licence number 0006/0143.

CYCLOSERINE

Presentation Capsules (red and grey) containing 125 mg Cycloserine BP, coded H39.

Capsules (red and grey) containing 250 mg Cycloserine BP, coded F04.

Uses Cycloserine inhibits cell wall synthesis in susceptible strains of Gram-positive and Gram-negative bacteria and in *Mycobacterium tuberculosis*.

Cycloserine is indicated in the treatment of active pulmonary and extra-pulmonary tuberculosis (including renal disease) when the organisms are susceptible to this drug and after failure of adequate treatment with the primary medications (streptomycin, isoniazid and aminosalicylic acid). Like all anti-tuberculous drugs, Cycloserine should be administered in conjunction with other effective chemotherapy and not as the sole therapeutic agent.

Cycloserine may be effective in the treatment of acute urinary tract infections caused by susceptible strains of Gram-positive and Gram-negative bacteria, especially *Klebsiella/Enterobacter* species and *Escherichia coli*. It is generally no more and may be less effective than other antimicrobial agents in the treatment of urinary tract infections caused by bacteria other than mycobacteria. Use of Cycloserine in these infections should be considered only when the more conventional therapy has failed and when the organism has been demonstrated to be sensitive to the drug.

Dosage and administration For oral administration. The usual dosage is 500 mg to 1 g daily in divided doses, monitored by blood levels. The initial adult dosage most

frequently given is 250 mg twice daily at 12-hour intervals for the first two weeks. The daily dosage of 1 g should not be exceeded.

Contra-indications, warnings, etc Administration is contra-indicated in patients with any of the following: Hypersensitivity to Cycloserine; epilepsy; depression, severe anxiety or psychosis; severe renal insufficiency; alcohol abuse.

Administration of Cycloserine should be discontinued or the dosage reduced if the patient develops allergic dermatitis or symptoms of central nervous system toxicity such as convulsions, psychoses, somnolence, depression, confusion, hyper-reflexia, headache, tremor, vertigo, paresis or dysarthria.

The toxicity of Cycloserine is closely related to excessive blood levels (above 30 mg/l), which are caused by high dosage or inadequate renal clearance. The ratio of toxic dose to effective dose in tuberculosis is small.

The risk of convulsions is increased in chronic alcoholics.

Patients should be monitored by haematological, renal excretion, blood level and liver function studies.

Usage in pregnancy: The safety of Cycloserine for use during pregnancy has not been established.

Usage in children: Safety and dosage have not been established for paediatric use.

Precautions: Before treatment with Cycloserine is begun, cultures should be taken and the susceptibility of the organism to the drug should be established. In tuberculous infections, sensitivity to the other anti-tuberculous agents in the regimen should also be demonstrated.

Blood levels should be determined at least weekly for patients having reduced renal function, for individuals receiving a daily dosage of more than 500 mg, and for those showing signs and symptoms suggestive of toxicity. The dosage should be adjusted to keep the blood level below 30 mg/l.

Anticonvulsant drugs or sedatives may be effective in controlling symptoms of central nervous system toxicity, such as convulsion, anxiety and tremor. Patients receiving more than 500 mg of Cycloserine daily should be closely observed for such symptoms. The value of pyridoxine in preventing CNS toxicity from Cycloserine has not been proved.

Administration of Cycloserine and other anti-tuberculous drugs has been associated in a few instances with vitamin B₁₂ and/or folic acid deficiency, megaloblastic anaemia and sideroblastic anaemia. If evidence of anaemia develops during treatment, appropriate studies and therapy should be instituted.

Overdosage – Symptoms – CNS depression with accompanying drowsiness, somnolence, dizziness, hyper-reflexia, mental confusion, convulsions and allergic dermatitis.

Treatment – Pyridoxine, 300 mg or more daily, and anticonvulsants may be given to relieve convulsions. General management may include symptomatic and supportive therapy such as gastric lavage, oxygen, artificial respiration, intravenous fluids, standard measures for management of circulatory shock and maintenance of body temperature.

Side-effects: Most adverse reactions occurring during therapy with Cycloserine involve the nervous system or are manifestations of drug hypersensitivity. The following side-effects have been observed:

Nervous system symptoms (which appear to be related

to higher dosages of drug, i.e. more than 500 mg daily): convulsions, drowsiness and somnolence, headache, tremor, dysarthria, vertigo, confusion and disorientation with loss of memory, psychoses, possibly with suicidal tendencies, hyper-irritability, aggression, paresis, hyper-reflexia, paraesthesiae, major and minor (localised) clonic seizures, coma.

Allergic (apparently not related to dosage): skin rash.

Miscellaneous: elevated serum aminotransferases, especially in patients with pre-existing liver disease.

Pharmaceutical precautions Keep containers tightly closed. Store below 25°C. Protect from moisture.

Legal category POM.

Package quantities Capsules 125 mg: Bottles of 100. Capsules 250 mg: Bottles of 40 and 100.

Further information Nil.

Product licence numbers

Capsules 125 mg 0006/5044

Capsules 250 mg 0006/5045

DIMELOR®

Presentation Tablets (yellow, scored, coded U07) each containing 500 mg Acetohexamide USP.

Uses The principal clinical indication for Dimelor is diabetes mellitus of the stable type (without such complications as ketosis or acidosis), variously described as relatively mild adult, maturity-onset, or non-ketotic type.

The use of Dimelor in insulin-dependent patients may reduce the insulin requirements.

Dosage and administration The daily dose of Dimelor may range from 250 mg to 1.5 g. Many patients are controlled on a single daily dose of 500 mg. Divided dosage may be advantageous where the daily requirements are higher. Patients who do not respond to 1.5 g daily are unlikely to benefit from a higher dose.

The use of Dimelor in children is not recommended.

Moderate diabetes: A loading dose technique can be used in cases which are fairly severe. New patients usually respond to 3 tablets (1.5 g) on the first day, 2 tablets on the second day and 1 tablet on subsequent days. Patients should be re-examined within a week for possible adjustment of dosage.

Mild diabetes: In the mild stable diabetic a loading dose is not necessary. Treatment can start with $\frac{1}{2}$ tablet (250 mg) daily before breakfast. The dose can be increased by 250–500 mg every five to seven days as needed.

Elderly patients: Because some elderly patients are unusually responsive, patients in this group should be started with a single daily dose of $\frac{1}{2}$ tablet (250 mg) before breakfast, and have their blood and/or urine sugar monitored after 24 hours. If satisfactory, this dose may then be continued or gradually increased if control is inadequate. Any tendency towards hypoglycaemia is an indication for reduction of dosage or for discontinuing the drug.

Transfer from other oral agents: Patients who have been maintained on other oral agents may be transferred directly to Dimelor. It should be remembered that Dimelor is intermediate in potency between tolbutamide and chlorpropamide, and the first dose of Dimelor should be only half the previous tolbutamide dose. When the

transfer is from chlorpropamide an eventual increase may be necessary.

Transfer from insulin: In general, patients who have been previously maintained on insulin in small dosage, 10 or 20 units per day, may be transferred to Dimelor directly. Patients on larger doses of insulin, 20–40 units or more, should have their insulin reduced by 25–30% a day or every other day, while Dimelor is begun at a dosage of 250 mg a day. Further reduction depends on the response to Dimelor.

During the period of insulin withdrawal, the patient should test his urine for sugar and acetone at least three times a day and report the results frequently to his physician, so that the appropriate adjustments can be made. Especial care should be observed in the elderly patient. Some cases may need to be treated in hospital during the transition period. Dimelor may be used with phenformin or insulin, when indicated, in suitable patients.

Contra-indications, warnings, etc Dimelor is contra-indicated in patients with hyperglycaemia and glycosuria which may be associated with primary renal disease. If reduction of the blood sugar becomes essential in these cases, insulin is indicated.

Usage in pregnancy: The safety of Dimelor for use during pregnancy has not been established. Therefore, the use of Dimelor is not recommended for the management of diabetes when complicated by pregnancy. The advisability of administering Dimelor to women of child-bearing age should be considered with caution.

Dimelor is of no value in diabetes complicated by acidosis and coma. These conditions require insulin.

In times of stress to the patient, such as fever of any cause, trauma, infection or surgical procedures, it may be necessary to return the patient to insulin therapy or to use insulin in addition to Dimelor.

Precautions: The principles of management of diabetes mellitus are necessary to ensure optimum control with Dimelor and are the same as for patients requiring insulin.

In patients with impaired hepatic and/or renal function and in debilitated or malnourished individuals, careful observation of the patient and adjustment of dosage are mandatory to prevent the occurrence of hypoglycaemia.

Thiazide-type diuretics may aggravate the diabetic state and alter the dosage of Dimelor required.

Preparations containing phenylbutazone interfere with the excretion of the active metabolite hydroxyhexamide; as a result, increased sulphonylurea levels depress the blood glucose. This may also be true of probenecid and the absorbed antimicrobial sulphas.

Sulphonylurea compounds, like antimicrobial sulpha drugs and barbiturates, may aggravate hepatic porphyria.

Patients receiving sulphonylureas may experience peculiar symptoms, referred to as the 'disulfiram reaction', following the ingestion of alcohol.

Secondary failures and the spontaneous tendency of diabetes to fluctuate in severity may occur. Therefore, patients should be seen by their physicians at regular intervals and their diabetes evaluated in order to avoid hyperglycaemic and hypoglycaemic episodes.

Hypoglycaemia may occur in those patients who do not eat regularly or who exercise without caloric supplementation. It is most likely to appear during the period of transition from insulin to Dimelor, and should be considered in patients who have hepatic or renal disease as well as those who are debilitated or malnourished.

Side-effects: These consist mainly of gastro-intestinal disturbances (nausea, epigastric fullness, heartburn) and headache. Both appear to be dose-related, and may disappear when dosage is reduced.

Allergic skin manifestations (pruritus, erythema, urticaria, morbilliform or maculopapular eruptions) occur but are usually transient and may disappear with continued dosage. If the skin reactions persist, the drug should be stopped. Photosensitivity reactions may be noted. Jaundice of both the cholestatic and mixed hepatic types have been observed with Dimelor.

As with other sulphonylurea drugs, leucopenia, thrombocytopenia, pancytopenia, agranulocytosis, aplastic anaemia and haemolytic anaemia may occur with Dimelor.

Pharmaceutical precautions Keep containers tightly closed.

Legal category POM.

Package quantities Bottles of 100 and 500.

Further information Nil.

Product licence number 0006/5069.

DOBUTREX®

Presentation Dobutrex (dobutamine hydrochloride) for injection is supplied in a sterile lyophilised form in 250 mg vials for intravenous use only.

Uses Actions: The primary action of dobutamine is to augment cardiac contractility by stimulating the β_1 receptors of the heart. It is a direct-acting agent and does not cause the release of endogenous noradrenaline as does dopamine.

Indications: Dobutrex is indicated for adults who require inotropic support in the treatment of heart failure associated with myocardial infarction, open heart surgery or cardiomyopathies.

Dosage and administration Dobutrex may be reconstituted with Water for Injections PhEur or 5% Dextrose Intravenous Infusion BP. To dissolve, add 10 ml of diluent to the vial. Reconstituted Dobutrex must be diluted further by injecting aseptically the contents of one vial (10 ml containing 250 mg dobutamine) into a 250 ml or 500 ml bottle of one of the following intravenous solutions:

Sodium Chloride Intravenous Infusion BP

5% Dextrose Intravenous Infusion BP

5% Dextrose + 0.9% Sodium Chloride Intravenous Infusion BP

5% Dextrose + 0.45% Sodium Chloride Intravenous Infusion BP

Sodium Lactate Intravenous Infusion BP

These dilutions will give a concentration for administration as follows:

250 ml contains 1,000 mcg/ml of dobutamine

500 ml contains 500 mcg/ml of dobutamine

These prepared solutions should be used within 24 hours.

Administration: After dilution, Dobutrex should be administered intravenously through an intravenous needle or catheter. An i.v. drip chamber or other suitable metering device is essential for controlling the rate of flow in drops per minute.

Recommended dosage: Most patients will respond satisfactorily to doses ranging from 2.5 to 10 mcg/kg/minute. Occasionally, however, a dose as low as 0.5 mcg/kg/minute will elicit a response. Rarely, a dose as high as 40 mcg/kg/minute is required.

The rate of administration and the duration of therapy should be adjusted according to the patient's response as determined by heart rate, blood pressure, urine flow, and, if possible, measurement of cardiac output.

Rather than abruptly discontinuing therapy with Dobutrex, it is often advisable to decrease the dosage gradually.

Side-effects, which are dose-related, are infrequent when Dobutrex is administered at rates below 10 mcg/kg/minute. Rates as high as 40 mcg/kg/minute have been used occasionally without significant adverse effects.

The final volume administered should be determined by the fluid requirements of the patient.

Contra-indications, warnings, etc

Contra-indications: None.

Warnings: If an undue increase in heart rate or systolic blood pressure occurs or if an arrhythmia is precipitated, the dose of dobutamine should be reduced or the drug should be discontinued temporarily.

Particular care should be exercised when dobutamine is used in patients with acute myocardial infarction because any significant increases in heart rate that occur may intensify ischaemia and cause anginal pain and ST segment elevation.

Dobutamine should be used with great caution in patients with idiopathic hypertrophic subaortic stenosis since positive inotropic agents may increase outlet obstruction in these patients.

No improvement may be observed in the presence of marked mechanical obstruction such as severe valvular aortic stenosis.

Minimal vasoconstriction has occasionally been observed, most notably in patients recently treated with a β -blocking drug. Because the inotropic effect of dobutamine stems from stimulation of cardiac β_1 receptors this effect is, of course, prevented by β -blocking drugs.

Usage in pregnancy: Reproduction studies performed in rats and rabbits have revealed no evidence of impaired fertility or harm to the fetus due to dobutamine. To date, the drug has not been administered to pregnant women and safety in this situation remains to be determined.

Paediatric use: The safety and efficacy of dobutamine for use in children have not been established.

Precautions: Hypovolaemia should be corrected when necessary with whole blood or plasma before dobutamine is administered.

Adverse reactions: A 10 to 20 mm rise in systolic blood pressure has been observed in most patients. Those with pre-existing hypertension may exhibit an exaggerated pressor response. An increase in heart rate of five to ten beats per minute may occur. In some instances, patients have developed excessive tachycardia or ectopic beats. Dobutamine may also increase the ventricular rate in patients with pre-existing atrial fibrillation. Temporary discontinuation of the infusion or a reduction in dosage will usually reverse these conditions.

The following side-effects have been reported rarely: nausea, headache, anginal pain, nonspecific chest pain, palpitations or shortness of breath.

No abnormal laboratory values attributable to dobutamine have been observed.

Overdosage: In cases of overdosage, as evidenced by excessive change in blood pressure or tachycardia, reduce the rate of administration or temporarily discontinue dobutamine until the patient's condition stabilises. Because the duration of action of dobutamine is short, any adverse effects are also short-lived.

Pharmaceutical precautions Unreconstituted vials: Store at room temperature (15°–25°C). Reconstituted solutions may be stored under refrigeration (0°–6°C) for 48 hours or at room temperature (15°–25°C) for six hours.

Prepared intravenous solutions are stable for 24 hours at room temperature. The pH of these solutions will be within the range of 2.5 to 5.5.

Do *not* add Dobutrex to 5% Sodium Bicarbonate Intravenous Infusion BP or to any other strongly alkaline solutions. Dobutrex should not be used in conjunction with other agents or diluents containing sodium metabisulphite.

Solutions containing Dobutrex may turn pink; the colour may intensify with time. This colour change is due to slight oxidation of the drug, but there is no significant loss of potency during the recommended storage periods.

Legal category POM.

Package quantities 25 ml vials containing 250 mg dobutamine as the hydrochloride.

Further information Nil.

Product licence number 0006/0134.

DOLASAN®

Presentation Tablets (orange, elliptical, coded C54) each containing: Dextropropoxyphene Napsylate BP 100 mg (equivalent to approximately 65 mg dextropropoxyphene hydrochloride or 60 mg dextropropoxyphene base).

Aspirin PhEur 325 mg.

Uses For the relief of mild to moderate pain.

Dosage and administration For oral administration to adults only. The usual dose, which should not normally be exceeded, is 1 tablet taken three or four times daily.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to dextropropoxyphene or aspirin, active peptic ulceration and haemophilia.

Warnings: Dextropropoxyphene is an analgesic with CNS depressant properties and should be used with caution in patients who are receiving other CNS depressant drugs, as an additive effect may occur. Patients should be warned to avoid alcohol.

As with other drugs which affect the CNS, care should be taken when prescribing for patients with personality or other psychological disorders. Tolerance, psychological and physical dependence may rarely occur.

Like other centrally acting drugs, dextropropoxyphene may impair patients' mental and physical reactions in the performance of potentially hazardous tasks (e.g. in driving ability, operation of machinery, etc.) to a varying extent, depending on dosage and individual susceptibility.

Salicylates should be used with caution in patients with asthma or coagulation abnormalities. They may also

induce gastro-intestinal haemorrhage, occasionally major.

Use in pregnancy: The safety of Dolasan for use during pregnancy has not been established. Aspirin may prolong labour and contribute to maternal and neonatal bleeding, and is best avoided at term.

Precautions: Aspirin may enhance the effect of anti-coagulants, inhibit the action of uricosuric agents, precipitate bronchospasm or induce attacks of asthma in susceptible individuals.

Side-effects: Side-effects such as dizziness, sedation, nausea and vomiting seem to be more prominent in ambulatory than in non-ambulatory patients, and some of these side-effects may be alleviated if the patient lies down.

Other reported side-effects include constipation, abdominal pain, skin rashes, lightheadedness, headache, weakness, euphoria, dysphoria and minor visual disturbances.

Overdosage: The chronic ingestion of dextropropoxyphene in doses exceeding 720 mg (as base) per day has caused toxic psychoses and convulsions.

Symptoms of acute toxicity may be rapid in onset, with the danger of respiratory arrest. Other recognised manifestations include respiratory depression, coma, circulatory collapse, pulmonary oedema, convulsions and cardiac arrhythmias.

Deterioration may be rapid, with fatal outcome.

The clinical picture may be complicated by salicylism.

Treatment: Primary attention should be given to the re-establishment of adequate respiratory exchange through provision of a patent airway and institution of assisted or controlled ventilation. The narcotic antagonist naloxone is a specific antidote against the respiratory depression produced by dextropropoxyphene. An appropriate dose of this antagonist should be administered, preferably by the intravenous route, simultaneously with efforts at respiratory resuscitation. Repeated doses of the antagonist may be necessary over a prolonged period due to the slow elimination of dextropropoxyphene. In addition to the use of a narcotic antagonist, the patient may require careful titration with an anticonvulsant to control seizures. Analeptic drugs (for example, caffeine or amphetamine) should not be used because of their tendency to precipitate convulsions. Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated.

Gastric lavage may be helpful. Activated charcoal can absorb a significant amount of ingested dextropropoxyphene. Dialysis is of little value in poisoning by dextropropoxyphene alone. Salicylates are dialysable.

Pharmaceutical precautions Keep containers tightly closed.

Legal category POM.

Package quantities Bottles of 100 tablets.

Further information Nil.

Product licence number 0006/0077.

DOLOXENE®

Presentation Capsules (opaque orange, coded H64) containing approximately 100 mg Dextropropoxyphene Napsylate BP (equivalent to approximately 65 mg dex-

tropropoxyphene hydrochloride or 60 mg dextropropoxyphene base).

Uses For the relief of mild to moderate pain.

Dosage and administration For oral administration to adults only. The usual dose is one capsule three or four times daily, and should not normally be exceeded.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to dextropropoxyphene.

Warnings: Dextropropoxyphene is an analgesic with CNS depressant properties and should be used with caution in patients who are receiving other CNS depressant drugs, as an additive effect may occur. Patients should be warned to avoid alcohol.

As with other drugs which affect the CNS, care should be taken when prescribing for patients with personality or other psychological disorders. Tolerance, psychological and physical dependence may rarely occur.

Use in pregnancy: The safety of Doloxene for use during pregnancy has not been established.

Side-effects: Side-effects such as dizziness, sedation, nausea and vomiting seem to be more prominent in ambulatory than in non-ambulatory patients, and some of these side-effects may be alleviated if the patient lies down.

Other reported side-effects include constipation, abdominal pain, skin rashes, lightheadedness, headache, weakness, euphoria, dysphoria and minor visual disturbances.

Overdosage: The chronic ingestion of dextropropoxyphene in doses exceeding 720 mg (as base) per day has caused toxic psychoses and convulsions.

Symptoms of acute toxicity may be rapid in onset, with the danger of respiratory arrest. Other recognised manifestations include respiratory depression, coma, circulatory collapse, pulmonary oedema, convulsions and cardiac arrhythmias.

Deterioration may be rapid, with fatal outcome.

Treatment: Primary attention should be given to the re-establishment of adequate respiratory exchange through provision of a patent airway and institution of assisted or controlled ventilation. The narcotic antagonist naloxone is a specific antidote against the respiratory depression produced by dextropropoxyphene. An appropriate dose of this antagonist should be administered, preferably by the intravenous route, simultaneously with efforts at respiratory resuscitation. Repeated doses of the antagonist may be necessary over a prolonged period due to the slow elimination of dextropropoxyphene.

In addition to the use of a narcotic antagonist, the patient may require careful titration with an anticonvulsant to control seizures. Anaesthetic drugs (for example, caffeine or amphetamine) should not be used because of their tendency to precipitate convulsions. Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated.

Gastric lavage may be helpful. Activated charcoal can absorb a significant amount of ingested dextropropoxyphene. Dialysis is of little value in poisoning by dextropropoxyphene alone.

Pharmaceutical precautions Keep containers tightly closed. Store below 25°C.

Legal category POM.

Package quantities Bottles of 100 and 500.

Further information Nil.

Product licence number 0006/5068.

DOLOXENE* Compound

Presentation Doloxene Compound is presented as hard gelatin capsules (light grey opaque cap, red opaque body) coded H91, each containing: Dextropropoxyphene Napsylate BP 100 mg (equivalent to approximately 65 mg dextropropoxyphene hydrochloride or 60 mg dextropropoxyphene base).

Aspirin PhEur 375 mg

Caffeine PhEur 30 mg

Uses For the relief of mild to moderate pain.

Dosage and administration For oral administration to adults only. The usual dose is one capsule three or four times daily, and should not normally be exceeded.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to any of the constituents, active peptic ulceration and haemophilia.

Warnings: Dextropropoxyphene is an analgesic with CNS depressant properties and should be used with caution in patients who are receiving other CNS depressant drugs, as an additive effect may occur. Patients should be warned to avoid alcohol.

As with other drugs which affect the CNS, care should be taken when prescribing for patients with personality or other psychological disorders. Tolerance, psychological and physical dependence may rarely occur.

Like other centrally acting drugs, dextropropoxyphene may impair patients' mental and physical reactions in the performance of potentially hazardous tasks (e.g. in driving ability, operation of machinery, etc.) to a varying extent, depending on dosage and individual susceptibility.

Salicylates should be used with caution in patients with asthma or coagulation abnormalities. They may also induce gastro-intestinal haemorrhage, occasionally major.

High doses of caffeine may cause tremors and palpitations.

Use in pregnancy: The safety of Doloxene Compound for use during pregnancy has not been established. Aspirin may prolong labour and contribute to maternal and neonatal bleeding, and is best avoided at term.

Precautions: Aspirin may enhance the effect of anticoagulants, inhibit the action of uricosuric agents, precipitate bronchospasm or induce attacks of asthma in susceptible individuals.

Side-effects: Side-effects such as dizziness, sedation, nausea and vomiting seem to be more prominent in ambulatory than in non-ambulatory patients, and some of these side-effects may be alleviated if the patient lies down.

Other reported side-effects include constipation, abdominal pain, skin rashes, lightheadedness, headache, weakness, euphoria, dysphoria and minor visual disturbances.

Overdosage: The chronic ingestion of dextropropoxyphene in doses exceeding 720 mg (as base) per day has caused toxic psychoses and convulsions.

Symptoms of acute toxicity may be rapid in onset, with the danger of respiratory arrest. Other recognised manifestations include respiratory depression, coma,

circulatory collapse, pulmonary oedema, convulsions and cardiac arrhythmias.

Deterioration may be rapid, with fatal outcome.

The clinical picture may be complicated by salicylism.

Treatment: Primary attention should be given to the re-establishment of adequate respiratory exchange through provision of a patent airway, and institution of assisted or controlled ventilation. The narcotic antagonist naloxone is a specific antidote against the respiratory depression produced by dextropropoxyphene. An appropriate dose of this antagonist should be administered, preferably by the intravenous route, simultaneously with efforts at respiratory resuscitation. Repeated doses of the antagonist may be necessary over a prolonged period due to the slow elimination of dextropropoxyphene.

In addition to the use of a narcotic antagonist, the patient may require careful titration with an anticonvulsant to control seizures. Analeptic drugs (for example, caffeine or amphetamine) should not be used because of their tendency to precipitate convulsions. Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated.

Gastric lavage may be helpful. Activated charcoal can absorb a significant amount of ingested dextropropoxyphene. Dialysis is of little value in poisoning by dextropropoxyphene alone. Salicylates are dialysable.

Pharmaceutical precautions Keep containers tightly closed. Store below 25°C.

Legal category POM.

Package quantities Bottles of 100 and 500.

Further information Nil.

Product licence number 0006/0091.

ELDISINE* ▼

Presentation Vials containing 5 mg Eldisine (vinde-sine sulphate) and 25 mg Mannitol BP. (Supplied in a combination package with an accompanying vial of diluting solution, 5 ml, containing 45 mg Sodium Chloride PhEur with 0.9% Benzyl Alcohol BP as a preservative.)

Uses Eldisine is an anti-neoplastic drug for intravenous use which can be used alone or in combination with other oncolytic drugs. Information available at present suggests that Eldisine as a single agent may be useful for the treatment of: acute lymphoblastic leukaemia of childhood resistant to other drugs, blastic crises of chronic myeloid leukaemia, malignant melanoma unresponsive to other forms of therapy.

Dosage and administration Extreme care must be used in calculating and administering the dose of Eldisine, since overdosage may have a very serious or fatal outcome.

It is recommended that the drug be administered intravenously in a single bolus injection at weekly intervals. The size of the dose is determined by body surface area. In adults the recommended starting dose is 3 mg/m², and children may be started at 4 mg/m². Thereafter, granulocyte counts should be made prior to each subsequent dose to determine the patient's sensitivity to the drug. Provided there is no granulocytopenia or other toxicity (see adverse reactions) the dosage may be increased in 0.5 mg/m² steps at weekly intervals.

The dose should not be increased after that dose which: (i) reduces the granulocyte count to below 1500 cells/mm³, or on rare occasions, (ii) reduces the platelet count to below 100,000/mm³, (iii) causes acute abdominal pain (see under precautions).

On each of the above occasions there should be full recovery before administering the next dose, which should be reduced from the one causing the adverse reaction. For most patients, however, the weekly dosage will prove to be in the range of 3.0 to 4.0 mg/m² in adults and 4.0 to 5.0 mg/m² in children. (A nomogram for calculation of body surface area is available on request.)

The use of small amounts of Eldisine daily for long periods is not advised, even though the resulting total weekly dosage may be similar to that recommended. Little or no added therapeutic advantage has been demonstrated when such regimens have been used, and side-effects are increased. Strict adherence to the recommended dosage schedule is very important.

To prepare a solution containing 1 mg/ml add the 5 ml of accompanying diluting solution to the 5 mg of Eldisine in the sterile vial. The drug dissolves rapidly to give a clear solution.

The dose of Eldisine solution (calculated to provide the desired number of milligrams per square metre of the patient's surface area) may be injected either into the tubing of a running intravenous infusion (*compatible infusions are 5% Dextrose Intravenous Infusion BP, Sodium Chloride Intravenous Infusion BP and dextrose/saline infusions*), or directly into a vein.

The latter procedure is readily adaptable to outpatient therapy. In either case, the injection should be completed in 1 to 3 minutes. If care is taken to ensure that the needle is securely within the vein and that no solution containing Eldisine is spilled extravascularly, cellulitis and/or phlebitis is unlikely to occur.

Because of the enhanced possibility of thrombosis, it is considered inadvisable to inject a solution of Eldisine into an extremity in which the circulation is impaired, or potentially impaired, by such conditions as compressing or invading neoplasm, phlebitis or varicosity.

Caution: If leakage into surrounding tissue should occur during intravenous administration of Eldisine, it may cause considerable irritation. The injection should be discontinued immediately, and any remaining portion of the dose should be introduced into another vein. Local injection of hyaluronidase or hydrocortisone and the application of moderate heat to the area of leakage help to disperse the drug, and are thought to minimise discomfort and the possibility of cellulitis.

Care must be taken to avoid contamination of the eye with concentrations of Eldisine used clinically. If accidental contamination occurs, severe irritation (or if the drug was delivered under pressure, even corneal ulceration) may result. The eye should be washed thoroughly and immediately with water.

Contra-indications, warnings, etc

Contra-indications: Intrathecal administration.

Use in patients who are granulocytopenic (less than 1500 granulocytes per mm³) unless the granulocytopenia is a result of the disease affecting the bone marrow. Eldisine should not be used in the presence of bacterial infection. Such infections must be brought under control with antiseptics or antibiotics before using Eldisine.

Warning - Usage in pregnancy: This product should not normally be administered to patients who are pregnant or to mothers who are breast feeding. Although no abnormalities of the human fetus have been reported

thus far, animal studies with Eldisine suggest that teratogenic effects may occur.

Precautions: Clinically, the dose-limiting toxicity of Eldisine is granulocytopenia, although, in general, oncolytic activity is obtained at doses causing little or no effect on the granulocytes.

When granulocytopenia occurs, the nadir in the granulocyte count may be expected to occur 3–5 days after the last day of drug administration. Recovery of the granulocyte count is rapid thereafter and is usually complete within 6–8 days after the last dose.

The thrombocyte count is usually either unaffected or increased by weekly therapy with Eldisine. However, significant thrombocytopenia has occurred occasionally, particularly when doses are given more frequently than once a week. It is probably more likely to occur when patients are thrombocytopenic (less than 100,000 cells/mm³) prior to therapy with Eldisine.

The effect of Eldisine upon the red blood cell count and haemoglobin concentration is usually insignificant when other treatment does not complicate the picture. It should be remembered, however, that patients with malignant disease may exhibit anaemia even in the absence of any treatment.

If granulocytopenia with less than 1000 granulocytes/mm³ occurs following a dose of Eldisine, the patient should be watched carefully for evidence of infection until the granulocyte count has returned to a safe level.

Whilst the neurotoxicity is not usually dose-limiting, particular attention should be given to dosage and neurological side-effects if Eldisine is administered to patients with pre-existing neuromuscular disease, and also when other drugs with neurotoxic potential are being used. The neurotoxicity associated with Eldisine therapy may be additive.

Care should be exercised when Eldisine has been the cause of acute abdominal pain, as paralytic ileus may be a significant risk if further doses of Eldisine are given, particularly if the dose is increased.

As Eldisine is excreted principally by the liver, it may be necessary to reduce initial doses in the presence of significantly impaired hepatic or biliary function.

When chemotherapy is being given in conjunction with radiation therapy through portals which include the liver, the use of Eldisine should be delayed until radiation therapy has been completed.

Adverse reactions: The incidence of side-effects appears to be related not only to the size of dose employed but also to the total accumulated dose given. Acute toxicity is more likely to occur if doses above 4 mg/m² are employed, and symptoms usually persist for no longer than 24 hours. The onset of peripheral neuropathy appears to be more related to the total accumulated dose given.

The following are manifestations which have been reported as adverse reactions:

Gastro-intestinal – dysphagia, anorexia, nausea, vomiting, dyspepsia, perforated duodenal ulcer, abdominal pain, ileus, diarrhoea, constipation.

Neurological – numbness, paraesthesiae, peripheral neuritis, loss of deep tendon reflexes, myalgia, jaw pain, foot-drop, convulsions.

Cutaneous – maculopapular rashes, mouth ulceration, cellulitis with extravasation, alopecia from mild to total. Alopecia is the commonest side-effect. Regrowth of hair may occur while still on therapy.

Haematological – granulocytopenia (the dose-limiting factor), thrombocytosis, thrombocytopenia, mild anaemia.

Miscellaneous – malaise, spikes of fever, rigors.

In preliminary assessments, neurotoxicity induced by Eldisine is generally less severe and less progressive in nature compared to effects observed with Oncovin (vincristine sulphate).

Pharmaceutical precautions Vials of Eldisine should be stored in a refrigerator between 0° and 6°C.

After reconstitution: After a portion of the solution has been removed from a vial, the remainder of the contents of the vial may be stored in a refrigerator for future use for 30 days without significant loss of potency. When the reconstituted vial of Eldisine is to be stored for more than 48 hours, it is essential to use the accompanying diluting solution or a diluent which contains a preservative.

Eldisine should never be mixed with any other drug.

Legal category POM.

Package quantities Vials 5 mg; Single vials.

Further information Nil.

Product licence numbers

Vials 5 mg 0006/0137

Diluent 0006/5174

FOLIC ACID

Presentation Folic acid is an orange-yellow, almost odourless and tasteless micro-crystalline powder. It is presented as tablets each containing 5 mg Folic Acid BP (coded J66).

Uses Folic acid is a member of the B group of vitamins. It is necessary for the normal production and maturation of red blood cells. Folic acid produces a haemopoietic response in nutritional macrocytic anaemia, megaloblastic anaemia of infancy and the anaemias of pregnancy, pellagra and sprue, the anaemia following gastrectomy, and in pernicious anaemia.

Dosage and administration For oral administration.

Adults: In the treatment of megaloblastic anaemia, an initial dose of 10–20 mg daily may be given for 14 days, or until a haemopoietic response is obtained. Daily maintenance dose 2.5–10 mg.

Children: 5–15 mg daily.

Contra-indications, warnings, etc Folic acid should not be given for the treatment of pernicious anaemia without adequate amounts of cyanocobalamin, because folic acid alone will not prevent the development of sub-acute combined degeneration of the spinal cord.

Side-effects: Folic acid is usually well tolerated, but anorexia, nausea, abdominal distension and flatulence have been reported in association with its use.

Pharmaceutical precautions Folic Acid tablets should be stored in airtight containers, protected from light.

Legal category POM.

Package quantities Bottles of 100 and 1,000 tablets.

Further information *Prophylaxis of megaloblastic anaemia of pregnancy*: A dose of 200–500 mcg daily is recommended.

Product licence number 0006/5113.

GLUCAGON

Presentation Glucagon in lyophilised form with accompanying diluting solution is available in two package sizes:

Vials containing 1 unit (1.09 mg) of glucagon as the hydrochloride with 49 mg of lactose. (Diluting solution, 1 ml, containing glycerin, 1.6%, with phenol, 0.2%, as a preservative. Sodium hydroxide and/or hydrochloric acid may have been added during manufacture to adjust the pH).

Vials containing 10 units (10.9 mg) of glucagon as the hydrochloride with 140 mg of lactose. (Diluting solution 10 ml, containing glycerin, 1.6%, with phenol, 0.2%, as a preservative. Sodium hydroxide and/or hydrochloric acid may have been added during manufacture to adjust the pH).

Crystalline glucagon is a white powder containing less than 0.01% zinc. It is relatively insoluble in water but is soluble at a pH of less than 3 or more than 9.5.

Uses *Actions*: Glucagon causes an increase in blood glucose concentrations and is used in the treatment of hypoglycaemic states. It is effective in small doses. Glucagon acts only on liver glycogen, converting it to glucose, and is therefore helpful only if liver glycogen is available. It is of little or no help in states of starvation, adrenal insufficiency or chronic hypoglycaemia. The patient with juvenile-type diabetes does not have as great a response in blood glucose levels as does the adult-type stable diabetic, therefore supplementary carbohydrate should be given as soon as possible, especially to juvenile patients.

Parenteral administration of glucagon produces relaxation of the smooth muscle of the stomach, duodenum, small bowel and colon.

Indications: Glucagon is indicated for counteracting severe hypoglycaemic reactions in diabetic patients or resulting from insulin shock therapy in psychiatric patients.

Glucagon is indicated as a diagnostic aid in the radiological examination of the stomach, duodenum, small bowel and colon, when a hypotonic state would be advantageous.

Glucagon is as effective for this examination as the anticholinergic drugs, but it has fewer side-effects. When glucagon is administered concomitantly with an anticholinergic agent, the response is not significantly greater than when either drug is used alone. However, the addition of the anticholinergic agent results in increased side-effects.

Dosage and administration The diluent is provided for use only in the preparation of glucagon for *intermittent* parenteral injection **and for no other use**.

Directions for the use of glucagon in hypoglycaemia:

1. Dissolve the lyophilised glucagon in the accompanying diluent.
2. Give 0.5–1 unit of glucagon by subcutaneous, intramuscular or intravenous injection. These doses are equally suitable for adults and children.
3. The patient will normally awaken in 5–20 minutes.

If the response is delayed, there is no contra-indication to the administration of 1 or 2 additional doses of glucagon: however, in view of the deleterious effects of cerebral hypoglycaemia and depending on the duration and depth of coma, the use of parenteral glucose must be considered.

4. Intravenous glucose *must* be given if the patient fails to respond to glucagon.

5. When the patient responds, give supplementary carbohydrate to restore the liver glycogen and prevent secondary hypoglycaemia.

Reversal of insulin shock therapy: Dissolve the lyophilised glucagon in the accompanying diluent. After one hour of coma, inject 0.5–1 unit of glucagon by the subcutaneous, intramuscular or intravenous route. Larger doses may be employed if desired. The patient will normally awaken in 10–25 minutes. If no response occurs within the desired interval, the dose may be repeated. Upon awakening, the patient should be fed orally as soon as possible, and the usual dietary regimen followed.

In very deep states of coma, such as Stage IV or Stage V of Himwich, intravenous glucose should be given in addition to glucagon for a more immediate response. Glucagon and glucose may be used together without decreasing the efficacy of glucose administration.

For use as a diagnostic aid: Dissolve the lyophilised glucagon in the accompanying diluting solution.

The following doses may be administered for relaxation of the stomach, duodenum and small bowel, depending on the time of onset of action and the duration of effect required for the examination. Since the stomach is less sensitive to the effect of glucagon, $\frac{1}{2}$ unit i.v. or 2 units i.m. are recommended.

Dose (units)	Route of administration	Time of onset of action (min)	Approximate duration of effect (min)
0.25–0.5	i.v.	1	9–17
1	i.m.	8–10	12–27
2†	i.v.	1	22–25
2†	i.m.	4–7	21–32

†2-unit doses are associated with a higher incidence of nausea and vomiting than the lower doses.

For examination of the colon, it is recommended that a 2-unit dose be administered intramuscularly approximately 10 minutes prior to initiation of the procedure. Relaxation of the colon and reduction of discomfort to the patient will allow the radiologist to perform a more satisfactory examination.

Contra-indications, warnings, etc

Contra-indications: None.

Warnings: Since glucagon is a protein, hypersensitivity is a possibility.

Glucagon should not be administered to patients with known or suspected insulinoma and/or pheochromocytoma. In patients with insulinoma, intravenous administration of glucagon will produce an initial increase in blood glucose, but, because of its insulin-releasing effect, may subsequently cause severe hypoglycaemia. Exogenous glucagon also stimulates the release of catecholamines, which can cause a marked increase in blood pressure in patients with pheochromocytoma.

Precautions: In the treatment of hypoglycaemic shock

with glucagon, liver glycogen must be available. Glucose by the intravenous route or by gavage should be considered in the hypoglycaemic patient.

Glucagon should be used with caution as a diagnostic aid in diabetic patients.

Side-effects: Glucagon is relatively free of adverse reactions, except for occasional nausea and vomiting, which may also occur with hypoglycaemia.

Pharmaceutical precautions Glucagon is stable in lyophilised form at room temperature (15°–25°C). It will remain potent in solution for as long as three months if kept under refrigeration (0°–6°C).

Legal category POM.

Package quantities Vials No. 666, 1 unit (1.09 mg) glucagon as the hydrochloride accompanied by Vials No. 667 containing 1 ml of diluent.

Vials No. 668, 10 units (10.9 mg) glucagon as the hydrochloride accompanied by Vials No. 669 containing 10 ml of diluent.

Further information Nil.

Product licence numbers

Vials 1 unit	0006/5110
Vials 10 units	0006/5111
Vials Diluting Solution	0006/5112

ILOTYCIN*

Presentation Tablets (special coated, red, coded C03), containing 250 mg Erythromycin BP.

Uses Antibiotic. Erythromycin is indicated in the treatment of conditions associated with the following micro-organisms:

Streptococcus pyogenes (group A beta-haemolytic) – Upper and lower respiratory tract, skin and soft tissue infections of mild to moderate severity.

Alpha-haemolytic streptococci (viridans group) – Short-term prophylaxis against bacterial endocarditis prior to dental or other operative procedures in patients with a history of rheumatic fever or congenital heart disease who are hypersensitive to penicillin.

Str. pneumoniae – Infections of the upper and lower respiratory tract of mild to moderate severity.

Staphylococcus aureus – Acute infections of skin and soft tissue which are mild to moderately severe. Resistance may develop during treatment.

Mycoplasma pneumoniae – Primary atypical pneumonia due to this organism.

Treponema pallidum – Erythromycin is an alternative choice of treatment for syphilis in penicillin-allergic patients.

Corynebacterium diphtheriae – As an adjunct to antitoxin, to prevent establishment of carriers, and to eradicate the organism in carriers.

S. minutissimum – In the treatment of erythrasma.

Entamoeba histolytica – In the treatment of intestinal amoebiasis only. Extra-enteric amoebiasis requires treatment with other agents.

Listeria monocytogenes – Infections due to this organism.

Bordetella pertussis – When given early after exposure to whooping cough, erythromycin may reduce the risk of development of classical symptoms.

Legionnaires' disease – Although no controlled clinical efficacy studies have been conducted, *in vitro* and limited preliminary clinical data suggest that erythromycin may be effective in treating Legionnaires' disease.

Dosage and administration For oral administration. Optimum blood levels are obtained when doses are given on an empty stomach.

Adults: The usual dosage is 250 mg every six hours. This may be increased up to 4 g or more per day according to the severity of the infection.

Children: Age, weight, and severity of the infection are important factors in determining the correct dosage. The usual regimen is 30–50 mg/kg/day in divided doses. For more severe infections, this dosage may be doubled.

If administration on a twice daily schedule is desirable in either adults or children, one-half of the total daily dose may be given every 12 hours, one hour before meals.

Streptococcal infections: In the treatment of group A beta-haemolytic streptococcal infections, a therapeutic dosage of erythromycin should be administered for at least 10 days.

Prophylaxis: In continuous prophylaxis of streptococcal infections in persons with a history of rheumatic heart disease, the dosage is 250 mg twice daily. When Ilotycin is used prior to surgery to prevent endocarditis caused by alpha-haemolytic streptococci, a recommended schedule for adults is 1 g 1.5–2 hours pre-operatively and 500 mg every six hours for eight doses post-operatively; for children, 20 mg/kg 1.5–2 hours pre-operatively and 10 mg/kg every six hours for eight doses post-operatively.

Syphilis: 30–40 g given in divided doses over a period of 10 to 15 days.

Amoebic dysentery: 250 mg four times daily for 10 to 14 days for adults; 30–50 mg/kg/day in divided doses for 10 to 14 days for children.

Pertussis: Although optimum dosage and duration of treatment have not been established, doses of erythromycin utilised in reported clinical studies were 40–50 mg/kg/day, given in divided doses for 5 to 14 days.

Legionnaires' disease: Although optimum doses have not been established, doses utilised in reported clinical data were 1–4 g erythromycin base daily in divided doses.

Contra-indications, warnings, etc

Contra-indication: Hypersensitivity to erythromycin.

Warnings: Since erythromycin is excreted principally by the liver, caution should be exercised in administering the antibiotic to patients with impaired hepatic function. There have been reports of hepatic dysfunction, with or without jaundice, occurring in patients taking oral erythromycin products.

Usage in pregnancy: Although laboratory and clinical studies have shown no evidence of teratogenicity, caution should be exercised when prescribing for the pregnant patient.

Precautions: The use of erythromycin in patients who are receiving concomitant high doses of theophylline may be associated with an increase in serum theophylline levels and potential theophylline toxicity. If symptoms of toxicity develop, the dose of theophylline should be reduced.

During prolonged or repeated therapy, there is a

possibility of overgrowth of non-susceptible bacteria or fungi. If such infections arise, the drug should be discontinued and appropriate therapy instituted.

Side-effects: The most frequent side-effects of erythromycin preparations are gastro-intestinal (e.g. abdominal cramping and discomfort) and are dose-related. Nausea, vomiting and diarrhoea occur infrequently with usual oral doses.

Mild allergic reactions, such as urticaria and other skin rashes, have occurred. Serious allergic reactions, including anaphylaxis, have been reported.

Overdosage: Symptoms are mainly confined to nausea, vomiting and diarrhoea.

Treatment: General management may consist of supportive therapy.

Pharmaceutical precautions Store in a cool place (6°–15°C). Keep containers tightly closed.

Legal category POM.

Package quantities Bottles of 100, 500 and 1,000.

Further information Nil.

Product licence number 0006/5105.

KEFADOL*

Presentation 10 ml vials containing cefamandole nafate equivalent to 500 mg cefamandole plus 31.5 mg sodium carbonate.

10 ml vials containing cefamandole nafate equivalent to 1 g cefamandole plus 63 mg sodium carbonate.

100 ml vials containing cefamandole nafate equivalent to 2 g cefamandole plus 126 mg sodium carbonate.

Uses Cefamandole is indicated in the treatment of infections of the respiratory tract, genito-urinary tract, bones and joints, bloodstream (septicaemia), skin and soft tissue, gall bladder and peritoneum, and pelvic inflammatory disease in women, when due to susceptible micro-organisms.

Prophylactic use: Perioperative administration of cefamandole may reduce the incidence of postoperative infections in patients undergoing contaminated or potentially contaminated surgical procedures associated with a high risk of infection, or where the occurrence of a postoperative infection could be especially serious.

Cefamandole is usually active against most strains of the following organisms:

Beta-haemolytic and other streptococci (many strains of enterococci, e.g., *Streptococcus faecalis*, are relatively resistant); Staphylococci, including coagulase-positive, coagulase-negative (e.g., *Staphylococcus epidermidis*), penicillinase-producing and most methicillin-resistant strains; *Streptococcus pneumoniae*; *Haemophilus influenzae* (including ampicillin-resistant strains); *Escherichia coli* and other coliform bacteria; *Klebsiella* spp.; *Proteus mirabilis*; *Proteus* spp. (indole-positive, including *Pr. rettgeri* and *Pr. vulgaris*); *Morganella morganii*; *Enterobacter* spp.; *Salmonella* spp. including *S. typhi*; *Serratia* spp. (many strains are relatively resistant). *Pseudomonas* species are resistant to cefamandole.

Cefamandole has demonstrated *in vitro* activity against the following anaerobic bacteria: Anaerobic streptococci, *Peptococcus* and *Peptostreptococcus* spp.; *Bacteroides* spp.; *Clostridium* spp.

Cefamandole is resistant to degradation by beta-

lactamases from *Staph. aureus* and certain members of the *Enterobacteriaceae*.

Dosage and administration Cefamandole nafate may be given intravenously or by deep intramuscular injection.

Adults: The dosage range for cefamandole is 500 mg to 2 g every four to eight hours, depending on the severity and site of infection.

Impaired renal function: When renal function is impaired, a reduced dosage must be employed and serum concentrations should be monitored when feasible. After an initial dose of 1 to 2 g (depending on the severity of infection), a maintenance dosage schedule should be followed (see table). Continued dosage should be determined by degree of renal impairment, severity of infection and susceptibility of the causative organism.

Maintenance dosage of cefamandole in patients with impaired renal function

Creatinine clearance ml/min/1.73m ²	50–80 (every 6 h)	25–50 (every 8 h)	10–25 (every 8 h)	2–10 (every 12 h)	<2 (every 12 h)
Life-threatening infections	2 g	2 g	1.25 g	1 g	0.75 g
Severe infections	1.5 g	1.5 g	0.75 g	0.75 g	0.5 g
Less severe infections	0.75 g	0.75 g	0.5 g	0.5 g	0.25 g

Intramuscular administration: Cefamandole should be reconstituted with Water for Injections PhEur or Sodium Chloride Intravenous Infusion BP. Shake well until dissolved.

Intravenous administration:

1. **For direct intermittent intravenous administration,** add 10 ml of Water for Injections PhEur, 5% Dextrose Intravenous Infusion BP, or Sodium Chloride Intravenous Infusion BP per gram of cefamandole. Slowly inject directly into the vein over a period of three to five minutes or give through the tubing of an administration set while the patient is also receiving one of the following intravenous fluids:

Sodium Chloride Intravenous Infusion BP
5% Dextrose Intravenous Infusion BP
10% Dextrose Intravenous Infusion BP
5% Dextrose and 0.9% Sodium Chloride Intravenous Infusion BP
5% Dextrose and 0.45% Sodium Chloride Intravenous Infusion BP
Sodium Lactate Intravenous Infusion BP

2. **Intermittent intravenous infusion with a Y-type administration set or volume control set** can also be accomplished while any of the above mentioned intravenous fluids are being infused. However, during infusion of the solution containing cefamandole, it is desirable to discontinue the other solution. When this technique is employed, careful attention should be paid to the volume of the solution containing cefamandole so that the calculated dose will be infused. When a Y-tube connection is used, 100 ml of an appropriate diluent should be added to the 2 g (100 ml) vial. If Water for Injections PhEur is used as the diluent, reconstitute with approximately 20 ml per g to avoid a hypotonic solution.

3. **For continuous intravenous infusion,** each gram of cefamandole should be diluted with 10 ml of Water for Injections PhEur. An appropriate quantity of the resulting

solution may be added to an i.v. bottle containing one of the following fluids:

- Sodium Chloride Intravenous Infusion BP
- 5% Dextrose Intravenous Infusion BP
- 10% Dextrose Intravenous Infusion BP
- 5% Dextrose and 0.9% Sodium Chloride Intravenous Infusion BP
- 5% Dextrose and 0.45% Sodium Chloride Intravenous Infusion BP
- Sodium Lactate Intravenous Infusion BP

If combination therapy with cefamandole and an aminoglycoside is indicated, each of these should be administered at separate sites.

Infants and children: Administration of 50 to 100 mg/kg/day in equally divided doses every four to eight hours has been effective for most infections susceptible to cefamandole. This may be increased to a total daily dose of 150 mg/kg (not to exceed the maximum adult dose) for serious infections.

Kefadol has been safely administered to infants under the age of thirty days.

Prophylactic use: The following schedules are recommended for perioperative use:

Adults: 1 or 2 g intravenously or intramuscularly one-half to one hour prior to surgical incision, followed by 1 or 2 g every six hours for 24 hours.

For patients undergoing procedures involving implantation of prosthetic devices, administration for up to 72 hours is recommended.

Children (more than three months of age): 50–100 mg/kg/day in equally divided doses by the same routes and schedule designated above.

If signs of infection occur, cultures should be obtained and appropriate therapy instituted.

Contra-indications, warnings, etc

Contra-indications: Cefamandole is contra-indicated in patients with known allergy to the cephalosporin group of antibiotics.

Warnings: This product should be given cautiously to penicillin-sensitive patients. There is some evidence of partial cross-allergenicity of the penicillins and the cephalosporins. Patients have been reported to have had severe reactions to both classes of drugs.

Antibiotics should be administered with caution to any patient who has demonstrated some form of allergy, particularly to drugs.

Usage in pregnancy: Safety of this product for use during pregnancy has not been established.

Precautions: Although cefamandole rarely produces alteration in kidney function, evaluation of renal status is recommended, especially in seriously ill patients receiving maximum doses. Patients with impaired renal function should be placed on the dosage schedule recommended under DOSAGE AND ADMINISTRATION. Usual doses in such individuals may result in excessive serum concentrations.

As with other broad-spectrum antibiotics, hypoprothrombinaemia, with or without bleeding, has been reported rarely, but it has been promptly reversed by administration of vitamin K. Such episodes usually have occurred in elderly, debilitated or otherwise compromised patients with deficient stores of vitamin K. Treatment of such individuals with antibiotics possessing significant Gram-negative and/or anaerobic activity is thought to alter the number and/or type of intestinal bacterial flora, with consequent reduction in synthesis of

vitamin K. Prophylactic administration of vitamin K may be indicated in such patients, especially when intestinal sterilisation and surgical procedures are performed.

Prolonged use of cefamandole may result in the overgrowth of non-susceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

A false positive reaction for glucose in the urine may occur with Benedict's or Fehling's solutions or with Clinistest tablets but not with Tes-Tape* (urine sugar analysis paper, Lilly). A false positive test for proteinuria may occur with acid and denaturation precipitation tests.

The results of experimental studies in animals suggest that the concurrent use of potent diuretics such as frusemide or ethacrynic acid may increase the risk of renal toxicity with cephalosporin antibiotics.

Side-effects – Hypersensitivity: Maculopapular rash, urticaria, eosinophilia and drug fever have been reported. These reactions are more likely to occur in patients with a history of allergy, particularly to penicillin.

Blood: Neutropenia and thrombocytopenia have been reported rarely. Some individuals have developed positive direct Coombs' tests during treatment with the cephalosporin antibiotics.

Liver: Transient rise in AST (SGOT), ALT (SGPT) and ALP levels have been noted.

Kidney: Rise in blood urea and decreased creatinine clearance have been reported, particularly in patients with prior renal impairment. The rôle of cefamandole in renal changes is difficult to assess, because other factors predisposing to pre-renal azotaemia or to acute renal failure usually have been present.

Local reactions: Pain on intramuscular injection is infrequent. Thrombophlebitis occurs rarely.

Pharmaceutical precautions *Unreconstituted vials:* Store at room temperature (15°–25°C). Protect from light. After reconstitution, store in a refrigerator (0°–6°C) and use within 96 hours. If kept at room temperature (15°–25°C) use within 24 hours. During storage at room temperature, carbon dioxide develops inside the vial after reconstitution. This pressure may be dissipated prior to withdrawal of the vial contents, or it may be used to aid withdrawal if the vial is inverted over the syringe needle and the contents are allowed to flow into the syringe.

Do not mix an aminoglycoside with cefamandole in the same intravenous fluid container.

Legal category POM.

Package quantities Vials 7060, 500 mg in 10 ml: individual vials in packs of 10 vials.

Vials 7061, 1 g in 10 ml: individual vials in packs of 10 vials.

Vials 7069, 2 g in 100 ml: individual vials.

Further information Solutions of cefamandole range from light yellow to amber, depending upon a variety of factors, including concentration and the diluent used.

Product licence number 0006/0111.

KEFLEX*

Presentation Tablets (pillow shaped, 16 mm long, peach, marked Lilly U49) containing 500 mg Cephalexin BP.

Tablets (9.5 mm diameter, peach, marked Lilly U57) containing 250 mg Cephalexin BP.

Capsules (pale green and dark green, coded H71) containing 500 mg Cephalexin BP.

Capsules (green and white, coded H69) containing 250 mg Cephalexin BP.

Suspension (pink granules) containing 125 mg Cephalexin BP per 5 ml.

Suspension (orange granules) containing 250 mg Cephalexin BP per 5 ml.

Uses Cephalexin is indicated in the treatment of the following infections due to susceptible micro-organisms: Respiratory tract infections, Otitis media, Skin and soft tissue infections, Bone and joint infections, Genito-urinary tract infections, including acute prostatitis, Dental infections.

Cephalexin is active against the following organisms *in vitro*: Beta-haemolytic streptococci; Staphylococci, including coagulase-positive, coagulase-negative and penicillinase-producing strains.

Streptococcus pneumoniae,

Escherichia coli,

Proteus mirabilis,

Klebsiella species,

Haemophilus influenzae,

Neisseria catarrhalis.

Most strains of enterococci (*Streptococcus faecalis*) and a few strains of staphylococci are resistant to Keflex. It is not active against most strains of *Enterobacter* species, *Morganella morganii* and *Pr. vulgaris*. It has no activity against *Pseudomonas* or *Herellea* species. When tested by *in vitro* methods, staphylococci exhibit cross-resistance between cephalexin and methicillin-type antibiotics.

Dosage and administration Keflex is administered orally.

Adults: The adult dosage ranges from 1–4 g daily in divided doses. For skin and soft tissue infections, streptococcal pharyngitis and mild, uncomplicated urinary tract infections, the usual dosage is 250 mg every 6 hours, or 500 mg every 12 hours. For more severe infections or those caused by less susceptible organisms, larger doses may be needed. If daily doses of cephalexin greater than 4 g are required, parenteral cephalosporins, in appropriate doses, should be considered.

Children: The usual recommended daily dosage for children is 25–50 mg/kg (10–20 mg/lb) in divided doses. For skin and soft tissue infections, streptococcal pharyngitis and mild, uncomplicated urinary tract infections, the total daily dose may be divided and administered every 12 hours.

Aged 2–4 years: 125 mg/5 ml: 20 ml in 2–4 divided doses.

Aged 5 years and over: 250 mg/5 ml: 20 ml in 2–4 divided doses.

In severe infections, the dosage may be doubled. In the therapy of otitis media, clinical studies have shown that a dosage of 75 to 100 mg/kg/day in 4 divided doses is required.

In the treatment of beta-haemolytic streptococcal infections, a therapeutic dose should be administered for at least 10 days.

Contra-indications, warnings, etc Keflex is contra-indicated in patients with known allergy to the cephalosporin group of antibiotics.

Warnings: Keflex should be given cautiously to patients who have shown hypersensitivity to other drugs. Cephalosporins should be given with caution to penicillin-sensitive patients, as there is some evidence of partial cross-allergenicity between the penicillins and the cephalosporins. Patients have had severe reactions (including anaphylaxis) to both drugs.

Usage in pregnancy: Although laboratory and clinical studies have shown no evidence of teratogenicity, caution should be exercised when prescribing for the pregnant patient.

Precautions: If an allergic reaction to Keflex occurs the drug should be discontinued and the patient treated with the appropriate agents. Prolonged use of Keflex may result in the overgrowth of non-susceptible organisms. Keflex should be administered with caution in the presence of markedly impaired renal function. Careful clinical and laboratory studies should be made because safe dosage may be lower than that usually recommended. A false positive reaction for glucose in the urine may occur with Benedict's or Fehling's solutions or with copper sulphate test tablets, but not with Tes-Tape[®] (urine sugar analysis paper, Lilly).

Side-effects: *Gastro-intestinal:* Nausea, vomiting, dyspepsia and abdominal pain have occurred. Diarrhoea has been reported infrequently. It is rarely severe enough to warrant cessation of therapy. Colitis, including rare instances of pseudomembranous colitis, has been reported.

Hypersensitivity: Allergies (in the form of rash, urticaria and angio-oedema) have been observed. These reactions usually subside upon discontinuation of the drug. Anaphylaxis has also been reported.

Haematological: Eosinophilia, neutropenia and positive Coombs' tests have been reported.

Hepatic: Slight elevations of AST (SGOT) and ALT (SGPT) have been observed.

Miscellaneous: Other reactions have included genital and anal pruritus, genital moniliasis, vaginitis and vaginal discharge, dizziness, fatigue and headache.

Pharmaceutical precautions Capsules and tablets: Keep containers tightly closed. Suspensions: After mixing, Keflex suspensions should be stored in a cool place (6°–15°C) or in a refrigerator (0°–6°C) and be used within 10 days. Where dilution is unavoidable, Syrup BP should be used after the suspension has been prepared according to the manufacturer's instructions.

Legal category POM.

Package quantities

Tablets 500 mg: Bottles of 20, 100 and 500.
Tablets 250 mg: Bottles of 20, 100 and 500.
Capsules 500 mg: Bottles of 20, 100 and 500.
Capsules 250 mg: Bottles of 20, 100 and 500.
Suspension 125 mg/5 ml: Bottles of 100 ml.
Suspension 250 mg/5 ml: Bottles of 100 ml.

Further information Nil.

Product licence numbers

Tablets 500 mg	0006/5096
Tablets 250 mg	0006/0073
Capsules 500 mg	0006/0076
Capsules 250 mg	0006/5103

Suspension 125 mg/5 ml 0006/5097
Suspension 250 mg/5 ml 0006/5098

KEFLIN®

Presentation Vials containing the equivalent of 1 g cephalothin as the sodium salt.

Uses Keflin is indicated in the treatment of serious infections of the respiratory tract, genito-urinary tract, soft tissue and skin, gastro-intestinal tract, bones and joints, blood stream and cardiovascular system when due to susceptible organisms. It has also been effective in cases of peritonitis and septic abortion.

Cases of staphylococcal and pneumococcal meningitis have also responded to treatment. However, as only low levels of Keflin are found in the cerebrospinal fluid, the drug is not reliable for the treatment of this condition and should only be considered when other more reliably effective antibiotics cannot be used.

Keflin is usually active against the following organisms *in vitro*: Staphylococci, including coagulase-positive, coagulase-negative and penicillinase-producing strains; Clostridia, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Escherichia coli* and other coliform bacteria, *Klebsiella* species, *Proteus mirabilis*, *Salmonella* species, *Shigella* species.

Beta-haemolytic and other streptococci (many strains of enterococci e.g. *Streptococcus faecalis*, are relatively resistant).

Pseudomonas species are resistant to Keflin, as are most indole-positive *Proteus* and motile *Enterobacter* species.

The administration of Keflin before, during and after operations has been beneficial in reducing the incidence of postoperative infection in patients undergoing contaminated or potentially contaminated surgical procedures associated with a high risk of infection, in surgical patients with reduced host resistance to bacterial infection, or when the occurrence of a postoperative infection could be especially serious. The best results are observed if Keflin is administered immediately prior to the operative procedure, thus providing adequate antibiotic concentration in the tissues before bacterial contamination occurs.

Postoperative administration of Keflin should be discontinued after twenty-four hours unless signs of infection are present, in which case cultures should be performed and appropriate therapy instituted. Longer courses of preventive antibiotic therapy may be considered necessary when surgical procedures involve implantation of prosthetic devices.

Dosage and administration

Adults: The usual dosage range in severe or life-threatening infections is 6–12 g per day. In milder infections a dose of 1 g every four to six hours may be indicated. Limit the dose to a maximum of 6 g daily in patients with oliguria or blood urea elevation above 17.8 mmol/l (107 mg/100 ml).

Infants and children: The dosage should be proportionately less in accordance with age, weight and severity of infection. Daily administration of 100 mg/kg (80–160 mg/kg) in divided doses has been found effective or most infections susceptible to Keflin.

Antibiotic therapy for beta-haemolytic streptococcal

infections should continue for at least 10 days. In staphylococcal infections, surgical procedures such as incision and drainage should be carried out in all cases when indicated.

Dosage and renal impairment: In patients with moderately severe oliguria or a blood urea above 17.8 mmol/l (107 mg/100 ml), a maximum dose of 6 g per day is generally adequate. In cases of anuria, after an intravenous loading dose (up to 6 g over the first 24 hours), total daily amounts of 1–3 g may be given in divided doses every 12–24 hours (or every 8–12 hours if dialysis is performed).

Keflin is best given intravenously.

For direct intravenous administration: A solution containing 1 g cephalothin in 5 ml of diluent may be slowly injected directly into the vein over a period of three to five minutes, or may be given through the tubing when the patient is receiving parenteral solutions. The cephalothin solution may be further diluted to a larger volume if desired to facilitate measurement of the rate of injection.

For continuous intravenous infusion: 4 g of cephalothin, diluted and well mixed with at least 20 ml of Water for Injections PhEur, may be added to 500 ml of 5% Dextrose Intravenous Infusion BP or Sodium Chloride Intravenous Infusion BP. The choice of saline or dextrose solution and the volume to be employed are dictated by the fluid and electrolyte management.

Intra-peritoneal dosage: In peritoneal dialysis procedures, cephalothin has been added to dialysis fluid in concentrations up to 6 mg/100 ml and instilled into the peritoneal space throughout an entire dialysis (16–30 hours). Careful assay procedures have shown that 44% of the administered drug was absorbed into the blood stream. Serum levels of 10 mg/l were reported, with no evidence of accumulation and no untoward or systemic reaction.

Contra-indications, warnings, etc

Contra-indication: Keflin is contra-indicated in persons who have shown hypersensitivity to cephalosporin antibiotics.

Warnings: Before cephalothin therapy is instituted careful enquiry should be made concerning previous hypersensitivity reactions to cephalosporins and penicillin. Cephalosporin C derivatives should be given cautiously to penicillin-sensitive patients.

There is some clinical and laboratory evidence of partial cross-allergenicity of the penicillins and the cephalosporins. Patients have been reported to have had severe reactions (including anaphylaxis) to both drugs.

Antibiotics should be administered with caution to any patient who has demonstrated some form of allergy, particularly to drugs.

Usage in pregnancy: The safety of this product for use during pregnancy has not been established.

Precautions: If an allergic reaction to Keflin occurs the drug should be discontinued.

Prolonged use of Keflin may result in the overgrowth of non-susceptible organisms.

A false-positive reaction for glucose in the urine may occur with Benedict's or Fehling's solutions or with copper sulphate test tablets, but not with Tes-Tape® (urine sugar analysis paper, Lilly).

Side-effects: Maculopapular rash, urticaria, reactions resembling serum sickness and anaphylaxis have been reported. Eosinophilia and drug fever have been observed

to be associated with other allergic reactions. These reactions are most likely to occur in patients with a history of allergy, particularly to penicillin.

Neutropenia, thrombocytopenia and haemolytic anaemia have been reported. Some individuals, particularly those with uraemia, have developed positive direct Coombs' tests during cephalothin therapy.

Transient rise in AST (SGOT) and alkaline phosphatase has been noted.

Rises in blood urea and decreased creatinine clearances have been reported, particularly in patients with prior renal impairment.

Pain, induration, tenderness and elevation of temperature have been reported following repeated intramuscular injections. Thrombophlebitis has occurred, and is usually associated with daily doses of over 6 g given by infusion for more than three days.

Pharmaceutical precautions Keflin solutions are compatible with the following commonly used intravenous solutions: Water for Injections PhEur, Sodium Chloride Intravenous Infusion BP, Dextrose Intravenous Infusion BP, Sodium Lactate Intravenous Infusion BP, Compound Sodium Lactate Intravenous Infusion BP, Sodium Chloride and Dextrose Intravenous Infusion BP.

Stability: Unreconstituted vials: Store in a cool place (6°–15°C). After reconstitution: When stored under refrigeration (0°–6°C), the solution has a satisfactory potency for 48 hours. Solutions may precipitate; they can be redissolved by being warmed. Intravenous infusions should be started within six hours and completed within 24 hours. For prolonged infusions, replace with a freshly prepared solution at least every 24 hours.

The concentrated solution will darken, especially at room temperature.

Legal category POM.

Package quantities Vials Keflin (cephalothin sodium) equivalent to 1 g cephalothin (No. 698): Pack of 10 vials.

Further information Nil.

Product licence number 0006/5099.

KEFZOL*

Presentation Kefzol is supplied in rubber-stoppered vials containing the equivalent of 500 mg and 1 g cephalozin as the sodium salt. The sodium content is 48.3 mg per g of cephalozin sodium.

Uses Kefzol is indicated in the treatment of the following infections due to susceptible micro-organisms:

- Respiratory tract infections
- Genito-urinary tract infections
- Skin and soft tissue infections
- Bone and joint infections
- Septicaemia
- Endocarditis

Kefzol may also be used as antibiotic cover during surgery on the biliary tract and for the treatment of biliary tract infections.

Cephalozin is active against the following organisms *in vitro*: *Staphylococcus aureus* (penicillin-sensitive and penicillin-resistant) Group A beta-haemolytic streptococci and other strains of streptococci (many strains of enterococci are resistant) – *Streptococcus pneumoniae*, *Escherichia coli*, *Klebsiella* species, *Proteus mirabilis*, *Haemophilus influenzae*, *Enterobacter aerogenes*.

Most strains of *Enterobacter cloacae*, *Morganella morganii* and indole-positive *Proteus* (*Pr. vulgaris*, *Pr. rettgeri*) are resistant. Methicillin-resistant staphylococci, *Serratia*, *Pseudomonas*, *Mima* and *Herellea* species are almost uniformly resistant to cephalozin.

Dosage and administration After reconstitution, Kefzol may be administered intramuscularly or intravenously.

Intramuscular administration: Reconstitute with Water for Injections PhEur, or 0.9% Sodium Chloride Intravenous Infusion BP according to Table 1. Shake well until dissolved. Kefzol should be injected into a large muscle mass.

Table 1. Dilution table

Vial size	Diluent to be added	Approximate available volume	Approximate average concentration
500 mg	4.0 ml	4.1 ml	125 mg/ml
500 mg	2.0 ml	2.2 ml	225 mg/ml
1 g	2.5 ml	3.0 ml	330 mg/ml

Intravenous administration: Kefzol may be administered by intravenous injection or by continuous or intermittent infusion. Total daily dosages are the same as for intramuscular injection.

Intermittent intravenous infusion: Kefzol may be administered along with primary intravenous fluid management programmes in a volume control set or in a separate secondary i.v. bottle. Reconstituted 500 mg or 1 g of Kefzol may be diluted in 50 to 100 ml Water for Injections PhEur or one of the following intravenous solutions:

0.9% Sodium Chloride Intravenous Infusion BP.

5% or 10% Dextrose Intravenous Infusion BP.

5% Dextrose in Compound Sodium Lactate Intravenous Infusion BP.

0.9% Sodium Chloride and 5% Dextrose Intravenous Infusion BP.

0.45% Sodium Chloride and 5% Dextrose Intravenous Infusion BP.

Compound Sodium Lactate Intravenous Infusion BP.

5% or 10% Invert Sugar in Water for Injections PhEur.

Direct intravenous injection: Dilute 500 mg or 1 g of reconstituted Kefzol in a minimum of 10 ml of Water for Injections PhEur and inject solution slowly over a period of three to five minutes. The injection may be made directly into a vein or, for patients receiving the above parenteral fluids, through the tubing.

Dosage: The usual adult dosages are given in Table 2.

Table 2. Usual adult dosage

Type of infection	Dose	Frequency
Pneumococcal pneumonia	500 mg	q 12 h
Mild infections caused by susceptible Gram-positive cocci	500 mg	q 8 h
Acute uncomplicated urinary tract infections	500 mg to 1 g	q 12 h
Moderate to severe infections	500 mg to 1 g	q 6 to 8 h

In adults with renal impairment, cephalozin is not readily excreted. After a loading dose of 500 mg, the

Table 3. Maintenance dosage of Kefzol in adults with reduced renal function

Renal function	Blood urea†		Creatinine clearance ml/min	Serum Creatinine†		Dosage		Serum half-life (hours)
	mg/100 ml	mmol/l		mg/100 ml	mmol/l	Mild to moderate infection	Moderate to severe infection	
Mild impairment	42–74	7.0–12.3	70–40	1.3–2.0	114.9–176.8	250–500 mg q 12 h	500 mg–1.25 g q 12 h	3–5
Moderate impairment	75–105	12.5–17.5	40–20	2.1–3.5	185.6–309.4	125–250 mg q 12 h	250–600 mg q 12 h	6–12
Severe impairment	106–160	17.7–26.7	20–5	3.6–7.0	318.2–618.8	75–150 mg q 24 h	150–400 mg q 24 h	15–30
Essentially no function	> 160	> 26.7	< 5	> 7.0	> 618.8	37.5–75 mg q 24 h	75–200 mg q 24 h	30–40

† If used to estimate degree of renal impairment, elevated blood urea and serum creatinine concentrations should reflect a steady state of renal azotaemia.

Following recommendations for maintenance dosage (Table 3) may be used as a guide.

Paediatric dosage: In children, a total daily dosage of 25 or 50 mg/kg of body weight, divided into three or four equal doses, is effective for most mild to moderately severe infections (Table 4). Total daily dosage may be increased to 100 mg/kg of body weight for severe infections.

In children with mild to moderate renal impairment (creatinine clearance of 70–40 ml/min), 60% of the normal daily dose given in divided doses q 12 h should be sufficient. In children with moderate impairment (creatinine clearance of 40–20 ml/min), 25% of the normal daily dose in divided doses q 12 h should be adequate. In children with marked impairment (creatinine clearance of 20–5 ml/min), 10% of the normal daily dose given q 24 h should be sufficient. All dosage recommendations apply after an initial loading dose.

Table 4. Paediatric dosage guide

Weight kg	25 mg/kg/day divided into 3 doses		25 mg/kg/day divided into 4 doses	
	Approximate single dose (q 8 h)	Vol. needed with dilution of 125 mg/ml	Approximate single dose (q 6 h)	Vol. needed with dilution of 125 mg/ml
4.5	40 mg	0.35 ml	30 mg	0.25 ml
9.0	75 mg	0.6 ml	55 mg	0.45 ml
13.5	115 mg	0.9 ml	85 mg	0.7 ml
18.0	150 mg	1.2 ml	115 mg	0.9 ml
22.5	190 mg	1.5 ml	140 mg	1.1 ml

Weight kg	50 mg/kg/day divided into 3 doses		50 mg/kg/day divided into 4 doses	
	Approximate single dose (q 8 h)	Vol. needed with dilution of 225 mg/ml	Approximate single dose (q 6 h)	Vol. needed with dilution of 225 mg/ml
4.5	75 mg	0.35 ml	55 mg	0.25 ml
9.0	150 mg	0.7 ml	110 mg	0.5 ml
13.5	225 mg	1.0 ml	170 mg	0.75 ml
18.0	300 mg	1.35 ml	225 mg	1.0 ml
22.5	375 mg	1.7 ml	285 mg	1.25 ml

Contra-indications, warnings, etc

Contra-indication: Cephazolin is contra-indicated in patients with known allergy to the cephalosporin group of antibiotics.

Warnings: Before instituting therapy with cephazolin, every attempt should be made to determine if the patient has had previous hypersensitivity reactions to the cephalosporins, penicillins, or other drugs, in which case this product should be given cautiously.

There is some evidence of partial cross-allergenicity between the penicillins and the cephalosporins. Patients have been reported to have had severe reactions (including anaphylaxis) to both drugs.

The results of experimental studies in animals given cephalosporins suggest that the concurrent use of potent diuretics, such as frusemide or ethacrynic acid, may increase the risk of renal toxicity.

Usage in pregnancy: The safety of this product for use during pregnancy has not been established.

Usage in neonates: The safety of this product for use in premature and infants under one month of age has not been established.

Precautions: If an allergic reaction to cephazolin occurs, the drug should be discontinued and the patient treated with the usual agents (e.g. adrenaline or other pressor amines, antihistamines, or corticosteroids).

Prolonged use of cephazolin may result in the overgrowth of non-susceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

When cephazolin is administered to patients with low urinary output due to impaired renal function, lower daily dosage is required (see Dosage and Administration).

A false positive reaction for glucose in the urine may occur with Benedict's or Fehling's solutions or with copper sulphate test tablets, but not with Tes-Tape* (urine sugar analysis paper, Lilly).

Side-effects: The following side-effects have been reported:

Drug fever, skin rash, vulvar pruritus, and eosinophilia. Neutropenia, leucopenia, thrombocythaemia, and positive direct and indirect Coombs' tests.

Transient rise in AST (SGOT), ALT (SGPT), blood urea and alkaline phosphatase levels without clinical evidence of renal or hepatic impairment.

Nausea, anorexia, vomiting, diarrhoea and oral candidiasis.

Up to 6% of patients have complained of pain, some with induration, following intramuscular injection. Rarely, phlebitis has been encountered upon intravenous injection.

Other side-effects have included genital and anal pruritus, genital moniliasis, and vaginitis.

Pharmaceutical precautions Extemporaneous mixtures with other antibiotics (including aminoglycosides) are not recommended.

Unreconstituted vials: Protect from light.

Stability: Reconstituted Kefzol and dilutions of Kefzol in the recommended intravenous fluids are stable for 24 hours at room temperature (15–25°C) and for 96 hours if stored under refrigeration (0–6°C).

Legal category POM.

Package quantities

500 mg vials (No. 767): Single vials in packs of 10.
1 g vials (No. 768): Single vials in packs of 10.

Further information Nil.

Product licence number 0006/0078.

MERTHIOATE* Tincture

Presentation Tincture, orange/red, 1:1000 of Thiomersal BP with alcohol 50%.

Uses A complex organic mercurial antiseptic, effective against all common pathogens (bacteria and fungi).

Tincture: Used for skin antiseptics before surgery and first-aid treatment for contaminated wounds. Has been used as an antifungal agent in athlete's foot.

Dosage and administration Topical application.

Contra-indications, warnings, etc Hypersensitivity to thiomersal.

Precautions: After application, Merthiolate Tincture should be permitted to dry before being covered by bandages or other occlusive dressings, otherwise the alcohol and acetone in the solution may be irritating. Merthiolate is incompatible with strong acids, salts of heavy metals and iodine, and should not be used with or immediately following their application. It may be used with or following soaps or sulphonamides. Prolonged or repeated application should be avoided.

Overdosage: The mercury ion in Merthiolate is closely bound. Symptoms of mercury poisoning are almost unknown even after accidental ingestion of large quantities. Account must also be taken of the alcohol and acetone content.

Side-effects: In the small number of patients who exhibit hypersensitivity to thio or mercuri radicals such as are contained in Merthiolate, symptoms include erythematous, papular and vesicular eruptions over the area of application.

Pharmaceutical precautions Keep containers tightly closed. Protect from light and excessive heat.

Legal category P.

Package quantities Bottles of 1 litre.

Further information Merthiolate contains 49% mercury in organic chemical combination. It is readily soluble

in water and is miscible with soap and alcohol. Unlike many other antiseptics, it remains effective in the presence of non-sanguineous drainage.

Product licence number 0006/5101.

NEBCIN*

Presentation Nebcin is presented in vials in the following strengths: 1 ml vials containing 40,000 units tobramycin sulphate equivalent to 40 mg tobramycin base.

2 ml vials containing 80,000 units tobramycin sulphate equivalent to 80 mg tobramycin base.

2 ml vials containing 20,000 units tobramycin sulphate equivalent to 20 mg tobramycin base.

Also containing 0.5% w/v Phenol BP with Sodium Metabisulphite BP and disodium edetate.

Uses Nebcin is indicated for the treatment of the following infections caused by susceptible micro-organisms:

central nervous system infections, including meningitis; septicaemia and neonatal sepsis; gastro-intestinal infections, including peritonitis; and other significant infections such as: complicated and recurrent urinary tract infections, including pyelonephritis and cystitis; lower respiratory tract infections, including pneumonia; bronchopneumonia and acute bronchitis; skin, bone and soft tissue infections, including burns.

Nebcin may be considered in serious staphylococcal infections for which penicillin or other less potentially toxic drugs are contra-indicated and when bacteria susceptibility testing and clinical judgement indicate its use.

Tobramycin is usually active against most strains of the following organisms:

Pseudomonas aeruginosa

Proteus species (indole-positive and indole-negative) including *Pr. mirabilis*, *Pr. rettgeri* and *Pr. vulgaris*; *Morganella morganii*, *Escherichia coli*, *Klebsiella-Enterobacter-Serratia* species, *Citrobacter* species, *Providencia* species, *Staphylococci* including *Staphylococcus aureus* (coagulase-positive and coagulase-negative).

Some strains of group D streptococci are susceptible *in vivo* although most strains of enterococci demonstrate resistance.

The combination of tobramycin and carbenicillin is synergistic *in vitro* against most strains of *Ps. aeruginosa*. Other Gram-negative organisms may be affected synergistically by the combination of tobramycin and a cephalosporin.

Dosage and administration Nebcin may be given intramuscularly or intravenously. The patient's pretreatment body weight should be obtained for calculation of correct dosage.

The intramuscular dose is the same as the intravenous dose.

Patients with normal renal function:

Adults: The usual recommended dosage for adults with serious infections is 3 mg/kg/day, administered in three equal doses every eight hours (see Table 1). For life-threatening infections, dosages up to 5 mg/kg/day may be administered in three or four equal doses. The dosage should be reduced to 3 mg/kg/day as soon as clinically

indicated. To prevent increased toxicity due to excessive blood levels, dosage should not exceed 5 mg/kg/day unless serum levels are monitored.

Table 1. Dosage schedule guide for adults with normal renal function
(Dosage at 8-hour intervals)

Patient weight kg	Usual dose for serious infections 1 mg/kg q 8 h (Total 3 mg/kg/day)		Maximum dose for life-threatening infections (Reduce as soon as possible) 1.66 mg/kg q 8 h (Total 5 mg/kg/day unless monitored)	
	mg/dose	ml/dose†	mg/dose	ml/dose†
120	120	3.0	200	5.0
100	100	2.5	166	4.0
80	80	2.0	133	3.0
60	60	1.5	100	2.5
40	40	1.0	66	1.6

† Applicable to 40 mg/ml product forms.

Mild to moderate infections of the urinary tract have responded to a dosage of 2–3 mg/kg/day administered as a single intramuscular injection.

Children: The recommended dosage is 6–7.5 mg/kg/day, administered in three or four equally divided doses. In some patients it may be necessary to administer higher doses.

Premature or full-term neonates (one week of age or less): Dosages of up to 4 mg/kg/day may be administered in two equal doses every 12 hours.

The usual duration of treatment is 7 to 10 days. A longer course of therapy may be necessary in difficult and complicated infections. In such cases, monitoring of renal, auditory and vestibular functions is advised, because neurotoxicity is more likely to occur when treatment is extended for longer than 10 days.

It is recommended that blood levels should be determined whenever possible to ensure the correct dosage is given. Blood levels should always be determined in patients with chronic infections such as cystic fibrosis, or where longer duration of treatment may be necessary, or in patients with decreased renal function.

Patients with impaired renal function: Following a loading dose of 1 mg/kg, subsequent dosage in these patients must be adjusted, either with lower doses administered at eight-hour intervals or with normal doses at prolonged intervals (see Table 2). Both of these regimens are suggested as guides to be used when serum levels of tobramycin cannot be measured directly. They are based on either the creatinine clearance or the serum creatinine of the patient, because these values correlate with the half-life of tobramycin. Neither regimen should be used when dialysis is being performed.

Reduced dosage at eight-hour intervals (Regimen I): An appropriately reduced dosage range can be found in the accompanying table for any patient for whom the blood urea, creatinine clearance or serum creatinine values are known. The choice of dose within the indicated range should be based on the severity of the infection, the sensitivity of the pathogen, and individual patient considerations, especially renal function. An alternative rough guide for determining reduced dosage at eight-hour intervals (for patients whose steady-state serum creatinine values are known) is to divide the normally recommended dose by the patient's serum creatinine value (mg/100 ml).

Normal dosage at prolonged intervals (Regimen II): Recommended intervals between doses are given in the accompanying table. As a general rule, the dosage frequency in hours can be determined by multiplying the patient's serum creatinine level (mg/100 ml) by six.

The dosage schedules derived from either method should be used in conjunction with careful clinical and laboratory observations of the patient and should be modified as necessary.

Table 2. Two maintenance regimens based on renal function and body weight following an initial dose of 1 mg/kg†

Renal function‡			Regimen I or Regimen II	
			Adjusted doses at 8-hour intervals	Normal dosage at prolonged intervals
Blood urea	Serum creatinine	Creatinine clearance	Weight	
mg/100 ml mmol/l	mg/100 ml mcml/l	ml/min	50–60 kg 60–80 kg	Weight/Dose 50–60 kg: 60 mg 60–80 kg: 80 mg
Normal:				
≤42 ≤7.0	≤1.3 ≤114.9	≥70	60 mg 80 mg	q 8 h
42–74 7.0–12.3	1.4–1.9 123.8–168	69–40	30–60 mg 50–80 mg	q 12 h
75–105 12.5–17.5	2.0–3.3 176.8–291.7	39–20	20–25 mg 30–45 mg	q 18 h
106–140 17.7–23.3	3.4–5.3 300.6–468.5	19–10	10–18 mg 15–24 mg	q 24 h
141–160 23.5–26.7	5.4–7.5 477.4–663	9–5	5–9 mg 7–12 mg	q 36 h
>160 >26.7	≥7.6 ≥671.8	≤4	2.5–4.5 mg 3.5–6 mg	q 48 h§

†For life-threatening infections, dosages 50% above those normally recommended may be used. The dosages should be reduced as soon as possible when improvement is noted.

‡If used to estimate degree of renal impairment, blood urea and serum creatinine concentrations should reflect a steady state of renal azotaemia.

§When dialysis is not being performed.

Intramuscular administration: Nebcin may be administered by withdrawing the appropriate dose directly from the vial.

Intravenous administration: Nebcin may be given by intravenous infusion or by direct intravenous injection. When given by infusion, the usual volume of diluent (0.9% Sodium Chloride Intravenous Infusion BP or 5% Dextrose Intravenous Infusion BP) for adult doses is 50–100 ml. For children, the volume of diluent should be proportionately less than for adults. The diluted solution should be infused over a period of 20–60 minutes. Nebcin may be administered by direct intravenous injection or into the tubing of a drip set. When given in this way, serum levels may exceed 12 mg/l for a short time (see Contra-indications, warnings, etc.).

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to tobramycin sulphate. Intrathecal administration.

Warnings: Patients treated with Nebcin should be under close observation because tobramycin and other aminoglycoside antibiotics have an inherent potential for causing nephrotoxicity and ototoxicity.

Both vestibular and auditory ototoxicity can occur. Eighth cranial nerve impairment may develop in patients with pre-existing renal damage and if Nebcin is administered for longer periods or in higher doses than those recommended. Therefore, renal and eighth cranial nerve function should be closely monitored in patients with known or suspected renal impairment and also in those whose renal function is initially normal but who develop signs of renal dysfunction during therapy. Evidence of impairment in renal, vestibular and/or auditory function requires discontinuation of the drug or dosage adjustment.

Serum concentrations should be monitored when feasible, and prolonged concentrations above 12 mg/l should be avoided. Urine should be examined for increased excretion of protein, cells and casts.

The risk of toxic reactions is low in patients with normal renal function who do not receive Nebcin in higher doses or for longer periods of time than those recommended.

Concurrent and sequential use of other neurotoxic and/or nephrotoxic antibiotics, particularly streptomycin, neomycin, kanamycin, gentamicin, cephaloridine, paromomycin, viomycin, polymyxin B, colistin, vancomycin and amikacin, should be avoided.

Nebcin should not be given concurrently with potent diuretics. Some diuretics themselves cause ototoxicity, and intravenously administered diuretics enhance aminoglycoside toxicity by altering antibiotic concentrations in serum and tissue.

Usage in pregnancy: The safety of this product for use during pregnancy has not been established.

Precautions: Nebcin should be used with caution in premature and neonatal infants because of their renal immaturity and the resulting prolongation of serum half-life of the drug.

Neuromuscular blockade and respiratory paralysis have been reported in cats receiving very high doses of tobramycin (40 mg/kg). The possibility that prolonged secondary apnoea may occur should be considered if tobramycin is administered to anaesthetised patients who are also receiving neuromuscular blocking agents such as succinylcholine or tubocurarine. If neuromuscular blockade occurs, it may be reversed by the administration of calcium salts.

The inactivation of tobramycin by carbenicillin has been demonstrated *in vitro* and in patients with severe renal impairment. Such inactivation has not been found in patients with normal renal function if the drugs are administered by separate routes.

Cross-allergenicity among aminoglycosides has been known to occur.

If overgrowth of non-susceptible organisms occurs, appropriate therapy should be initiated.

Side-effects: Renal function changes, as shown by rising blood urea, non-protein nitrogen and serum creatinine and by oliguria, cylindruria and increased proteinuria, have been reported, especially in patients with a history of renal impairment who are treated for longer periods or with higher doses than those recommended. These changes can occur in patients with initially normal renal function.

Side-effects on both vestibular and auditory branches of the eighth cranial nerve have been reported, especially in patients receiving high doses or prolonged therapy. Symptoms include dizziness, vertigo, tinnitus, roaring in the ears and hearing loss.

Other reported side-effects, possibly related to tobramycin, include increased AST (SGOT), ALT (SGPT), and increased serum bilirubin; anaemia, granulocytopenia and thrombocytopenia; and fever, rash, itching, urticaria, nausea, vomiting, headache and lethargy.

Treatment of overdosage: In the event of overdosage or toxic reactions, haemodialysis or peritoneal dialysis will help remove tobramycin from the blood. Between 25%–70% of the administered dose may be removed, depending on the duration and type of dialysis employed; haemodialysis is the more effective method.

Pharmaceutical precautions Unreconstituted vials: Store at room temperature (15°–25°C). Nebcin should not be physically premixed with other drugs but should be administered separately according to the recommended dose and route.

Legal category POM.

Package quantities Boxes of 10 rubber-stoppered injection vials.

Further information Nil.

Product licence numbers

40 mg per 1 ml 0006/0084

10 mg per 1 ml 0006/0085

NU-SEALS* Aspirin

Presentation Enteric sealed tablets of aspirin. Nu-Seals Aspirin is available in two sizes containing 300 mg (coded B01) and 600 mg (coded B06) Acetylsalicylic Acid PhEur covered in a special coating, red in colour.

Uses Aspirin has analgesic, antipyretic and anti-inflammatory actions. Nu-Seals Aspirin is indicated wherever high and prolonged dosage of aspirin is required. The special coating resists dissolution in gastric juice, but will dissolve readily in the relatively less acid environment of the duodenum. Owing to the delay that the coating imposes on the release of the active ingredient, Nu-Seals Aspirin is unsuitable for the short-term relief of pain.

Dosage and administration Nu-Seals Aspirin is for oral administration. The usual adult dose of aspirin is 300–900 mg repeated three to four times daily according to clinical needs. In acute rheumatic disorders the dose

is in the range of 4–8 g daily, taken in divided doses. Nu-Seals Aspirin should not be given to children under the age of 5 years, as the usually recommended maximum single dose is less than that provided by the smaller size tablet. Children aged 6–12 years may be given 300 mg up to four times daily.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to aspirin. Hypo-prothrombinaemia, haemophilia and active peptic ulceration.

Warnings: Salicylates should be used with caution in patients with peptic ulceration or coagulation abnormalities. They may also induce gastro-intestinal haemorrhage, occasionally major.

In large doses, salicylates may also decrease insulin requirements.

Usage in pregnancy: Although clinical and epidemiological evidence would suggest the safety of aspirin for use during pregnancy, caution should be exercised when prescribing for pregnant patients. Aspirin may prolong labour and contribute to maternal and neonatal bleeding, and is best avoided at term.

Precautions: Salicylates may enhance the effect of anticoagulants and inhibit the uricosuric effect of probenecid. They may also precipitate bronchospasm or induce attacks of asthma in susceptible subjects.

Side-effects: Salicylates may induce hypersensitivity, asthma, urate kidney stones, chronic gastro-intestinal blood loss, tinnitus, nausea and vomiting. The special coating of Nu-Seals Aspirin helps to reduce the incidence of side-effects resulting from gastric irritation.

Overdosage: Overdosage produces dizziness, tinnitus, sweating, nausea and vomiting, confusion and hyper-ventilation. Gross overdosage may lead to CNS depression with coma, cardiovascular collapse and respiratory depression. If overdosage is suspected, the patient should be kept under observation for at least 24 hours, as symptoms and salicylate blood levels may not become apparent for several hours. Treatment of overdosage consists of gastric lavage and forced alkaline diuresis. Haemodialysis may be necessary in severe cases.

Pharmaceutical precautions Keep containers tightly closed.

Legal category P.

Package quantities Bottles of 100 and 500.

Further information Nil.

Product licence numbers

Tablets 300 mg 0006/5093

Tablets 600 mg 0006/5094

ONCOVIN*

Presentation Vials containing 1 mg Oncovin (Vincristine Sulphate BP) and 10 mg Lactose BP.

Vials containing 2 mg Oncovin (Vincristine Sulphate BP) and 20 mg Lactose BP.

Vials containing 5 mg Oncovin (Vincristine Sulphate BP) and 50 mg Lactose BP.

Oncovin is supplied in a combination package with an accompanying vial of diluting solution, 10 ml containing 90 mg Sodium Chloride BP with 0.9% Benzyl Alcohol BP as a preservative.

Uses Oncovin is an anti-neoplastic drug for intravenous use.

Information available at present suggests that Oncovin may be useful either alone or in conjunction with other oncolytic drugs for the treatment of:

1. Acute leukaemias.
2. Malignant lymphomas, including Hodgkin's disease, lymphosarcoma and reticulum cell sarcoma.
3. Other neoplasms, e.g. neuroblastoma, Wilms' tumour and rhabdomyosarcoma.

Dosage and administration Extreme care must be used in calculating and administering the dose of Oncovin since overdosage may have a very serious or fatal outcome.

The drug is administered intravenously at weekly intervals. The size of the dose is determined by body weight. In children, remissions from acute leukaemia have been induced with weekly doses of 0.05–0.15 mg/kg of body weight.

In acute leukaemia of children the following incremental approach to dosage may be employed:

First dose 0.05 mg/kg

Second dose 0.075 mg/kg

Third dose 0.1 mg/kg, and

Fourth dose 0.125 mg/kg up to a maximum of 0.15 mg/kg

There is no need to advance the dosage beyond that level which produces therapeutic benefit. After remission has been obtained, the dosage may be reduced in some cases to a maintenance level of 0.05 to 0.075 mg/kg/week.

In adult leukaemia the suggested dosage is 0.025–0.075 mg/kg of body weight per weekly dose.

Oncovin has also been used successfully either in sequence or in combination with other available agents effective in the treatment of leukaemia.

For malignancies other than leukaemia, a suggested dosage for Oncovin is 0.025 mg/kg/week intravenously until some beneficial effect is seen. Thereafter much smaller weekly doses in the range of 0.005–0.010 mg/kg may be employed for maintenance therapy for so long as an antitumour effect can be maintained.

The dosage must always be adjusted individually because of the narrow range between therapeutic and toxic levels, and individual variations in response.

Solutions of Oncovin ranging from 0.01 mg to 1 mg/ml have been administered with equally satisfactory results. With these concentrations, there have been no reports of phlebitis or cellulitis at the site of injection unless extravasation occurred. Various solvents have been employed for the drug, including Water for Injections BP and Sodium Chloride Intravenous Infusion BP. Both of the latter appear to be equally satisfactory.

To prepare a solution containing 1 mg/ml add 1 ml of the accompanying diluting solution to the 1 mg vial, 2 ml to the 2 mg vial, or 5 ml to the 5 mg vial. The drug dissolves rapidly to give a clear solution. The calculated dose of the resulting solution is drawn up into a syringe and injected either directly into a vein or into the tubing of a running intravenous infusion, whichever is more suitable for the patient. Care should be taken to avoid infiltration of subcutaneous tissues. Injection of Oncovin may be completed in about one minute.

Caution: If leakage into surrounding tissue should occur during intravenous administration of Oncovin, it may cause considerable irritation. The injection should be discontinued immediately and any remaining portion of

the dose should then be introduced into another vein. Local injection of hyaluronidase or hydrocortisone and the application of moderate heat to the area of leakage help to disperse the drug and are thought to minimise discomfort and the possibility of cellulitis.

It is important to avoid contamination of the eyes with concentrations of Oncovin used clinically. If accidental contamination occurs, severe irritation (or if the drug was delivered under pressure, even corneal ulceration) may result. The eye should be washed with water thoroughly and immediately.

Contra-indications, warnings, etc

Contra-indication: The intrathecal administration of Oncovin is usually fatal.

Warning: *Usage in pregnancy:* Caution is necessary with the use of all oncolytic drugs during pregnancy. Information on the use of Oncovin during pregnancy is very limited. Although no abnormalities of the human fetus have been reported thus far, animal studies with Oncovin would suggest that teratogenic effects may occur.

This product should not normally be administered to patients who are pregnant or to mothers who are breast feeding, unless the potential benefits clearly outweigh the risks.

Precautions: Effective therapy with Oncovin is less likely to be followed by granulocytopenia than is the case with Velbe (vinblastine sulphate) and other oncolytic agents. A study of the side-effects of Oncovin in all age groups reveals that it is usually neuromuscular rather than bone marrow toxicity that limits dosage. However, because of the possibility of granulocytopenia both clinician and patient should remain alert for signs of any complicating infection. Although pre-existing granulocytopenia does not necessarily contra-indicate the administration of Oncovin, the appearance of granulocytopenia during treatment warrants careful consideration before giving the next dose. Acute uric acid nephropathy, which may occur after administration of oncolytic agents, has also been reported with Oncovin.

As Oncovin is excreted principally by the liver, it may be necessary to reduce initial doses in the presence of significantly impaired hepatic or biliary function.

When chemotherapy is being given in conjunction with radiation therapy through portals which include the liver, the use of Oncovin should be delayed until radiation therapy has been completed.

Adverse reactions: The use of small amounts of Oncovin daily for long periods is not advised as this leads to the prolongation of otherwise short term side-effects (i.e. those lasting less than 7 days).

The incidence of side-effects appears to be related not only to the size of dose employed, but also to the total accumulated dosage given, particularly in the case of neurotoxicity.

Neuromuscular (often dose limiting)–neuritic pain, sensory loss, paraesthesiae, difficulty in walking, slapping gait, loss of deep tendon reflexes, muscle wasting, ataxia, foot drop and cranial nerve palsies. Frequently, there appears to be a sequence in the development of neuromuscular side-effects. Initially, one may encounter only sensory impairment and paraesthesiae. With continued treatment, neuritic pain may appear and later, motor difficulties. No reports have yet been made of any agent that can reverse the neuromuscular manifestations of Oncovin.

Haematological – granulocytopenia; Oncovin does not appear to have any constant or significant effect upon

the platelets or the red blood cells. If thrombocytopenia is present when treatment with Oncovin is begun, it may actually improve before the appearance of marrow remission.

Gastro-intestinal – constipation, abdominal cramps, paralytic ileus, vomiting and diarrhoea. The constipation which may be encountered responds well to such usual measures as enemas and laxatives. Constipation may take the form of upper colon impaction and the rectum may be found to be empty on physical examination. Colicky abdominal pain, coupled with an empty rectum, may mislead the clinician. A flat film of the abdomen is useful in demonstrating this condition. A routine prophylactic regimen against constipation is recommended for all patients receiving Oncovin.

Cutaneous – alopecia, oral ulceration.

Miscellaneous – weight loss, fever, polyuria, dysuria and headache. Convulsions, frequently with hypertension, have been reported in a few patients receiving Oncovin. Rare occurrences of the syndrome attributed to disorder of antidiuretic hormone secretion have also been observed. This syndrome has been described in association with several disease states. There is high urinary sodium excretion in the presence of hyponatraemia. Renal or adrenal disease, hypotension, dehydration, uraemia and clinical oedema are absent. With fluid deprivation, improvement occurs in the hyponatraemia and in the renal loss of sodium.

With single weekly doses, granulocytopenia, neuritic pain, constipation and difficulty in walking are usually of short duration (i.e. less than seven days). When subsequent dosage is reduced these side-effects may lessen or disappear. Other side-effects, such as alopecia, sensory loss, paraesthesiae, slapping gait, loss of deep tendon reflexes and muscle wasting, do not reverse so rapidly but persist for at least as long as treatment is continued. In most instances, these side-effects have disappeared by about the sixth week after discontinuing treatment, but in some patients neuromuscular difficulties may persist for prolonged periods.

Overdosage: Side-effects following the use of Oncovin are dose related. Therefore, following administration of more than the recommended dose, patients can be expected to experience these effects in an exaggerated fashion.

Treatment: Supportive care should include: (a) prevention of side-effects that result from the syndrome of inappropriate secretion of antidiuretic hormone. This includes restriction of fluid intake and perhaps the use of a diuretic acting on the loop of Henle and distal tubule function; (b) administration of an anticonvulsant; (c) use of cathartics to prevent ileus; (d) monitoring the patient's cardiovascular system; and (e) daily blood counts for guidance in transfusion requirement. Animal studies indicate that folic acid is effective in the treatment of overdosage. A suggested schedule is to administer 15 mg of folic acid intravenously every 3 hours for 24 hours and then every 6 hours for at least 48 hours.

Pharmaceutical precautions Vials of Oncovin should be stored in a refrigerator between 0° and 6°C.

After reconstitution: After a portion of the solution has been removed from a vial, the remainder of the contents of the vial may be stored in a refrigerator for further use for 14 days without significant loss of potency. When the reconstituted vial of Oncovin is to be stored for more

than 48 hours, it is essential to use the accompanying diluting solution or a diluent which contains a preservative. Oncovin should never be mixed with any other drug.

Legal category POM.

Package quantities

Vials 1 mg: Single vials.

Vials 2 mg: Single vials.

Vials 5 mg: Single vials.

Further information The use of Oncovin either alone or in combination with other oncolytic drugs in the treatment of malignant conditions other than leukaemia has been investigated and reported by various workers. The clinician is referred to the medical literature. A nomogram dosage card is available on request for the guidance of clinicians who prefer to relate dosage to body surface area. In acute leukaemia a dose of 1.5–2 mg/m² weekly has been employed.

If central nervous system leukaemia is diagnosed, additional agents and routes of administration will be required, since Oncovin does not cross the blood brain barrier in therapeutic amounts.

Product licence numbers

Vials 1 mg 0006/5070

Vials 2 mg 0006/5070

Vials 5 mg 0006/5071

Diluent 0006/5174

PROGESIC*

Presentation Tablets each containing fenoprofen calcium equivalent to 200 mg of fenoprofen. The tablets are round, yellow, 9.5 mm in diameter and marked Lilly 4015.

Uses Analgesic. For the relief of mild/moderate pain. Pyrexia.

Dosage and administration For oral administration to adults only, and not recommended for administration to children.

Dosage: 200 mg three or four times a day; in more intractable pain the dose may be doubled. The maximum daily dose should not exceed 3 g.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to the drug. Active peptic ulceration.

Warnings: Adverse effects may include gastro-intestinal intolerance and episodes of bleeding. Although fenoprofen has been associated with less gastro-intestinal microbleeding than aspirin, patients with a history of peptic ulcer or gastro-intestinal bleeding should be closely supervised during fenoprofen therapy.

Bronchospasm may be precipitated in patients suffering from, or with a previous history of, bronchial asthma or allergic disease.

Although cross-sensitivity has not been established, the drug should not be given to patients in whom salicylates induce the syndrome of asthma, rhinitis or urticaria.

Usage in pregnancy: The safety of fenoprofen for use during pregnancy or lactation has not been established; therefore it should not be administered to pregnant women or nursing mothers unless the potential benefits clearly outweigh any potential risk. Animal studies showed prolongation of parturition.

Precautions: Because of its affinity for albumin, fenoprofen may displace other drugs from their binding sites, and this may lead to drug interaction. In patients receiving coumarin-type anticoagulants, the addition of fenoprofen could prolong the prothrombin time. Patients receiving hydantoins or sulphonylureas should be carefully monitored.

When aspirin and fenoprofen are administered concurrently, plasma concentrations of fenoprofen are reduced. It may be advisable to discontinue the concomitant use of aspirin to maximise the beneficial effects of fenoprofen. However, single or intermittent doses of aspirin may be administered if they are indicated.

Since fenoprofen is eliminated primarily by the kidney, the drug should not be administered to patients with significantly impaired renal function.

Patients with initial low haemoglobin values who are receiving long-term therapy should be monitored, as transient reduction of haemoglobin and haematocrit values due to fenoprofen have been reported.

Elevation of AST (SGOT), LDH and ALP levels have been reported occasionally, and it is therefore recommended that fenoprofen be discontinued if any significant liver abnormalities occur.

Side-effects: Gastro-intestinal – These are the most commonly observed side-effects and include dyspepsia, constipation, diarrhoea, ulceration of the buccal mucosa, nausea, vomiting, anorexia and occult blood in the stool. Cases of peptic ulceration, including some complicated by bleeding, have occurred.

Renal – Rare cases of acute renal insufficiency, in association with allergic nephritis, nephrosis or papillary necrosis, have been reported. As a general rule, these are reversible on withdrawal of the drug. Episodes of dysuria, cystitis and haematuria have occurred.

Haematological – Various syndromes involving the bone marrow have been reported rarely; thrombocytopenia, pancytopenia and aplastic anaemia have occurred.

Allergic – Pruritus, rash, urticaria, Stevens-Johnson syndrome and angioneurotic oedema have been reported.

Neurological – Reactions reported include headache, somnolence, dizziness, tremor, confusion and insomnia.

Miscellaneous – Tinnitus, hearing decrease, amblyopia, blurred vision, palpitations, increased sweating, nervousness and peripheral oedema have been reported.

Overdosage: Information is available on two cases of intentional overdose. A patient who ingested 7.5 g fenoprofen developed severe lower abdominal pain, scrotal pain, burning on micturition, haematuria and proteinuria. All symptoms subsided within forty-eight hours.

A second patient who ingested 33 g fenoprofen over a seven-hour period developed abdominal pain followed by vomiting, and excessive perspiration. She was anuric for twenty-four hours, despite supportive therapy, and during this time developed severe headache and tinnitus. Subsequent urinalysis indicated haematuria. Symptoms gradually resolved and recovery was uneventful.

Treatment: Standard therapy to evacuate gastric contents and to support vital functions should be employed. Since fenoprofen is acidic and is excreted in the urine, it would seem theoretically beneficial to try forced alkaline diuresis.

Pharmaceutical precautions Store at room temperature (15°–25°C).

Legal category POM.

Package quantities Tablets 200 mg. Blister packs of 96 tablets.

Further information Nil.

Product licence number
Tablets 200 mg 0006/0141.

SECONAL[®] Sodium

Presentation Capsules (orange, coded F42) containing 50 mg Secobarbitone Sodium BP.

Capsules (orange, coded F40) containing 100 mg Secobarbitone Sodium BP.

Uses The rapid onset and short duration of action of Seconal Sodium makes it a valuable hypnotic for the patient whose chief difficulty is that of getting off to sleep, but who generally sleeps fairly well thereafter.

Seconal Sodium is also used for pre-anaesthetic medication in surgery, or wherever a rapidly acting sedative or hypnotic effect is desired.

Dosage and administration

Hypnosis: Adults: 50–100 mg. Occasionally as much as 200 mg may be required.

Pre-anaesthetic – Adults: 200–300 mg.

Children: 50–100 mg.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to secobarbitone sodium. Patients with a history of porphyria should not receive barbiturates in any form. Barbiturates may stimulate the enzymes responsible for metabolising many other drugs, in particular they should not be administered concurrently with coumarin-type anticoagulants. They may also effect the metabolism of endogenous steroids. Barbiturates should not be administered in the presence of uncontrolled pain, because excitement may be produced.

Warning: May be habit-forming.

Precautions: Seconal Sodium should be used with caution in patients with decreased liver function, since a prolongation of effect may occur. The central nervous system depressant effect of secobarbitone sodium may be additive with that of other CNS depressants, including alcohol.

Except in emergencies, barbiturates should not be given to persons who are known to be, or are likely to become, dependent on sedative or hypnotic drugs. The repeated prescribing of any barbiturate drug for the same patient calls for careful consideration by the physician.

Usage in pregnancy: The safety of secobarbitone sodium for use during pregnancy or for the nursing mother has not been established.

Adverse reactions: Idiosyncrasy, manifested as excitement, hangover or pain, may occur. Hypersensitivity reactions occur in some patients, especially in those with asthma, urticaria or angioneurotic oedema.

Overdosage: Symptoms include respiratory depression, depression of superficial and deep reflexes, constriction of the pupils to a slight degree (although in severe poisoning they may dilate), decreased urine formation, hypothermia and coma.

Treatment: General management should consist of symptomatic and supportive therapy, including gastric lavage, administration of intravenous fluids and maintenance

of blood pressure, body temperature and adequate respiratory exchange. Haemodialysis will increase the rate of removal of barbiturates from the body fluids.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities

Capsules 50 mg: Bottles of 100.

Capsules 100 mg: Bottles of 100 and 500.

Further information Nil.

Product licence numbers

Capsules 50 mg 0006/5065

Capsules 100 mg 0006/5066

Sodium AMYTAL[®]

Presentation Ampoules for injection, containing 250 mg or 500 mg Amobarbital Sodium BP.

Capsules (blue, coded F23) each containing 60 mg Amobarbital Sodium BP.

Capsules (blue, coded F33) each containing 200 mg Amobarbital Sodium BP.

Tablets (uncoated, white, coded U43) each containing 60 mg Amobarbital Sodium BP.

Tablets (uncoated, white, coded U16) each containing 200 mg Amobarbital Sodium BP.

Uses As a routine hypnotic, Sodium Amytal 200 mg in the adult patient will provide eight hours or more of sleep. Considerably larger doses are sometimes employed, under supervision, for control of refractory patients in the mental hospital.

Sodium Amytal is of value as a daytime sedative in the neurotic patient, who may be helped to function without breakdown and without loss of mental acuity.

Because of its rapid onset of action, Sodium Amytal may be used parenterally to control status epilepticus, but it is not the barbiturate of choice in the routine treatment of grand mal epilepsy.

Dosage and administration Capsules and tablets for oral administration.

Sedation: 60 mg two or three times daily.

Hypnosis: 60–200 mg. Occasionally a larger dose may be necessary.

Ampoules for parenteral (intramuscular or intravenous) administration: 250 mg–1 g. See package literature accompanying the ampoules. The rate of intravenous injection must not exceed 1 ml per minute. Either too-rapid injection or relative overdosage may cause apnoea or hypotension. Respiratory depression is more likely to occur if other central nervous system agents have been used concurrently. The maximum single adult dose should not exceed 1 g. The maximum intramuscular dose should not exceed 0.5 g. No greater volume than 5 ml, whatever the concentration, should be injected intramuscularly at any one site.

Several minutes may be required for the drug to dissolve completely, but under no circumstances should a solution be injected if it has not become absolutely clear within five minutes' time. Also, a solution that forms a precipitate after clearing should not be used. Sodium Amytal hydrolyses in solution or upon exposure to air. Not more than 30 minutes should elapse from the time the ampoule is opened until its contents are injected. Sodium Amytal supplied in capsules should not be used for injection purposes.

Caution: The intravenous administration of Sodium Amytal carries with it the potential dangers inherent in the intravenous use of any potent hypnotic.

Contra-indications, warnings, etc Hypersensitivity to amobarbital sodium. Patients with a history of porphyria should not receive barbiturates in any form. Barbiturates may stimulate the enzymes responsible for metabolising many other drugs; in particular they should not be administered concurrently with coumarin-type anticoagulants. They may also affect the metabolism of endogenous steroids. Barbiturates should not be administered in the presence of uncontrolled pain, because excitement may be produced.

Warning: May be habit-forming.

Precautions: Sodium Amytal should be used with caution in patients with decreased liver function, since a prolongation of effect may occur. The central nervous system depressant effect of amobarbital sodium may be additive with that of other CNS depressants, including alcohol.

Except in emergencies, barbiturates should not be given to persons who are known to be, or are likely to become, dependent on sedative or hypnotic drugs. The repeated prescribing of any barbiturate drug for the same patient calls for careful consideration by the physician.

The patient should be warned about the possibility of drowsiness if he must operate dangerous machinery or drive a vehicle.

Dosage and rate of administration should be selected with great care in patients with hypertension, hypotension or pulmonary or cardiovascular diseases.

Sodium Amytal is not recommended as an anaesthetic agent, but if a patient develops physical signs of severe depression, he should be treated as though deeply anaesthetised. Pulmonary oedema may complicate long periods of unconsciousness.

If the condition of the patient justifies the intravenous administration of Sodium Amytal, close hospital supervision is also indicated.

If rapidly induced, deep, or protracted hypnosis is not necessary, the effect of Sodium Amytal should be obtained with oral preparations.

Use in pregnancy: The safety of Sodium Amytal for use during pregnancy or for the nursing mother has not been established.

Adverse reactions: Idiosyncrasy, manifested as excitement, hangover or pain, may occur. Hypersensitivity reactions occur in some patients, especially in those with asthma, urticaria or angioneurotic oedema.

Overdosage: Symptoms include respiratory depression, depression of superficial and deep reflexes, constriction of the pupils to a slight degree (although in severe poisoning they may dilate), decreased urine formation, hypothermia and coma.

Treatment: General management should consist of symptomatic and supportive therapy, including gastric lavage, administration of intravenous fluids and maintenance of blood pressure, body temperature and adequate respiratory exchange. Haemodialysis will increase the rate of removal of barbiturates from the body fluids.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities

Ampoules 250 mg: Single ampoules.

Ampoules 500 mg: Single ampoules.

Capsules 60 mg: Bottles of 100 and 500.
Capsules 200 mg: Bottles of 100 and 500.
Tablets 60 mg: Bottles of 100 and 1,000.
Tablets 200 mg: Bottles of 100 and 1,000.

Further information Nil.

Product licence numbers

Ampoules 250 mg 0006/5086

Ampoules 500 mg 0006/5087

Capsules 60 mg 0006/5084

Capsules 200 mg 0006/5085

Tablets 60 mg 0006/5080

Tablets 200 mg 0006/5082

TUINAL*

Presentation Capsules (orange and blue, coded F65) containing 100 mg Tuinal (50 mg Secobarbitone Sodium BP and 50 mg Amobarbital Sodium BP).

Uses Tuinal combines the short onset of action of Seconal Sodium with the more prolonged effect of Sodium Amytal and is indicated whenever prompt and moderately sustained hypnosis is required. Not suitable for continuous daytime sedation.

Dosage and administration *Adults:* 100–200 mg at bedtime.

Contra-indications, warnings, etc Hypersensitivity to either constituent. Patients with a history of porphyria should not receive barbiturates in any form. Barbiturates may stimulate the enzymes responsible for metabolising many other drugs; in particular they should not be administered concurrently with coumarin-type anticoagulants. They may also affect the metabolism of endogenous steroids. Barbiturates should not be administered in the presence of uncontrolled pain, because excitement may be produced.

Warning: May be habit-forming.

Precautions: Tuinal should be used with caution in patients with decreased liver function, since a prolongation of effect may occur. The central nervous system depressant effect of Tuinal may be additive with that of other CNS depressants, including alcohol.

Except in emergencies, barbiturates should not be given to persons who are known to be, or are likely to become, dependent on sedative or hypnotic drugs. The repeated prescribing of any barbiturate drug for the same patient calls for careful consideration by the physician.

Use in pregnancy: the safety of Tuinal for use during pregnancy or for the nursing mother has not been established.

Adverse reactions: Idiosyncrasy, manifested as excitement, hangover or pain, may occur. Hypersensitivity reactions occur in some patients, especially in those with asthma, urticaria or angioneurotic oedema.

Overdosage: Symptoms include respiratory depression, depression of superficial and deep reflexes, constriction of the pupils to a slight degree (although in severe poisoning they may dilate) decreased urine formation, hypothermia and coma.

Treatment: General management should consist of symptomatic and supportive therapy, including gastric lavage, administration of intravenous fluids and maintenance of blood pressure, body temperature and adequate respiratory exchange. Haemodialysis will increase the rate of removal of barbiturates from the body fluids.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities

Capsules 100 mg: Bottles of 100 and 500.

Further information Nil.

Product licence numbers

Capsules 100 mg 0006/5077

V-CIL-K*

PENICILLIN V POTASSIUM

Presentation *V-Cil-K*:

1. Phenoxymethylpenicillin Potassium Capsules BP (pink, coded H37) containing the equivalent of 250 mg phenoxymethylpenicillin.

2. Phenoxymethylpenicillin Potassium Tablets BP (white, coded C29) containing the equivalent of 250 mg phenoxymethylpenicillin.

3. Phenoxymethylpenicillin Potassium Tablets BP (white, coded C27) containing the equivalent of 125 mg phenoxymethylpenicillin.

4. Syrup (M-142): pink/white granules for the preparation of Phenoxymethylpenicillin Elixir BPC. Each 5 ml contains the equivalent of 250 mg phenoxymethylpenicillin.

5. Paediatric syrup (M-126): orange/pink granules for the preparation of Phenoxymethylpenicillin Elixir BPC. Each 5 ml contains the equivalent of 125 mg phenoxymethylpenicillin.

6. 'Pedipacs' (M-126): orange/pink granules for the preparation of Phenoxymethylpenicillin Elixir BPC. Each foil sachet contains the equivalent of 125 mg phenoxymethylpenicillin.

Penicillin V Potassium (M-751):

Paediatric Syrup: orange/pink granules for the preparation of Phenoxymethylpenicillin Elixir BPC. Each 5 ml contains the equivalent of 62.5 mg phenoxymethylpenicillin.

Uses Penicillin exerts high activity *in vitro* against: staphylococci (except penicillinase-producing strains), streptococci (groups A, C, G, H, L and M), pneumococci, *Corynebacterium diphtheriae*, *Bacillus anthracis*, *Actinomyces bovis*, *Streptobacillus moniliformis*, *Listeria monocytogenes*, *Neisseria gonorrhoeae*, *Treponema pallidum*, *Clostridium* species and *Leptospira*.

Phenoxymethylpenicillin and potassium phenoxymethylpenicillin are indicated in the treatment of mild to moderately severe infections associated with micro-organisms whose susceptibility to penicillin is within the range of serum levels attained with these dosage forms.

The following infections will normally respond to adequate doses: *Streptococcal infections (without bacteraemia)*: Mild to moderate infections of the upper respiratory tract, scarlet fever and mild erysipelas. *Note*: Streptococci in groups A, C, G, H, L and M are very sensitive to penicillin. Other groups, including group D (enterococci), are resistant.

Pneumococcal infections: Mild to moderately severe infections of the respiratory tract.

Staphylococcal infections sensitive to penicillin: Mild infections of the skin and soft tissues.

Fusospirochaetosis (Vincent's gingivitis and pharyngitis): Mild to moderately severe infections of the oropharynx usually respond to therapy with oral penicillin.

Prophylactic usage: Prophylaxis with oral penicillin has proved effective in preventing recurrence of rheumatic fever and chorea.

Patients with a past history of rheumatic fever receiving continuous prophylaxis may harbour penicillin-resistant organisms. In these patients, the use of another prophylactic agent should be considered. *Note*: Oral penicillin should not be used as adjunctive prophylaxis for genitourinary instrumentation or surgery, lower intestinal tract surgery, sigmoidoscopy, and childbirth.

Dosage and administration For oral administration.

Adults: 125 mg or 250 mg every four to six hours depending on the severity of the condition.

Children over 5 years: The adult dose.

Children 5 years or less: 125 mg every six hours.

Infants (up to 1 year): 62.5 mg every six hours.

In all but the most serious cases, the last dose of the day may be doubled to avoid disturbing sleep. Ideally, each dose should be given half an hour before (or at least three hours after) a meal.

Diluents: For syrup, if dilution is necessary, Syrup BP should be used after the solution has been prepared according to the manufacturer's instructions.

Contra-indications, warnings, etc A previous hypersensitivity reaction to any penicillin is a contra-indication.

Warnings: All degrees of hypersensitivity including fatal anaphylaxis have been observed with oral penicillin. These reactions are more likely to occur in individuals with a history of sensitivity to multiple allergens, and enquiry should be made for such a history before therapy is begun. If an allergic reaction occurs, the drug should be discontinued and the patient treated with the usual agents (e.g. adrenaline and other pressor amines, antihistamines and corticosteroids).

Precautions: Penicillin should be used with caution in individuals with histories of significant allergies and/or asthma.

Oral therapy should not be relied upon in patients with severe illness, or with nausea, vomiting, gastric dilatation, cardiospasm or intestinal hypermotility. Occasionally patients do not absorb therapeutic amounts of orally administered penicillin.

Streptococcal infections should be treated for a minimum of 10 days, and post-therapy cultures should be performed to confirm the eradication of the organisms.

Prolonged use of antibiotics may promote the overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, appropriate measures should be taken.

Adverse reactions: The most common adverse reactions to oral penicillin are nausea, vomiting, epigastric distress, diarrhoea and black hairy tongue. Hypersensitivity reactions observed may be skin eruptions, urticaria, reactions resembling serum sickness; chills, fever, oedema, arthralgia and prostration; laryngeal oedema and anaphylaxis. Fever and eosinophilia may frequently be the only reactions observed. Haemolytic anaemia, leucopenia, thrombocytopenia, neuropathy and nephropathy are infrequent reactions and are usually associated with high doses of parenteral penicillin.

Pharmaceutical precautions Keep containers tightly closed.

Capsules: Store below 25°C.

Tablets: Store in a cool place (6°–15°C).

Syrup: After mixing, syrup can be stored in a cool place (6–15°C) for seven days without significant loss of potency.

Legal category POM.

Package quantities V-Cil-K:

Capsules 250 mg: Bottles of 100, 500 and 1,000.

Tablets 250 mg: Bottles of 100, 500 and 1,000.

Tablets 125 mg: Bottles of 100, 500 and 1,000.

Syrup (M-142) 250 mg/5 ml: Bottles of 100 ml.

Paediatric syrup (M-126) 125 mg/5 ml: Bottles of 100 ml.

'Pedipacs' (M-126): Packs of 12 and 144.

Penicillin V Potassium (M-751):

Paediatric syrup 62.5 mg/5 ml: Bottles of 100 ml.

Further information Nil.

Product licence numbers

Capsules 250 mg 0006/5126

Tablets 250 mg 0006/5164

Tablets 125 mg 0006/5163

Syrup 250 mg/5 ml 0006/5129

Paediatric syrup 125 mg/5 ml 0006/5128

'Pedipacs' 0006/5128

Paediatric syrup 62.5 mg/5 ml 0006/5162

VANCOCIN®

Presentation Rubber-stoppered 10 ml vials each containing Vancomycin Hydrochloride BP, 500,000 Units, equivalent to 500 mg vancomycin, as a lyophilised plug.

Screw-cap containers each containing Vancomycin Hydrochloride for Oral Solution USP, 10,000,000 Units, equivalent to 10 g vancomycin.

Uses Vancocin is a glycopeptide antibiotic derived from *Streptomyces orientalis*, and is bactericidal against many Gram-positive bacteria.

Vancomycin is indicated in potentially life-threatening infections which cannot be treated with other effective, less toxic antimicrobial drugs, including the penicillins and cephalosporins.

Vancomycin is useful in the therapy of severe staphylococcal infections in patients who cannot receive or who have failed to respond to the penicillins and cephalosporins or who have infections with staphylococci resistant to other antibiotics. Vancomycin has been used successfully alone in the treatment of staphylococcal endocarditis.

Its effectiveness has been documented in other infections due to staphylococci, including osteomyelitis, pneumonia, septicaemia and soft tissue infections. When staphylococcal infections are localised and purulent, antibiotics are used as adjuncts to appropriate surgical measures.

Vancomycin may be used orally for the treatment of staphylococcal enterocolitis and pseudomembranous colitis due to *Clostridium difficile*.

Vancomycin is not absorbed from the gastro-intestinal tract and is therefore not effective by the oral route for other types of infection; parenteral administration may be used concomitantly if required.

Dosage and administration *For parenteral use – Adults:* The usual intravenous dose is 500 mg (in Sodium Chloride Intravenous Infusion BP or 5% Dextrose Intravenous Infusion BP) every six hours or 1 g every 12 hours. The majority of patients with infections caused by

organisms sensitive to the antibiotic show a therapeutic response within 48–72 hours. The total duration of therapy is determined by the type and severity of the infection and the clinical response of the patient. In staphylococcal endocarditis, treatment for three weeks or longer is recommended.

Children: The total daily dosage of Vancocin, calculated on the basis of 44 mg/kg of body weight, can be administered in divided doses in the child's 24-hour requirement of fluid.

Preparation of solution: At the time of use, add 10 ml of Water for Injections PhEur to the vial of dry, sterile Vancocin powder.

Further dilution is required. Read instructions which follow:

1. Intermittent infusion (the preferred method of administration). The above solution (containing 500 mg Vancocin) can be added to 100–200 ml Sodium Chloride Intravenous Infusion BP or 5% Dextrose Intravenous Infusion BP. The intravenous infusion may be given over a period of 20–30 minutes every six hours.

2. Continuous infusion (should be used only when intermittent infusion is not feasible). Two to four vials of the above (1–2 g) can be added to a sufficiently large volume of Sodium Chloride Intravenous Infusion BP or 5% Dextrose Intravenous Infusion BP to permit the desired daily dose to be administered slowly by intravenous drip over a 24-hour period.

For oral administration: Since vancomycin is not significantly absorbed from the gastro-intestinal tract, potential systemic toxicity is not a constraint upon its oral use.

Adults: The usual dose given is 1–2 g daily in divided doses. Each dose may be reconstituted in 30 ml water and either given to the patient to drink, or administered by nasogastric tube.

Children: The total daily dose is 44 mg/kg of body weight in divided doses.

Either the oral preparation or the contents of the 500 mg vial for parenteral administration may be used.

Contra-indications, warnings, etc

Contra-indication: Hypersensitivity to vancomycin.

Warnings: Because of its ototoxicity and nephrotoxicity, Vancocin should be avoided in patients with renal insufficiency. The risk of toxicity is appreciably increased by high blood concentrations or prolonged therapy. If it is necessary to use Vancocin in such patients, doses of less than 2 g/day usually will provide satisfactory blood levels.

Vancomycin should also be avoided in patients with previous hearing loss. If it is used in such patients, the dose of Vancocin should be regulated, if possible, by periodic determination of the drug level in the blood. Deafness may be preceded by tinnitus. The elderly are more susceptible to auditory damage. Experience with other antibiotics suggests that deafness may be progressive despite cessation of treatment.

Concurrent and sequential use of other neurotoxic and/or nephrotoxic antibiotics, particularly streptomycin, neomycin, kanamycin, gentamicin, cephaloridine, paromomycin, viomycin, polymyxin B, colistin and tobramycin, should be avoided.

Usage in pregnancy: The safety of this product for use during pregnancy has not been established.

Precautions: Patients with borderline renal function and individuals over the age of 60 should be given serial tests of auditory function and of vancomycin blood levels. All

patients receiving the drug should have periodic haematological studies, urine analysis, and liver and renal function tests.

Vancocin is very irritating to tissue, and causes necrosis when injected intramuscularly; it must be injected intravenously. Pain and thrombophlebitis occur in many patients receiving Vancocin and are occasionally severe. The frequency and severity of thrombophlebitis can be minimised if the drug is administered in a volume of at least 200 ml of a recommended diluent and if the sites of injection are regularly changed.

The use of Vancocin may result in overgrowth of non-susceptible organisms. If new infections due to bacteria or fungi appear during treatment, appropriate measures should be taken.

Adverse reactions: Nausea, chills, fever, urticaria and macular rashes have been associated with the administration of Vancocin. It may also produce eosinophilia and anaphylactoid reactions.

Pharmaceutical precautions Store at room temperature (15°–25°C) and keep containers tightly closed. After reconstitution, solutions of Vancocin may be stored for up to two weeks in a refrigerator (0°–6°C) without significant loss of potency. In order to maintain sterility, it is recommended that Vancocin for parenteral use should be stored in a refrigerator and used within 96 hours.

Legal category POM.

Package quantities Vials 500 mg (500,000 Units Vancomycin): Single vials.

For oral use: 10 g (10,000,000 Units Vancomycin): Single containers.

Further information Nil.

Product licence numbers

Vials 500 mg 0006/5076

Containers 10 g 0006/0081

VELBE*

Presentation Vials containing 10 mg Velbe (Vinblastine Sulphate BP) in the form of a lyophilised plug.

Velbe is supplied in a combination package with an accompanying vial of diluting solution, 10 ml containing 90 mg Sodium Chloride PhEur, with 0.9% Benzyl Alcohol BP as a preservative.

Uses Velbe is an anti-neoplastic drug for intravenous use.

Information available at present suggests that Velbe may be useful, either alone or in combination with other oncolytic drugs for the treatment of: Generalised Hodgkin's disease (Stages III and IV). Lymphosarcoma. Reticulum cell sarcoma. Mycosis fungoides. Neuroblastoma. Histiocytosis X (Letterer-Siwe disease). Seminoma and embryonal tumours of the testis. Carcinoma of the breast, unresponsive to appropriate endocrine surgery and hormonal therapy. Some carcinomas of the skin and mucosa. Methotrexate-resistant choriocarcinoma.

Other neoplasms occasionally show a marked response to Velbe, but less frequently than the more susceptible conditions listed above.

Dosage and administration There are variations in the depth of the granulocytopenic response to Velbe. For this reason, it is recommended that the drug be given no more frequently than *once every seven days*. It is wise

to begin therapy with a single intravenous dose of 0.1 mg/kg. A nomogram dosage card is available on request for the guidance of clinicians who prefer to relate dosage to body surface area. Thereafter, granulocyte counts should be made to determine the patient's sensitivity to the drug. A simplified and conservative incremental approach to dosage at weekly intervals may be outlined as follows:

First dose	0.1 mg/kg
Second dose	0.15 mg/kg
Third dose	0.2 mg/kg
Fourth dose	0.25 mg/kg
Fifth dose	0.3 mg/kg

The same increases may be used until a maximum dose (not exceeding 0.5 mg/kg) is reached. The dose should not be increased after that dose which reduces the granulocyte count to approximately 1,500 cells/mm³. In some patients, 0.1 mg/kg may produce this granulocytopenia, others may require more than 0.3 mg/kg and very rarely as much as 0.5 mg/kg may be necessary. For most patients, however, the weekly dosage will prove to be in the range of 0.15–0.2 mg/kg.

When the dose of Velbe which will produce the above degree of granulocytopenia has been established, a dose *one increment smaller* than this should be administered at weekly intervals for maintenance. Thus, the patient is receiving the maximum dose that does not cause granulocytopenia. *It should be emphasised that, even though seven days have elapsed, the next dose of Velbe should not be given until the granulocyte count has returned to at least 2000/mm³.* In some cases, oncolytic activity may be encountered before granulocytopenic effect. When this occurs there is no need to increase the size of subsequent doses. Maintenance therapy of indefinite duration should consist of the maximum dose than can be administered regularly on an outpatient basis every seven to fourteen days without reducing the granulocyte count to a dangerous level.

Many authorities in recent years have investigated and reported good results with the use of Velbe in combination with other cancer chemotherapeutic agents.

To prepare a solution containing 1 mg/ml add 10 ml of the accompanying diluting solution to the 10 mg vial. The drug dissolves rapidly to give a clear solution.

The dose of Velbe solution (calculated to provide the desired number of milligrams per kilogram of the patient's weight) may be injected either into the tubing of a running intravenous infusion or directly into a vein. The latter procedure is readily adaptable to outpatient therapy. In either case, the injection may be completed in about one minute. If care is taken to ensure that the needle is securely within the vein and that no solution containing Velbe is spilled extravascularly, cellulitis and/or phlebitis will not occur.

Because of the enhanced possibility of thrombosis, it is considered inadvisable to inject a solution of Velbe into an extremity in which the circulation is impaired, or potentially impaired, by such conditions as compressing or invading neoplasm, phlebitis or varicosity.

Caution: If leakage into surrounding tissue should occur during intravenous administration of Velbe, it may cause considerable irritation. The injection should be discontinued immediately, and any remaining portion of the dose should then be introduced into another vein. Local injection of hyaluronidase or hydrocortisone and the application of moderate heat to the area of leakage help to disperse the drug, and are thought to minimise discomfort and the possibility of cellulitis.

It is important to avoid contamination of the eyes with concentrations of Velbe used clinically. If accidental contamination occurs, severe irritation (or if the drug was delivered under pressure, even corneal ulceration) may result. The eye should be washed with water thoroughly and immediately.

Contra-indications, warnings, etc

Contra-indications: Intrathecal administration. Velbe is contra-indicated in patients who are granulocytopenic. It should not be used in the presence of bacterial infection. Such infections must be brought under control with antiseptics or antibiotics before using Velbe.

Warning – Usage in pregnancy: Caution is necessary with the use of all oncolytic drugs during pregnancy. Information on the use of Velbe during pregnancy is very limited. Although no abnormalities of the human fetus have been reported thus far, animal studies with Velbe would suggest that teratogenic effects may occur.

This product should not normally be administered to patients who are pregnant or to mothers who are breast feeding, unless the potential benefits clearly outweigh the risks.

Precautions: Clinically, granulocytopenia is an expected effect of Velbe, and the level of the granulocyte count is an important guide to treatment. In general, the larger the dose employed, the more profound and longer lasting the granulocytopenia will be. The fact that the granulocyte count returns to normal levels after drug-induced granulocytopenia is an indication that the granulocyte-producing mechanism is not permanently depressed. Usually, the granulocyte count has completely returned to normal after the virtual disappearance of granulocytes from the peripheral blood.

Following therapy with Velbe, the nadir in the granulocyte count may be expected to occur five to ten days after the last day of drug administration. Recovery of the granulocyte count is fairly rapid thereafter and is usually complete within another seven to fourteen days. With the smaller doses employed for maintenance, granulocytopenia may not be a problem.

Although the thrombocyte count is not usually significantly lowered by therapy with Velbe, patients whose bone marrow has been recently impaired by prior therapy with radiation or with other oncolytic drugs may show thrombocytopenia (less than 150,000 platelets/mm³). When other chemotherapy or radiation has not been employed previously, thrombocyte reduction below the level of 150,000/mm³ is rarely encountered, even when Velbe may be causing significant granulocytopenia. Rapid recovery from thrombocytopenia within a few days is the rule.

The effect of Velbe upon the red blood cell count and haemoglobin is usually insignificant when other treatment does not complicate the picture. It should be remembered, however, that patients with malignant disease may exhibit anaemia even in the absence of any treatment.

If granulocytopenia with less than 1,000 granulocytes/mm³ occurs following a dose of Velbe, the patient should be watched carefully for evidence of infection until the granulocyte count has returned to a safe level.

When cachexia or ulcerated areas of the skin surface are present, there may be a more profound granulocytopenic response to the drug. Its use should be avoided in older persons suffering from either of these conditions.

In patients with malignant-cell infiltration of the bone

marrow, the granulocyte and platelet counts have sometimes fallen drastically after moderate doses of Velbe. Further use of the drug in such patients is inadvisable.

The use of small amounts of Velbe daily for long periods is not advised, even though the resulting total weekly dosage may be similar to that recommended. Little or no added therapeutic effect has been demonstrated when such regimens have been used. Strict adherence to the recommended dosage schedule is very important. When amounts equal to several times the recommended weekly dosage were given in seven daily instalments for long periods, convulsions, severe and permanent central nervous system damage, and even death occurred.

As Velbe is excreted principally by the liver, it may be necessary to reduce initial doses in the presence of significantly impaired hepatic or biliary function.

When chemotherapy is being given in conjunction with radiation therapy through portals which include the liver, the use of Velbe should be delayed until radiation therapy has been completed.

Adverse reactions: In general, the incidence of side-effects attending the use of Velbe appears to be related to the size of dosage employed. With the exception of alopecia and granulocytopenia, adverse reactions have not usually persisted for longer than 24 hours. Granulocytopenia, the most common adverse reaction, is usually the dose-limiting factor.

Gastro-intestinal – nausea, vomiting, constipation, ileus, diarrhoea, anorexia, abdominal pain, rectal bleeding, pharyngitis, haemorrhagic enterocolitis, bleeding from an old peptic ulcer.

Neurological – numbness, paraesthesiae, peripheral neuritis, mental depression, loss of deep tendon reflexes, headache, convulsions.

Cutaneous – ulceration of the mouth and skin, and alopecia. When alopecia develops it is frequently not total, and, in some cases, hair regrows while maintenance therapy continues.

Miscellaneous – malaise, weakness, dizziness and pain in tumour site.

Overdosage: Side-effects following the use of Velbe are dose related. Therefore, following administration of more than the recommended dose patients can be expected to experience these effects in an exaggerated fashion.

In addition, neurotoxicity similar to that seen with Oncovin (vincristine sulphate) may be observed.

Treatment: Supportive care should include: 1) prevention of the side-effects that result from the syndrome of inappropriate secretion of antidiuretic hormone. This includes restriction of fluid intake and perhaps the use of a diuretic acting on the loop of Henle and distal tubule function; 2) administration of an anticonvulsant; 3) prevention and treatment of ileus; 4) monitoring the patient's cardiovascular system; and 5) daily blood counts for guidance in transfusion requirement.

The major effect of excessive doses of Velbe will be on granulocytopenia, and this may be life-threatening.

Pharmaceutical precautions Vials of Velbe should be stored in a refrigerator between 0° and 6°C.

After reconstitution: After a portion of the solution has been removed from a vial, the remainder of the contents of the vial may be stored in a refrigerator for further use for 30 days without significant loss of potency. When the reconstituted vial of Velbe is to be stored for more

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than 48 hours, it is essential to use the accompanying diluting solution or a diluent which contains a preservative. Velbe should never be mixed with any other drug.

Legal category POM.

Package quantities Vials 10 mg: Single vials.

Further information Nil.

Product licence numbers

Vials 10 mg: 0006/5073

Diluent: 0006/5174

**Trade Mark*

Lipha Pharmaceuticals Limited

Old Farm Road

West Drayton

Middlesex UB7 7LD

IONAMIN*

Presentation *Ionamin 15*: Grey and yellow opaque capsule size No. 3 containing cationic exchange resin complex equivalent to 15 mg phentermine.

Ionamin 30: Yellow opaque capsule size No. 3 containing cationic exchange resin complex equivalent to 30 mg phentermine.

Uses Ionamin is useful and effective as an adjunct in weight-control problems, indicated for the treatment of simple obesity.

Dosage and administration *Adults*: 15–30 mg (usually 15 mg) daily before breakfast or 10–14 hours before retiring.

Children: 6–12 years: 1 capsule Ionamin 15 at breakfast time.

Contra-indications, warnings, etc Ionamin is contra-indicated in severe cardiovascular disease, severe hypertension, hyperthyroidism, agitation-depression states, known allergy or hypersensitivity to phentermine, concomitant or recent use of monoamine oxidase inhibitors, and of adrenergic neurone-blocking anti-hypertensive agents. Ionamin should be used with caution in patients treated with thyroid medication, psychotropic drugs, cough and cold remedies or local anaesthetics containing sympathomimetic amines.

Ionamin is not recommended in the first trimester of pregnancy.

Side-effects: When these occur they may include dryness of the mouth, insomnia, palpitations and other signs of mild central nervous stimulation.

Overdosage: Accidental overdose may be treated by lavage and sedation.

Pharmaceutical precautions No special storage precautions are required.

Legal category POM.

Package quantities Available in Bottles of 100.

Further information Chemically Ionamin contains phentermine as an ion-exchange resin complex of sulphonated polystyrene.

Experimental study has confirmed previous predictions of activity based on structural relationship of sympathomimetic amines. Phentermine is a sympathomimetic agent relatively weak in peripheral and central excitatory effects. Ionamin exerts its effect within one hour of administration and is gradually released from the ion-exchange resin complex over 10–14 hours. This smooth and prolonged activity further minimises the possible occurrence of CNS effects such as insomnia.

Product licence numbers

Capsules 15 mg 3759/0007

Capsules 30 mg 3759/0008

NITROLINGUAL* SPRAY ▼

Presentation A metered-dose aerosol which delivers 0.4 mg Nitroglycerin per spray emission. This presentation provides for very rapid buccal absorption from the spray droplets producing an almost immediate effect.

Uses For the treatment and prophylaxis of angina pectoris and the treatment of variant angina.

Dosage and administration Patients should be instructed: not to inhale the spray; to position canister touching the mouth and spray the dose onto the oral mucosa, preferably onto or under the tongue. The mouth should then be closed immediately after each spray dose.

Adults: At the onset of an attack: one or two metered-doses to be sprayed onto the oral mucosa. No more than three metered-doses are generally recommended at any one time. For the prevention of exercise-induced angina or in other precipitating conditions: One or two metered-doses to be sprayed onto the oral mucosa immediately prior to the event.

During application the canister should be held vertical with the valve head uppermost and the spray orifice as close to the mouth as possible. Patients should be instructed to familiarize themselves with the position of the spray orifice, which can be identified by a small indentation in the nozzle, in order to facilitate orientation for administration at night.

Children: The spray is not recommended.

Contra-indications, warnings, etc

Contra-indications: As with all nitrates: Hypersensitivity to this drug; shock and marked hypotension; cerebral haemorrhage and brain trauma; mitral stenosis and angina caused by hypertrophic obstructive cardiomyopathy.

Precautions: The spray is not recommended for use during pregnancy. As with other nitrates tolerance to this drug and cross tolerance to other nitrates may occur. The hypotensive effect may be enhanced by alcohol.

Adverse Reactions: These are common to all nitrates used for the treatment of angina pectoris. Cutaneous vasodilatation with flushing, tachycardia and occasionally unexplained bradycardia. Headache may occur but can usually be controlled by reducing the dose, or by the administration of analgesics.

Postural hypotension which may cause cerebral ischaemia and present as transient episodes of dizziness and weakness.

Overdosage – Signs and Symptoms: As with all nitrates large doses may cause flushing of the face, severe headache, a feeling of suffocation, hypotension and fainting. Rarely cyanosis and methaemoglobinaemia may occur. In a few patients there may be a reaction comparable to shock with nausea, vomiting, weakness, sweating and syncope.

Overdosage – Treatment: Recovery often occurs without

special treatment. Hypotension may be corrected by elevation of the legs to promote venous return. Methaemoglobinemia should be treated by intravenous methylene blue.

In the event of more serious overdosage symptomatic treatment should be given for respiratory and circulatory defects.

Pharmaceutical precautions Nitrolingual Spray should be stored in a cool place, protected from frost and direct heat or sunlight. The canister should not be broken, punctured or burnt, even when apparently empty.

Shelf life 3 years.

Legal category P

Package quantities Canisters containing 200 metered-doses.

Further information Nitroglycerin relieves angina pectoris by reducing the work load, and hence oxygen requirement of the myocardium and simultaneously improving the blood supply to ischaemic areas of the heart.

Unlike glyceryl trinitrate sublingual tablets, Nitrolingual Spray does not deteriorate on storage. No loss of potency occurs throughout the 3 year shelf-life of the product.

Nitroglycerin is also known as Glyceryl trinitrate, Trinitroglycerin and Trinitrin.

Product licence number 3759/0010.

PRAXILENE*

Presentation Pale pink capsules overprinted 'PRAXILENE-Lipha' each containing 100 mg of naftidrofuryl oxalate.

Uses *Indications:* Peripheral vascular disorders – intermittent claudication, night cramps, rest pain, incipient gangrene, trophic ulcers, Raynaud's syndrome, diabetic arteriopathy and acrocyanosis.

Cerebral vascular disorders – cerebral insufficiency and cerebral atherosclerosis, particularly where these manifest themselves as mental deterioration and confusion in the elderly.

Pharmacology: Praxilene has been shown to exert a direct effect on intracellular metabolism. Thus it has been demonstrated in animals and man that it produces an increase of ATP levels and a decrease of lactic acid levels in ischaemic conditions, evidence for an enhancement of cellular oxidative capacity. Furthermore Praxilene is a powerful spasmolytic agent.

Dosage and administration Peripheral vascular disorders: 1 to 2 capsules three times daily for a minimum of three months, or at the discretion of the Physician.

Cerebral vascular disorders: 1 capsule three times daily for a minimum of three months, or at the discretion of the Physician.

Contra-indications, warnings, etc

Contra-indications: Praxilene is contra-indicated in those patients who show a hypersensitivity to it.

Side-effects: Praxilene is normally well tolerated in the dosage recommended. Occasionally nausea and epigastric pain have been noted.

Overdosage: When this occurs, gastric lavage should be employed. Following overdosage, there may be depression of cardiac conduction, and, in severe cases,

treatment with Isoprenaline injection or electrical pacing should be considered. Convulsive crises may also be observed and these may be managed by diazepam.

Pharmaceutical precautions Store in a cool place away from light.

Legal category POM.

Package quantities Packs of 100 and 500 × 100 mg capsules.

Further information For the treatment of peripheral vascular disorders when symptoms of gross ischaemia, rest pain, or incipient gangrene are present, and for severe Raynaud's syndrome, parenteral treatment with Praxilene Forte should be given in conjunction with oral therapy. The recommended dosing schedule is one 200 mg (10 ml) Praxilene Forte ampoule twice daily, given by infusion, for 7 to 10 days, together with 1 to 2 capsules three times daily.

Product licence number

3759/0002

PRAXILENE FORTE*

Presentation Clear, colourless, 10 ml ampoules imprinted 'PRAXILENE FORTE', each containing 200 mg of naftidrofuryl oxalate (20 mg/ml).

Uses *Indications:* For the treatment of peripheral vascular disease when symptoms of gross ischaemia, rest pain or incipient gangrene are present. Raynaud's syndrome.

Pharmacology: Praxilene has been shown to exert a direct effect on intracellular metabolism. Thus, it has been demonstrated in animals and man that it produces an increase of ATP levels and a decrease of lactic acid levels in ischaemic conditions, evidence for an enhancement of cellular oxidative capacity. Furthermore, Praxilene is a powerful spasmolytic agent.

Dosage and administration One 10 ml ampoule twice daily administered by intravenous or intra-arterial infusion in 250–500 ml of saline, dextrose or low molecular weight dextran, over a minimum of 90 minutes, for a period of 7 to 10 days.

Contra-indications, warnings, etc

Contra-indications: Praxilene Forte should not be given to patients with atrioventricular block, or to those who show a hypersensitivity to the drug.

Precautions: Care should be exercised in patients with severe cardiac insufficiency and conduction disorders. The possibility of an additive effect occurring between Praxilene Forte and antiarrhythmic and beta-adrenergic blocking drugs should be considered.

Side-effects: Praxilene Forte is normally well tolerated in the dosage recommended; however, nausea has been occasionally noted.

Overdosage: When this occurs, there may be depression of cardiac conduction and, in severe cases, treatment with isoprenaline injection or electrical pacing should be considered. Convulsive crises may also be observed and these may be managed by diazepam.

Warning: Must not be administered by bolus injection.

Pharmaceutical precautions Store in a cool place away from light.

Praxilene Forte should not be given in solutions containing calcium ions.

Legal category POM.

Package quantities Packs of 10 ampoules.

Further information Praxilene capsules containing 100 mg of naftidrofuryl oxalate should be given together with the infusion therapy at a dosage of 1 capsule three

times daily. On completion of the infusion therapy, the patient should continue on oral treatment, 1 or 2 capsules three times daily for a minimum of three months, or at the discretion of the Physician.

Product licence number 3759/0004.

** Trade Mark*

Luitpold-Werk (Munich)

Medical & Scientific Office in UK

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Product licences held by
Farillon Limited
Bryant Avenue
Romford
Essex, RM3 0PJ



ANACAL* SUPPOSITORIES ANACAL* RECTAL OINTMENT

Presentation

	<i>Anacal Suppository (torpedo-shaped, off-white colour) (g%)</i>	<i>Anacal Rectal Ointment (a white odourless, soft ointment) (g%)</i>
Mucopolysaccharide polysulphuric acid ester (Heparinoid)	0.2	0.2
Prednisolone	0.05	0.15
Oxypolyethoxydodecane (Lauromacrogol-400)	2.5	5.0
Hexachlorophane	0.25	0.5

Uses *Pharmacology:* Mucopolysaccharide polysulphuric acid ester stimulates the metabolism of connective tissue, helps to break up microthrombi in the capillaries of the submucous tissue and has anti-exudative properties. Prednisolone is anti-inflammatory, anti-exudative and anti-allergic. Oxypolyethoxydodecane has local analgesic properties, thus relieving acute pain and itching. Hexachlorophane is strongly bactericidal, prevents growth of pathogenic micro-organisms and eradicates infection.

Indications: Haemorrhoids (including perianal haematomas), perianal eczema, pruritus, anal fissure, proctitis, periproctitis and after-care of haemorrhoids treated by surgery or injection.

Dosage and administration *Anacal Suppositories:* 1 suppository to be inserted once or twice daily.

Anacal Rectal Ointment: To be applied one to four times daily, as required. (Nozzle supplied for internal application.)

Contra-indications, warnings, etc

Not intended for administration to children below the age of 7 years.

Pharmaceutical precautions Store suppositories in a cool place.

Legal category POM.

Package quantities *Anacal Suppositories:* Packs of 10 (2 g).

Anacal Rectal Ointment: Tubes of 30 g.

Further information Chronic constipation, faulty dietary habits and alcohol may worsen haemorrhoids. These factors should be taken into account and, if possible, avoided.

Product licence numbers

Anacal Suppositories 0542/5004
Anacal Rectal Ointment 0542/5005

COMBIZYM*

Presentation Combizym two-step coated tablets, of yellow colour, contain in the outer layer plant enzymes (from *Aspergillus oryzae*) 120 mg (proteases, hemicellulases, cellulase, amylase), in the kernel Pancreatin BP triplex 220 mg (lipase 12 U, trypsin 20 U, amylase 14 U minimum content after Willstätter).

Uses *Pharmacology:* *Aspergillus* enzymes break up protein and carbohydrates in the stomach and duodenum. Pancreatic enzymes, released in the jejunum and ileum, complete the breakdown of food proteins, carbohydrates and fats.

Indications: Digestive disorders due to enzyme imbalance, pancreatic insufficiency, disorders of fat digestion, dyspepsia, enteritis, malabsorption syndrome.

Dosage and administration *Adults and children:* 1 or 2 tablets to be swallowed with meals.

Contra-indications, warnings, etc None.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Packs of 50 and 150 tablets.

Further information Nil.

Product licence number 0542/5002.

COMBIZYM COMPOSITUM*

Presentation Combizym Compositum two-step coated tablets, of orange colour, contain in the outer layer enzyme concentrate from *Aspergillus oryzae* (protease 126 Willstätter units, cellulase 185 Grassmann units, hemicellulase 64 Grassmann units, amylase 1.3 Willstätter units) 120 mg, in the kernel pancreatin (four times the activity of the USNF XII preparation) (lipase 26 Willstätter units, protease 36 Willstätter units, amylase 26 Willstätter units) 400 mg, and ox bile extract (USNF XI) 60 mg.

Uses *Pharmacology:* *Aspergillus* enzymes break up protein and carbohydrates in the stomach and duodenum. Pancreatic enzymes, released in the jejunum and ileum, complete the breakdown of food proteins, carbohydrates and fats. Ox bile extract stimulates biliary and pancreatic secretions, activates lipase and intensifies lipolysis by emulsification of fats.

Indications: Dyspepsia, pancreatic exocrine failure, chronic disorders of the pancreas, steatorrhoea, digestive disorders due to imbalance of digestive enzymes, digestive disorders in the old, gastric and intestinal disorders due to intolerance to drugs.

Dosage and administration *Adults and children:* 1 tablet to be swallowed during or after each meal.

Contra-indications, warnings, etc None.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Packs of 20, 100 and 500 tablets.

Further information Nil.

Product licence number 0542/5003.

HIRUDOID* CREAM HIRUDOID* GEL

Presentation Hirudoid Cream contains Organo-heparinoid 'Luitpold' 0.3 g (25,000 units) in 100 g of a white vanishing-cream base.

Hirudoid Gel contains the same active constituent in a colourless gel base.

Uses *Pharmacology:* The active constituent of Hirudoid speedily penetrates the skin, acting uniformly and persistently on diseased tissue. Hirudoid inhibits proteolysis and the spreading of hyaluronidase. It thus counteracts inflammation of traumatic, infective, toxic or allergic origin. It promotes the absorption of traumatic and inflammatory oedema, inhibits the formation and further growth of thrombi, assists in dissolving thrombi, regulates blood and lymph flow, stimulates metabolism and regeneration of damaged connective tissue, and quickly relieves pain from tissue tension.

Indications: Superficial thrombophlebitis, varicose veins and their concomitant symptoms, superficial soft-tissue injuries.

Dosage and administration *Hirudoid Cream:* Two to six inches (5–15 cm) to be applied up to four times daily to the affected area and gently massaged into the skin. If the area is tender to touch or if there is evidence of thrombosis, Hirudoid Cream should be applied thickly to the skin and covered with gauze or lint. In such cases it may be massaged very gently into the skin surrounding the affected area.

Hirudoid Gel: To be applied as a thin layer up to four times daily. Recommended when its cooling effect and rapid action are especially required (e.g. tired, aching legs and sports injuries).

Contra-indications, warnings, etc *Hirudoid Cream:* None.

Hirudoid Gel: The gel contains an alcohol and therefore should not be brought into direct contact with open wounds or mucous membranes.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities *Hirudoid Cream or Gel:* Tubes of 40 g.

Further information Nil.

Product licence numbers

Hirudoid Cream 0542/5000

Hirudoid Gel 0542/0005

MOVELAT* CREAM MOVELAT* GEL

Presentation Movelat Cream contains mucopolysaccharide polysulphuric acid ester (Heparinoid) 0.2 g, adrenocortical extract 1.0 g (equivalent to 20 mg of corticosteroids), and salicylic acid 2.0 g in a white vanishing-cream base to 100 g.

Movelat Gel contains the same active constituents in a colourless gel base.

Uses *Pharmacology:* The standardised adrenocortical extract is anti-inflammatory and anti-exudative. Mucopolysaccharide-polysulphuric acid ester arrests proteolysis and hyaluronidase activity, so that the anti-inflammatory and anti-exudative effects of the adrenocortical extract are enhanced. Salicylic acid facilitates penetration of the skin by the other active constituents and acts as a powerful analgesic.

Indications: Rheumatic disorders: osteo-arthritis, fibrositis. Non-rheumatic disorders of the locomotor apparatus: sprains, muscular strains and spasms, soft tissue injuries.

Dosage and administration *Movelat Cream:* Two to six inches (5–15 cm) to be massaged into the affected area up to four times daily. The Cream may also be used as a dressing, when it should be applied thickly.

Movelat Gel: To be applied gently to the affected area up to four times daily.

Contra-indications, warnings, etc *Movelat Cream:* None.

Movelat Gel: The gel contains an alcohol and therefore should not be brought into direct contact with open wounds or mucous membranes.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities *Movelat Cream or Gel:* Tubes of 50 g.

Further information Nil.

Product licence numbers

Movelat Cream 0542/5001

Movelat Gel 0542/0006

PROPAIN*

Presentation Yellow compressed tablets with a scored bisect line on one side, each containing:

Paracetamol PhEur	400 mg
Codeine Phosphate PhEur	10 mg
Diphenhydramine Hydrochloride BP	5 mg
Caffeine PhEur	50 mg

Uses Analgesic in the treatment of headache, migraine, muscular pain, period pain and toothache. The associated symptoms of tension pain are relieved by the inclusion of diphenhydramine hydrochloride.

Dosage and administration *For adults and children over 12 years of age:* 1 or 2 tablets orally every four hours, up to a maximum of ten tablets in 24 hours.

Contra-indications, warnings, etc Propain may cause drowsiness and, if affected, the patient should not drive or operate machinery. The effect of alcohol and other sedatives may be potentiated. Safety in pregnancy has not been established. Patients should avoid excessive intake of coffee and tea when taking these tablets. Propain should not be given to patients with known liver or renal impairment.

Overdosage: The effects of overdosage are predominantly those of paracetamol and hepatic necrosis can occur. Treat symptomatically as for paracetamol.

Pharmaceutical precautions Nil.

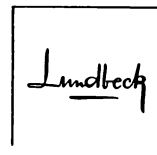
Legal category P.

Package quantities Strip packed in cartons of 12 tablets. Bulk containers of 100 tablets.

Further information Nil.

Product licence number 0542/0015.

**Trade Mark*



BLEOMYCIN INJECTION

Presentation Bleomycin Lundbeck Injection is a whitish-yellow freeze-dried plug of bleomycin sulphate equivalent to 15 mg bleomycin (standard NIHJ) in clear glass ampoule.

Active ingredients: 15 mg bleomycin per ampoule, as the sulphate.

Uses Pharmacology: Bleomycin is a basic water-soluble glycopeptide with cytotoxic activity. The mechanism of action of bleomycin is believed to involve single-strand scission of DNA, leading to inhibition of cell division, of growth and of DNA synthesis in tumour cells.

Apart from its antibacterial and antitumour properties, bleomycin is relatively free from biological activity. When injected intravenously it may have a histamine-like effect on blood pressure and may cause a rise in body temperature. Blood concentrations of bleomycin in patients indicate that the drug is excreted more rapidly after intravenous than after intramuscular injection and that up to one third of the dose is excreted unchanged in the urine within 24 hours.

Indications:

1. Squamous cell carcinoma affecting the mouth, nasopharynx and paranasal sinuses, larynx, oesophagus, external genitalia, cervix or skin. Well-differentiated tumours usually respond better than anaplastic ones.
2. Hodgkin's disease and other malignant lymphomas, including mycosis fungoides.
3. Testicular teratoma.
4. Malignant effusions of serous cavities.
5. Secondary indications in which bleomycin has been shown to be of some value (alone or in combination with other drugs) include metastatic malignant melanoma, carcinoma of the thyroid, lung and bladder.

Dosage and administration Adults: Bleomycin is usually administered intramuscularly but may be given intravenously (bolus or drip), intra-arterially, intrapleurally or intraperitoneally as a solution in physiological saline. Local injection directly into the tumour may occasionally be indicated.

1. Squamous cell carcinoma and testicular teratoma: The following dosage schedules are recommended for adults:

Age in years	Total dose (mg)	Dose per week (mg)
80 and over	100	15
70-79	150-200	30
60-69	200-300	30-60
Under 60	500	30-60

These doses may need to be adjusted when bleomycin is used in combination therapy.

A total dose of 500 mg should not normally be exceeded, but young men with testicular tumours have frequently tolerated twice this amount.

Used alone normal dose frequency is 15 mg three times a week or 30 mg twice a week, either intramuscularly or intravenously until the total dose indicated in the above table is administered. Continuous intravenous infusion at a rate of 15 mg/24 hours for up to 10 days, or 30 mg/24 hours for up to five days may produce a therapeutic effect more rapidly. The development of stomatitis is the most useful guide to the determination of individual tolerance of maximum therapeutic dose.

2. Malignant lymphomas: Used alone the recommended dosage regimen is 15 mg once or twice a week, intramuscularly, to a total dose of 225 mg. For patients 60 years and over, 75% of the dosage recommended in 1 above should be used. These doses may need to be adjusted when bleomycin is used in combination chemotherapy.

3. Malignant effusions (particularly those associated with carcinoma of breast): After drainage of the serous cavity affected 60 mg bleomycin dissolved in 100 ml physiological saline is introduced via the drainage needle or cannula, which is then withdrawn.

Bleomycin is commonly used in conjunction with radiotherapy, particularly in the treatment of cancer of the head and neck region. Such a combination may enhance mucosal reactions if full doses of both forms of treatment are used and bleomycin dosage may require reduction, e.g. to 5 mg at the time of each radiotherapy fraction five days a week. Bleomycin is frequently used as one of the drugs in multiple chemotherapy regimens (e.g. in squamous cell carcinoma, testicular teratoma, lymphoma). The mucosal toxicity of bleomycin should be borne in mind in the selection and dosage of drugs with similar toxic potential used in such combinations.

Children: Until further data are available, administration of bleomycin to children should take place only under exceptional circumstances and in special centres. The dosage should be based on that recommended for adults and adjusted to body surface area or body weight.

Reduced kidney function: With serum creatinine values of 2-4 mg%, half the above individual dosage is recommended. With serum creatinine above 4 mg%, a further reduction in dose is indicated.

Preparation of solutions: For intramuscular injections the required dose is dissolved in up to 5 ml of a suitable solvent such as physiological saline. If pain occurs at the site of injection a 1% solution of lignocaine may be used as a solvent.

For intravenous injections the dose required is dissolved in 5-200 ml of physiological saline and injected slowly or added to the reservoir of a running intravenous infusion. For intra-arterial administration a slow infusion in physiological saline is used. For intra-cavitary injection 60 mg is dissolved in 100 ml normal saline.

For local injections bleomycin is dissolved in physiological saline to make a 1–3 mg/ml solution.

Contra-indications, warnings, etc This product should not normally be administered to patients who are pregnant or to mothers who are breast feeding. It is also contra-indicated in patients with acute pulmonary infection or greatly reduced lung function.

Adverse reactions: Like most cytotoxic agents bleomycin can give rise both to immediate and to delayed toxic effects. The most immediate effect is fever on the day of injection. Anorexia, tiredness or nausea also may occur. Pain at the injection site, or in the region of the tumour, has occasionally been reported, and other rare adverse effects are hypotension and local thrombophlebitis after intravenous administration. A few cases of acute fulminant reactions have been observed after intravenous injections of doses higher than those recommended. Hypotension, hyperpyrexia and drug related deaths have been reported rarely following intracavitary injection.

The most serious delayed effect is interstitial pneumonia, which may develop during, or occasionally after, a course of treatment. This condition may sometimes develop into fatal pulmonary fibrosis, although such an occurrence is rare on recommended doses. Previous or concurrent radiotherapy to the chest is an important factor in increasing the incidence and severity of lung toxicity. It has been suggested that those patients who have received bleomycin preoperatively are at a greater risk of developing pulmonary toxicity, and a reduction in inspired oxygen concentration during the operation and post-operatively is recommended.

The majority of patients who receive a full course of bleomycin develop lesions of the skin or oral mucosa. Induration, hyperkeratosis, reddening, tenderness, and swelling of the tips of the fingers, ridging of the nails, bulla formation over pressure points such as elbows, loss of hair and stomatitis are rarely serious and usually disappear soon after completion of the course.

Precautions: Patients undergoing treatment with bleomycin should have chest X-rays weekly. These should continue to be taken for up to four weeks after completion of the course. If breathlessness or infiltrates, not obviously attributable to tumour or to co-existent lung disease, appear, administration of the drug must be stopped immediately and patients should be treated with a corticosteroid (e.g. hydrocortisone 100 mg i.m. as the sodium succinate daily for five days, followed by oral prednisone 10 mg twice daily) and a broad-spectrum antibiotic. No specific clinical incompatibilities with other drugs or food have been encountered.

Overdosage: No specific antidote. The acute reaction to an overdosage with bleomycin would probably include hypotension, fever, rapid pulse and general symptoms of shock. Treatment is purely symptomatic. In the event of respiratory complications, the patient should be treated with a corticosteroid and a broad-spectrum antibiotic.

Pharmaceutical precautions Freeze-dried bleomycin has a shelf life of two years from the date of manufacture when stored at room temperature. Bleomycin should be administered as a freshly prepared solution.

Because of possible skin changes, direct contact of bleomycin with the skin should be avoided.

Pharmaceutical incompatibilities: Bleomycin solutions should not be mixed with solutions of essential amino acids, riboflavin, ascorbic acid, dexamethasone, aminophylline or frusemide.

Legal category POM.

The supply of bleomycin is restricted to centres with special experience in the chemotherapy of malignant diseases and is available on prescription only.

Package quantities Boxes of 10 × 15 mg ampoules.

Further information Bleomycin has little or no toxic effect on the bone marrow, and has no immunosuppressive action.

Product licence number 0458/0009.

CCNU LUNDBECK CAPSULES

Presentation Blue/white gelatin capsules containing 10 mg lomustine, and blue gelatin capsules containing 40 mg lomustine.

Active ingredient: 10 mg and 40 mg lomustine (CCNU; 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea).

Uses The mechanism of action is believed to be partly as an alkylating agent and partly by inhibition of several vital enzymatic processes. Cross-resistance with other nitrosoureas is usual but cross-resistance with conventional alkylating agents is unusual.

Indications: As palliative or supplementary treatment, usually in combination with radiotherapy and/or surgery or as part of multiple drug regimens in:

brain tumours (primary or metastatic);
lung tumours (especially oat-cell carcinoma);
Hodgkin's disease (resistance to conventional combination chemotherapy);
malignant melanoma (metastatic).

CCNU may also be of value as second-line treatment in non-Hodgkin's lymphoma, myelomatosis, gastrointestinal tumours, carcinoma of the kidney, the testis, the ovary, the cervix uteri and the breast.

Dosage and administration *Adults:* CCNU is given by mouth. The recommended dose in patients with normally functioning bone marrow receiving CCNU as their only chemotherapy is 120–130 mg/m² as a single dose every six to eight weeks (or as a divided dose over three days, e.g. 40 mg/m²/day).

Dosage is reduced if:

- CCNU is being given as part of a drug regimen which includes other marrow-depressant drugs, and
- in the presence of leucopenia below 3,000/mm³ or thrombocytopenia below 75,000/mm³.

Marrow depression after CCNU is longer sustained than after nitrogen mustards and recovery of white cell and platelet counts may not occur for six weeks or more. Blood elements depressed below the above levels should be allowed to recover to 4,000/mm³ (WBC) and 100,000/mm³ (platelets) before repeating CCNU dosage.

Administration to children: Until further data are available administration of CCNU to children with malignancies other than brain tumours should be restricted to specialised centres and exceptional situations. Dosage in children, like that in adults, is based on body surface area (120–130 mg/m² every six to eight weeks, with the same qualifications as apply to adults).

Contra-indications, warnings, etc This product should not normally be administered to patients who are pregnant or to mothers who are breast feeding. Other

contra-indications are: 1. Previous hypersensitivity to nitrosoureas; 2. Previous failure of the tumour to respond to other nitrosoureas; 3. Severe bone marrow depression.

Precautions: Patients receiving CCNU chemotherapy should be under the care of doctors experienced in cancer treatment. Blood counts should be carried out before starting the drug and at frequent intervals (preferably weekly) during treatment. Treatment and dosage is governed principally by the haemoglobin, white cell count and platelet count. Liver function should also be assessed periodically.

Adverse effects: Haematological: The principal adverse effect is marrow toxicity of a delayed or prolonged nature. Thrombocytopenia appears about four weeks after a dose of CCNU and lasts one to two weeks at a level around 80–100,000/mm³; leucopenia appears after six weeks and persists for one to two weeks at about 4–5,000/mm³. The haematological toxicity may be cumulative, leading to successively lower white cell and platelet counts with successive doses of the drug.

Gastrointestinal: Nausea and vomiting usually occur four to six hours after a full single dose of CCNU and last for 24–48 hours, followed by anorexia for two to three days. The effects are less troublesome if the six-weekly dose is divided into three doses and given on each of the first three days of the six-week period. Gastrointestinal tolerance is usually good, however, if prophylactic antiemetics are given (e.g. metoclopramide or chlorpromazine). Transient elevation of liver enzymes (SGOT, SGPT, LDH or alkaline phosphatase) are occasionally observed. More rarely patients are troubled by stomatitis.

Other side-effects: Loss of scalp hair has been reported infrequently.

Overdosage: There is no specific antidote. In the event of dangerously low red cell, white cell or platelet counts, cross-matched whole blood should be given as necessary.

Pharmaceutical precautions: The capsules should be stored in the original container and protected from light and moisture. The preparation has a shelf life of two years from the date of manufacture, when stored at room temperature.

Legal category POM.

The supply of CCNU capsules is restricted to centres with special experience in the chemotherapy of malignant disease. CCNU capsules are available on prescription only.

Package quantities: Bottles of 20 capsules each containing 10 mg or 40 mg lomustine.

Further information: Nil.

Product licence number: 0458/0018.
0458/0024

CLOPIXOL® INJECTION

Presentation: Clopixol Injection is a 20% sterile, straw-coloured solution of cis[Z]-clopenthixol decanoate in thin vegetable oil. It is presented in a clear glass ampoule (1 ml) and vials (10 ml).

Active ingredient: cis[Z]-clopenthixol decanoate 200 mg per 1 ml.

Uses Pharmacology: Clopenthixol is a potent neuroleptic of the thioxanthene group. In addition to its pronounced antipsychotic effect, it possesses a marked

specific calming effect and a non-specific sedative action. Clopenthixol itself is relatively short-acting, but Clopixol Injection, its decanoic acid ester dissolved in thin vegetable oil, provides a predictable slow release depot preparation of the active constituent. Pharmacokinetic studies in humans show that peak serum levels are attained towards the end of the first week and gradually decline over a period of three to four weeks after intramuscular injection. Clinical experience correlates well with the pharmacokinetic findings, using a dosage interval of two to four weeks.

Indications: Clopixol Injection is a depot neuroleptic preparation for the treatment of psychoses, especially schizophrenia and particularly for patients with features of agitation or aggression.

Dosage and administration Adults: Clopixol Injection is administered by deep intramuscular injection into the upper, outer buttock or lateral thigh in doses of 200–400 mg (1–2 ml) every two to four weeks. A few patients may need higher doses or shorter intervals between doses. The maximum recommended dose is 600 mg (3 ml) a week. Doses greater than 400 mg (2 ml) should be distributed between two injection sites. Treatment is usually started with 100 mg. One week later, or when symptoms recur (but not more than four weeks later) a second injection of 100–200 mg or more is given.

Note: As with all oily injections it is important to ensure by aspiration before injection, that inadvertent intravascular entry does not occur.

Children: Clopixol Injection should not be administered to children.

Transfer of patients to Clopixol Injection:

1. Those not previously treated with a long-acting antipsychotic injection should start with an initial dose of 100 mg intramuscularly and the patient's response and the appearance of extrapyramidal side-effects monitored carefully. Oral neuroleptic therapy should be gradually phased out.

2. Patients being transferred from phenothiazine depot injections should receive a dose in the ratio of 200 mg Clopixol Injection equivalent to 25 mg fluphenazine decanoate.

3. Patients whose schizophrenic symptoms may have been treated with flupenthixol decanoate (Depixol Injection) because of features such as anergia or withdrawal at the time of starting depot neuroleptic treatment may pass to a phase of their psychosis in which features such as agitation or aggression predominate. Such a change in the clinical picture would warrant consideration of a change of treatment to Clopixol Injection, using a comparable antipsychotic dose (200 mg Clopixol Injection = 40 mg Depixol Injection).

Contra-indications, warnings, etc

Contra-indications and precautions: Clopixol Injection is contra-indicated in acute alcohol, barbiturate or opiate poisoning.

Clopixol is unsuitable for patients whose psychoses are accompanied by features of apathy or withdrawal, for those who do not tolerate oral neuroleptic drugs, or for those with Parkinsonism; severe arteriosclerosis; senile confusional states; or advanced renal, hepatic or cardiovascular disease. In common with other therapies it is recommended that Clopixol Injection should not be administered during pregnancy, particularly the first trimester, unless the importance of control of psychotic

symptoms outweighs the theoretical hazard of foetal malformations.

Warning: Ability to drive a car or operate machinery may be affected. Therefore, caution should be exercised initially, until the individual reaction to the treatment is known.

Adverse reactions: Extrapyramidal side-effects may occur, especially during the first few days after injection and during the early phase of treatment. In most cases these side-effects can be satisfactorily controlled by anti-Parkinson drugs though their routine use is not recommended. Initial drowsiness has been reported and in a few patients slight changes in weight. Occasional local reactions such as erythema, swelling or tender fibrous nodules have been reported. Tardive dyskinesia, galactorrhoea and amenorrhoea are adverse effects of the general group of neuroleptic drugs. They have not been reported in patients treated with Clopixol Injection, but the theoretical hazard should be borne in mind.

Overdosage: Overdosage should be treated:

1. By anticholinergic anti-Parkinson drugs if extrapyramidal symptoms occur.
2. By sedation (with benzodiazepines) if akathisia occurs, or in the unlikely event of agitation, excitement or convulsions.
3. By noradrenaline in saline intravenous drip if the patient is in shock. Otherwise observation and symptomatic management should be adequate.

Pharmaceutical precautions Store at room temperature. Under these conditions the preparation has a shelf life of two years from the date of manufacture.

In accordance with normal practice partially used vials should be discarded at the end of each session.

Legal category POM.

Clopixol is available through hospitals, clinics and on prescription only through registered pharmacies for patients whose treatment has been initiated by a psychiatrist.

Package quantities Boxes of 10 × 200 mg (1 ml) ampoules.

Boxes of 1 × 10 ml vials.

Further information Nil.

Product licence number 0458/0017.

DEPIXOL[®] INJECTION

Presentation Depixol Injection is a 2% sterile, straw-coloured solution of cis(Z)-flupenthixol decanoate in thin vegetable oil. It is presented in clear glass ampoules, syringes (1 ml and 2 ml) and vials (10 ml).

Active ingredient: cis(Z)-flupenthixol decanoate 20 mg per ml.

Uses **Pharmacology:** Flupenthixol is a potent, non-sedating, neuroleptic drug of the thioxanthene series. In addition to a marked antipsychotic action it has been shown to possess activating, alerting, and anxiolytic effects and, in low doses, antidepressant activity. Flupenthixol itself is relatively short-acting, but Depixol Injection, its decanoic acid ester dissolved in thin vegetable oil, provides a predictable, slow-release depot preparation of the active constituent. Pharmacological studies in animals indicate a duration of action of two to four weeks after intramuscular injection. This has been

confirmed in man by pharmacokinetic studies using radioimmunoassay of flupenthixol, which indicate a slow release of active substance after intramuscular injection giving a maximal blood concentration about four to seven days after injection and a plateau lasting from two to three weeks. Further corroboration of this absorption pattern is provided by clinical studies where Depixol Injection has been successfully used by administration at intervals of two to four weeks.

Indications: Depixol Injection is a depot neuroleptic preparation and is indicated in the treatment and maintenance of schizophrenic patients, especially those who are unreliable in taking oral medicines prescribed for them. Features of the illness most likely to benefit are apathy, inertia, withdrawal, anxiety, hallucinations and paranoid delusions.

Dosage and administration **Adults.** Depixol Injection is administered by deep intramuscular injection into the upper, outer buttock or lateral thigh in doses of 20–40 mg (1–2 ml) at intervals of two to four weeks depending on the response. Some patients may need larger doses, or need them at shorter intervals. Doses greater than 40 mg (2 ml) should be distributed between two injection sites.

Note: As with all oily injections it is important to ensure, by aspiration before injection, that inadvertent intravascular entry does not occur.

Children: Depixol Injection should not be administered to children.

Transfer of patients to Depixol Injection:

1. Those not previously treated with long-acting antipsychotic injections should start with a test dose of 20 mg (1 ml) and the patient's response and the appearance of extra-pyramidal symptoms carefully studied during the following 5–10 days. Oral neuroleptic drugs should be continued, but in diminishing dosage.

2. Patients being transferred from phenothiazine depot injections should receive a dose in the ratio of 40 mg Depixol Injection equivalent to 25 mg fluphenazine decanoate.

3. Patients whose psychotic symptoms may have been treated with cis(Z)-clopenthixol decanoate (Clopixol Injection) because of features such as agitation or aggression at the time of starting depot neuroleptic therapy may pass to a phase in their psychoses in which features such as anergia or withdrawal predominate. Such a change in the clinical picture would warrant consideration of a change of treatment to Depixol Injection, using a comparable antipsychotic dose (40 mg Depixol Injection = 200 mg Clopixol Injection).

Two to four weeks later a second dose of 40 mg (2 ml) or more is then given, depending on the response and appearance of unwanted effects. This part of the treatment should normally be given in hospital. Subsequently the dose and frequency of administration should be adjusted for each individual patient so as to achieve maximum control of psychotic symptoms with a minimum of side-effects.

Contra-indications, warnings, etc Depixol Injection is not recommended for excitable or overactive patients since its activating effect may lead to exaggeration of these characteristics. It is also unsuitable for patients who do not tolerate oral neuroleptic drugs, or for those with Parkinsonism, severe arteriosclerosis, senile confusional states, or advanced renal, hepatic or cardiovascular disease. Depixol should be avoided in

pregnancy. However teratological studies in three animal species have failed to reveal any specific effect of flupenthixol or its decanoate on foetal anatomy. Therefore, it is reasonable, particularly after the first trimester, to persevere with treatment in a previously unrecognised pregnancy if psychiatric indications outweigh the theoretical hazard of foetal malformation.

Adverse reactions: The commonest unwanted effect is the appearance of extrapyramidal symptoms, both hypokinetic and hyperkinetic. When these appear, they generally do so one to three days after injection and last for about five days. The incidence seems to be greater after the first few injections, and to diminish thereafter. Routine anti-Parkinson drug treatment is not recommended. Tardive dyskinesia has been observed very occasionally; these rare cases have been almost exclusively in patients taking concurrent anticholinergic anti-Parkinson drugs. No specific clinical incompatibilities with other drugs or food have been encountered. However on theoretical pharmacodynamic grounds it may be wise to allow an interval of not less than seven days between completion of MAOI treatment and the initiation of Depixol therapy. Occasional depressive reactions have been reported after administration of Depixol Injection, but they appear to be less frequent than after other depot neuroleptics. Occasional local reactions such as erythema, swelling or tender fibrous nodules have been reported. Amenorrhoea has occurred in patients receiving high doses. Galactorrhoea is a rare side-effect of the drug which may be severe enough to warrant reduction of dosage or withdrawal of neuroleptic treatment. No anticholinergic, hepatic, renal, haematological or cardiovascular (e.g. hypotension) side-effects have been confirmed, nor have flupenthixol-induced photosensitivity or alterations in the cornea or lens been reported.

Overdosage: Overdosage should be treated:

1. By anticholinergic anti-Parkinson drugs if extrapyramidal symptoms occur.
2. By sedation (with benzodiazepines) in the unlikely event of agitation or excitement.
3. By noradrenaline in saline intravenous drip if the patient is in shock. Otherwise observation and symptomatic management should be adequate.

Pharmaceutical precautions Store at room temperature and protect from light. Under those conditions the preparation has a shelf life of two years from date of manufacture.

In accordance with normal practice partially used vials should be discarded at the end of each session.

Legal category POM.

For use in hospitals and hospital clinics and in registered pharmacies for dispensing prescriptions in respect of patients stabilised on Depixol. Depixol is available on prescription only.

Package quantities Boxes of 10 × 20 mg (1 ml) ampoules and syringes.

Boxes of 10 × 40 mg (2 ml) ampoules and syringes.
Boxes of 1 × 10 ml vials.

Further information Nil.

Product licence number 0458/0007.

DEPIXOL®-CONC. INJECTION

Presentation Depixol-Conc. Injection is a 10% sterile, straw-coloured solution of cis(Z)-flupenthixol decanoate in thin vegetable oil. It is presented in glass ampoules (1 ml) and vials (5 ml).

Active ingredient: cis(Z)-flupenthixol decanoate 100 mg per ml.

Uses Pharmacology: Flupenthixol is a potent, non-sedating neuroleptic drug of the thioxanthene series. In addition to a marked antipsychotic action it has been shown to possess activating, alerting and anxiolytic effects and, in low doses, antidepressant activity. Flupenthixol itself is relatively short-acting, but its decanoic acid ester dissolved in thin vegetable oil, provides a predictable, slow-release depot preparation of the active constituent. Pharmacological studies in animals indicate a duration of action of two to four weeks after intramuscular injection. This has been confirmed in man by pharmacokinetic studies using radioimmunoassay of flupenthixol which indicate a slow release of active substance after intramuscular injection, giving a maximal blood concentration about four to seven days after injection and a plateau lasting from two to three weeks. Further corroboration of this absorption pattern is provided by clinical studies where Depixol-Conc. Injection has been successfully used by administration at intervals of two to four weeks.

Indications: Depixol-Conc. Injection is a depot neuroleptic preparation and is indicated for the treatment of moderate to severe schizophrenia and allied psychoses. Patients for whom the drug is especially appropriate are:

1. Those believed by the Physician to be unreliable in taking oral medication.
2. Patients who are already receiving treatment with Depixol Injection at high dose levels and who may experience discomfort as a result of the large injection volume.
3. Patients who hitherto could not receive effective treatment with depot neuroleptics because of the high doses, and hence large volumes, required to achieve satisfactory therapeutic blood levels.

Features of the illness most likely to benefit are hallucinations, paranoid delusions, apathy, inertia, withdrawal and anxiety.

Dosage and administration Depixol-Conc. Injection is a solution of flupenthixol decanoate five times more concentrated than Depixol (standard) Injection and Depixol-Conc. Injection is therefore appropriate for the treatment of patients requiring single doses of 100 mg or more of the drug. Doses greater than 200 mg (2 ml) should be distributed between two injection sites.

Adults: Depixol-Conc. is administered by deep intramuscular injection into the upper, outer buttock or lateral thigh, usually in doses of 100–200 mg (1–2 ml) every two to four weeks. Individual dosage and intervals between injection should be adjusted according to therapeutic response. Dosage for most patients falls between 100 mg (1 ml) every four weeks and 300 mg (3 ml) every two weeks but some, especially during an exacerbation or acute relapse of the disease, may require single injections of as much as 400 mg (4 ml) fortnightly or even weekly. Adequate control of severe symptoms by Depixol-Conc. Injection is usually achieved within four to six months and this may justify return to lower dose maintenance with standard Depixol 2% injections.

Note: As with all oily injections it is important to ensure, by aspiration before injection, that inadvertent intravascular entry does not occur.

Children: Depixol-Conc. Injection should not be administered to children.

Transfer of patients to Depixol-Conc. Injection:

1. From Depixol Injection. Patients should be transferred on the basis of 1 ml Depixol-Conc. equivalent to 5 ml of Depixol Injection. Control of severe symptoms by Depixol-Conc. Injection (usually achieved within four to six months) may justify a return to low dose maintenance with Depixol Injection. Extrapyramidal effects may occur in a minority of patients, their incidence and severity being of the same order as are encountered in patients treated with Depixol Injection.

2. Patients being transferred from phenothiazine depot injections should start with an equivalent or higher dose in the ratio of 100 mg Depixol-Conc. Injection equivalent to 62.5 mg fluphenazine decanoate.

3. Those not previously treated with long-acting antipsychotic injections should start with a small test dose of Depixol Injection 20 mg (1 ml), (see Depixol Injection Data Sheet), and the response and possible emergence of extrapyramidal symptoms observed over the following 5–10 days. During this period oral medication should be gradually withdrawn. This part of the treatment should normally be given in hospital.

Contra-indications, warnings, etc Depixol-Conc. Injection is not recommended for patients who do not tolerate oral neuroleptic drugs, or for those with Parkinsonism, severe arteriosclerosis, senile confusional states, or advanced renal, hepatic or cardiovascular disease. Depixol-Conc. should be avoided in pregnancy. However teratological studies in three animal species have failed to reveal any specific effect of flupenthixol or its decanoate on foetal anatomy. Therefore, it is reasonable, particularly after the first trimester, to persevere with treatment in previously unrecognised pregnancy if psychiatric indications outweigh the theoretical hazard of foetal malformation.

Adverse reactions: The commonest side-effect is the appearance of extrapyramidal symptoms, both hypokinetic and hyperkinetic. When these appear they generally do so one to three days after injection and last for about five days. The incidence seems to be greater after the first few injections and to diminish thereafter. The incidence and severity of extrapyramidal side-effects is no greater with flupenthixol doses in the higher range (for which Depixol-Conc. Injection is appropriate) than with lower doses (for which Depixol standard injection solution is more appropriate) and routine anti-Parkinson drug treatment is not recommended. Tardive dyskinesia has been observed very occasionally: these rare cases have been almost exclusively in patients taking concurrent anticholinergic anti-Parkinson drugs. No specific clinical incompatibilities with other drugs or food have been encountered. However on theoretical pharmacodynamic grounds it may be wise to allow an interval of not less than seven days between completion of MAOI treatment and the initiation of Depixol therapy.

Occasional depressive reactions have been reported after administration of Depixol-Conc. Injection, but they appear to be less frequent than after other neuroleptics. Occasional local reactions such as erythema, swelling or tender fibrous nodules have been reported. Amenorrhoea has occurred in patients receiving high doses. Galactorrhoea is a rare side-effect of the drug which may

be severe enough to warrant reduction of dosage or withdrawal of neuroleptic treatment. Blood dyscrasias have been observed on rare occasions in patients treated with high-dose neuroleptics. It is, therefore, prudent to carry out periodical blood counts in patients receiving high doses of Depixol-Conc. Injection. No anticholinergic, hepatic, renal or cardiovascular (e.g. hypotension) side-effects have been confirmed nor have flupenthixol-induced photosensitivity or alterations in the cornea or lens been reported.

Overdosage: Overdosage should be treated:

1. By anticholinergic anti-Parkinson drugs if extrapyramidal symptoms occur.

2. By sedation (with benzodiazepines) in the unlikely event of agitation or excitement.

3. By noradrenaline in saline intravenous drip if the patient is in shock. Otherwise observation and symptomatic management should be adequate.

Pharmaceutical precautions Store at room temperature and protect from light. Under these conditions the preparation has a shelf life of two years from date of manufacture.

In accordance with normal practice partially used vials should be discarded at the end of each session.

Legal category POM.

For use in hospitals and hospital clinics and from registered pharmacies on prescription only.

Package quantities Boxes of 10 × 100 mg (1 ml) ampoules.

Boxes of 1 × 5 ml vials.

Further information Nil.

Product licence number 0458/0015.

DEPIXOL* TABLETS 3 mg

Presentation Depixol Tablets 3 mg contain flupenthixol 3 mg as the dihydrochloride. The tablets are round, biconvex, yellow sugar-coated, with a diameter of about 9 mm. The Lundbeck logo is printed in black on one face.

Uses Pharmacology: Flupenthixol is a potent neuroleptic with a rapid onset of antipsychotic, alerting and anxiolytic effects. It is rapidly metabolised and excreted and is relatively short-acting. When sustained action is required, a depot intramuscular injection of Depixol Injection or Depixol-Conc. Injection in the form of flupenthixol decanoate will provide a therapeutic effect for two to four weeks (see Depixol Injection and Depixol Conc. Injection data sheets).

Indications: Depixol Tablets 3 mg are indicated in the treatment of schizophrenia and other psychoses. Its alerting effect makes Depixol particularly useful in patients who are withdrawn, apathetic, anergic or depressed, or in whom neuroleptics with a marked sedative effect cause fatigue or drowsiness.

Dosage and administration **Adults:** 1–3 tablets twice daily, to a maximum of 18 mg [6 tablets] per day. Doses should be reduced in patients with intercurrent disease.

Children: Until further clinical evidence is available it is recommended that this product should not be administered to children.

Contra-indications, warnings, etc Depixol Tablets should be used with caution in patients with Parkinson-

ism, severe arteriosclerosis, senile confusional states, or advanced renal, hepatic or cardiovascular disease. They are not recommended for excitable or overactive patients in doses below 6 mg daily since the activating effect may lead to exaggeration of these characteristics. Depixol should be avoided in pregnancy. However teratological studies in three animal species have failed to reveal any specific effect of flupenthixol on foetal anatomy. Therefore, it is reasonable, particularly after the first trimester, to persevere with treatment in previously unrecognised pregnancy if psychiatric indications outweigh the theoretical hazard of foetal malformation.

Adverse reactions: Extrapyramidal symptoms occur in approximately 25% of patients but are usually mild and controllable by dose reduction or concurrent anti-Parkinson (anticholinergic) drugs. Routine anti-Parkinson drug treatment is not recommended. At high dosage a sedative effect may occur in the occasional patient. No adverse interactions have been reported between Depixol Tablets and tricyclic antidepressants and no specific clinical incompatibilities with other drugs or food have been encountered. However on theoretical pharmacodynamic grounds it may be wise to allow an interval of not less than seven days between completion of MAOI treatment and the initiation of Depixol therapy. Amenorrhoea may occur in patients receiving high doses. Tardive dyskinesia and galactorrhoea are adverse effects of the general group of neuroleptic drugs; neither has been reported in patients treated with Depixol Tablets, but the theoretical hazard should be borne in mind.

Overdosage: Overdosage should be treated by gastric lavage.

Pharmaceutical precautions The tablets should be stored in their original container, protected from light and moisture. Under these conditions, the preparation has a shelf life of five years from date of manufacture.

Legal category POM.

Package quantities Bottles of 100 tablets of 3 mg.

Further information Nil.

Product licence number 0458/0013.

ESTRACYT* CAPSULES

Presentation Off-white gelatin capsules each containing 140 mg estramustine phosphate as the disodium salt.

Active ingredient: 140 mg Estramustine phosphate – oestra-1,3,5 (10)-triene-3,17 β -diol-3-bis-(2-chloroethyl) carbamate-17-disodium phosphate.

Uses *Pharmacology:* Estracyt is a chemical compound of oestradiol and normustine and has both oestrogenic and cytotoxic activity. Its oestrogenic effect is weaker than that of oestradiol and this is reflected by the lower incidence of gynaecomastia and other feminising side-effects in patients treated with Estracyt for prostatic carcinoma. Estracyt also has antioestrogenic activity in that it antagonises the uterotrophic effect of oestrone in juvenile mice, anti-gonadotrophic activity in that it causes atrophy of the testes and accessory sex organs in rats, and anti-androgenic activity in that it inhibits testosterone-induced growth of the ventral prostate of castrated animals.

Estracyt's cytotoxic activity is weaker than that of conventional alkylating agents. It is concentrated ten

times more efficiently than oestradiol in prostatic tissue and has a greater affinity for prostatic than for other tissue. Though active against experimental animal tumours (rat DMBA-induced mammary tumour and hepatoma AH130), Estracyt has weak general cytostatic effects and causes little or no marrow depression at conventional therapeutic dosage. It has no immunosuppressant effect.

Estracyt appears to lose its phosphate moiety in the gut, liver and in phosphatase-rich human tissue, and following breakage of the carbamate linkage the steroid and alkylating moieties are excreted independently. Absorption of Estracyt from the gut is about 75% complete.

Indications Carcinoma of the prostate, especially in cases unresponsive to, or relapsing after, treatment by conventional oestrogens (stilboestrol, polyoestradiol phosphate (Estradurin), etc) or by orchidectomy. The response rate to Estracyt in such oestrogen-resistant cases is about 30% to 50%.

Dosage and administration *Adults:* Dosage range may be from 1 to 10 capsules a day by mouth with meals. Standard starting dosage is 4 capsules a day, with later adjustment to between 3 and 6 according to response and gastrointestinal tolerance. One to 2 capsules a day may be adequate for maintenance therapy.

Patients unresponsive to, ceasing to respond to, or intolerant of conventional oestrogens, who may be candidates for treatment with Estracyt, should be given a daily dose of 4 Estracyt capsules initially. This dose should provide symptomatic relief of bone pain at least comparable to that conferred by standard doses of conventional oestrogens. Subsequent Estracyt dosage should be adjusted, in all categories of patient, according to objective and subjective response and drug tolerance.

Children: Adenocarcinoma of the prostate is almost unknown in young boys and no relevant clinical studies of Estracyt have been carried out. Estracyt should not be administered to children.

Contra-indications, warnings, etc Peptic ulceration, severe liver disease and severe cardiac disease.

Precautions: Caution should be exercised in administering Estracyt to patients with moderate to severe bone marrow depression.

Adverse reactions: Adverse effects which may be encountered in treatment are gastrointestinal upset (most commonly transient nausea, but occasionally vomiting, and rarely diarrhoea); rarely transient disturbance of liver function (discernible as elevation of serum transaminases or bilirubin); rarely thrombocytopenia below 100,000/mm³; gynaecomastia (seen in less than 5% of patients); cardiovascular (with an incidence of angina no greater than that encountered in patients treated with conventional oestrogens, but including rare drug-related deaths from myocardial infarction); and allergy (manifest as a rash and/or fever).

Overdosage: There is no specific antidote. In the event of dangerously low levels of red cell, white cell or platelet counts; cross-matched whole blood should be given as necessary. It may also be advisable to monitor liver function.

Pharmaceutical precautions Store in a cold place (2°C to 8°C). The preparation has a shelf life of three years from the date of manufacture.

Legal category POM.

For use in hospitals and hospital clinics, and supplied to retail pharmacies for dispensing prescriptions for patients whose treatment has been initiated in hospital practice. Estracyt capsules are available on prescription only.

Package quantities Bottles of 100 capsules each containing 140 mg estramustine phosphate as the sodium salt.

Further information Nil.

Product licence number 0458/0016.

ESTRADURIN* INJECTION

Presentation Estradurin Injection contains 40 mg or 80 mg polyoestradiol phosphate per vial, for reconstitution with water for injection.

Estradurin 40 mg vial:

Polyoestradiol phosphate	40 mg
Mepivacaine	5 mg
Nicotinamide	25 mg
Phenylmercuric nitrate	0.02 mg

Estradurin 80 mg vial:

Polyoestradiol phosphate	80 mg
Mepivacaine	5 mg
Nicotinamide	40 mg
Phenylmercuric nitrate	0.02 mg

Uses Pharmacology: Estradurin is a water-soluble polymer in which molecules of oestradiol-17 β alternate with phosphate groups. After intramuscular injection it acts primarily as a long-acting form of oestradiol, but it also has an inhibitory action on acid and alkaline phosphatases.

The prolonged action of Estradurin is attributed to the slow progressive breakdown of the polymer by phosphatases *in vivo*. Since Estradurin has an inhibiting effect on phosphatases this breakdown is very slow, providing sustained oestrogen activity for up to four weeks after a single injection.

Indications: The treatment of oestrogen-responsive carcinoma of the prostate, particularly in men suspected of unreliability in the taking of conventional oral oestrogen.

Dosage and administration Adults: The recommended starting dose is 80–160 mg every four weeks for two to three months. Thereafter the dose may be reduced, in accordance with the patient's clinical and biochemical progress, to 40–80 mg every four weeks.

NB. Estradurin must be administered by *deep* intramuscular injection.

Children: Estradurin should not be administered to children.

Contra-indications, warnings, etc There are no contra-indications for Estradurin, but it should be used with caution in patients with serious liver impairment or thromboembolic cardiovascular disease.

Adverse reactions: Certain characteristic oestrogenic side-effects occur (e.g. gynaecomastia, feminisation), but their incidence and severity are considerably less than those encountered in patients receiving conventional stilboestrol therapy. Gastrointestinal disturbances have not been reported during treatment with Estradurin.

Overdosage: There is no specific antidote. Treatment should be purely symptomatic.

Pharmaceutical precautions Store at room temperature.

The product has a shelf life of five years from the date of manufacture. Estradurin solution is prepared by adding 2 ml water for injection to the vial and shaking until solution is complete.

It is recommended that solutions of Estradurin be prepared immediately before use.

Legal category POM.

Package quantities

10 × 40 mg vials: (with 10 × 2 ml ampoules water for injection).

10 × 80 mg vials: (with 10 × 2 ml ampoules water for injection).

Further information Mepivacaine, a local anaesthetic, is included to minimise discomfort at the site of injection.

Nicotinamide is included to enhance solubility of the polymer.

Product licence numbers

Estradurin 40 mg 0458/5000

Estradurin 80 mg 0458/5001

FLUANXOL* TABLETS 0.5 mg

Presentation Fluanxol Tablets 0.5 mg contain flupenthixol 0.5 mg as the dihydrochloride. The tablets are round, biconvex, red, sugar-coated, with a diameter of 6 mm. The Lundbeck logo is printed in black on one face.

Uses Pharmacology: Flupenthixol is a dopamine receptor blocker (perhaps principally pre-synaptic), with a rapid onset of both antidepressant and anxiolytic effects.

Indications: Fluanxol Tablets 0.5 mg are indicated in the treatment of depression (with or without anxiety) and in psychiatric conditions associated with fatigue, apathy, despondency, lack of initiative, depression or inertia. Patients with obsessive-compulsive neuroses may also benefit.

Patients often respond to Fluanxol within two to three days. If no effect has been observed within one week at maximum dosage the drug should be withdrawn.

Dosage and administration Adults: Two 0.5 mg tablets in the morning and two in the afternoon. The total daily dose may be increased by increments of 0.5 mg to a maximum of 3 mg. A maintenance dose of 0.5 mg b.d. may be appropriate after an adequate response has been noted. In view of the activating properties of Fluanxol it is advisable to give the last dose of the day no later than 4 p.m.

Children: Until further clinical evidence is available it is recommended that this product should not be administered to children.

Contra-indications, warnings, etc Fluanxol should be used with caution in patients with Parkinsonism, severe arteriosclerosis, senile confusional states, or advanced renal, hepatic or cardiovascular disease. It is not recommended for excitable or overactive patients since its activating effect may lead to exaggeration of these characteristics. Fluanxol should be avoided in pregnancy, particularly during the first trimester.

Adverse reactions: Restlessness or insomnia have occasionally been noted at the recommended doses. Extrapyramidal symptoms are rare at this dosage. A sedative effect may paradoxically occur in the occasional patient.

Overdosage: Overdosage should be treated by gastric lavage.

Pharmaceutical precautions The tablets should be stored in their original container, protected from light and moisture. Under these conditions the preparation has a shelf life of five years from date of manufacture.

Legal category POM.

Package quantities Bottles of 100 tablets of 0.5 mg.

Further information In the treatment of depressed patients (with or without anxiety) it is reassuring that the drug does not give rise to habituation and that abstinence symptoms have not been observed after discontinuation. Another advantage of Fluanxol, in view of the great suicide risk in the depressed patient, is its high therapeutic index. Anti-Parkinsonian medication should be administered only if extrapyramidal symptoms develop. No adverse interactions have been reported between Fluanxol and tricyclic antidepressants or benzodiazepines.

Product licence number 0458/0011.

MEDICOAL®

Presentation Medicoal is a granular formulation of activated charcoal that effervesces in water to form a suspension. The suspension is tasteless and suitable for conventional oral administration or for gastric lavage.

Active ingredient: Each sachet of Medicoal contains 5 g of activated charcoal.

Uses Emergency treatment of acute poisoning or drug overdosage. Medicoal has high adsorptive capacity for a wide range of plant and inorganic poisons and most drugs used in medicine, including those most commonly taken in accidental or deliberate overdosage, e.g. salicylates, barbiturates and tricyclic anti-depressants.

Indications: In the alimentary tract, Medicoal adsorbs (and thus reduces or prevents systemic absorption of) most inorganic and organic compounds of low or high molecular weight. It is indicated, preferably after emptying of the stomach contents by emesis or gastric wash-out, in cases of poisoning or drug overdosage with:

Vegetable poisons

aconite	hemlock	quinine
belladonna	ipecacuanha	salicylates
cocaine	morphine	strychnine
delphinine	muscarine	veratrine
digitalis	nicotine	
elaterin	opium	

Drugs

amphetamines	chlorpromazine	phenobarbital
antipyrine	(and related	tone (and
aspirin	phenothiazines)	other
atropine	dextroamphetamine	barbiturates)
chlorpheniramine	digoxin	phenytoin
(and related anti-histamines)	nortriptyline (and other tricyclic anti-depressants)	propoxyphene
		penicillin

Inorganic compounds and elements

antimony	silver	mercuric chloride
arsenic	tin	
iodine	titanium	potassium permanganate
phosphorus		

Dosage and administration

1. **Conventional oral administration:** Medicoal should be given orally as a suspension in water (one sachet in about 100 ml) as soon as possible after ingestion or suspected ingestion of the potential poison, or after induced emesis or stomach wash-out. The rate and degree of adsorption to activated charcoal varies from substance to substance according to ionisation, pH and molecular size. Many drugs require more than double their dose of charcoal for complete adsorption.

When the dose of drug or poison is known the standard dose of Medicoal is 5–10 times that dose. This is given as an initial dose of one or two sachets, followed by a similar dose 20 minutes later, repeated at 15–20 minute intervals until the appropriate total dose has been given. Higher or more frequent dosage of Medicoal may induce vomiting of the suspension. When the dose of ingested drug or poison is unknown a similar treatment schedule is followed to a maximum Medicoal dose of 10 sachets (50 g activated charcoal).

Medicoal may be effective even several hours after ingestion of the drug or poison in cases where the compound ingested is:

- an anticholinergic, slowing gastric emptying.
- absorbed and excreted in the bile; or where fear or nausea inhibits gastrointestinal motility.

2. **Gastric lavage:** Medicoal is added to the irrigation water in a dose of 30–50 g in $\frac{1}{2}$ –1 litre. Subsequent conventional oral dosage of Medicoal is governed by the proportion of dose or suspected dose of drug or poison ingested that is retrieved by stomach wash-out.

Children: The dose of Medicoal is related more to the dose or suspected dose of poison or drug than to the age, weight or surface area of the child, but the volume of the suspension at each administration may need to be reduced.

Contra-indications, warnings, etc

Contra-indications: Medicoal is valueless and contra-indicated in poisoning by strong acids or alkalis. Its adsorptive capacity for the following poisons and drugs is too low to be useful and other more specific forms of treatment should be used:

ferrous sulphate (and other iron salts)	cyanides
malathion	tolbutamide (and other sulphonylureas)
DDT	

Warnings: Activated charcoal should not be used simultaneously with systemically acting oral emetics such as ipecacuanha, since it adsorbs the drug, rendering it unavailable for systemic absorption and emetic activity. If an emetic is required it should be used to induce vomiting before giving Medicoal.

Medicoal is appropriate for the treatment of paracetamol poisoning, either alone or in conjunction with parenteral antidotes such as N-acetylcysteine or cysteamine. However, should a specific oral antidote such as methionine be used, Medicoal is contra-indicated since it will adsorb methionine in the gastrointestinal tract.

Precautions: Although the adsorption of dietary factors such as vitamins and minerals by Medicoal is of no consequence in the treatment of acute poisoning, it should be remembered that concurrent medication, for example for shock or associated infection, should be given parenterally since orally administered drugs may be partly or totally adsorbed and retained in the gut.

Adverse effects: No adverse effects are attributable to activated charcoal, but the release of carbon dioxide from the effervescent suspension may cause belching or vomiting of the dose administered if this is excessive.

Pharmaceutical precautions Medicoal should remain sealed in the sachets until required. The effervescent and dispersive properties of the granules are adversely affected by moisture. The product has a shelf life of five years from the date of manufacture.

Legal category P.

Package quantities Cartons of 5 and 30 sachets, each containing activated charcoal 5 g, as granules.

Further information Care should be exercised in the preparation and administration of Medical Suspension, since it may stain if spilt on clothing.

Product licence number 0458/0019.

*Trade Mark

NICORETTE* ▼

Presentation Square pieces of chewing gum containing 2 mg or 4 mg nicotine.

Active ingredient: 2 mg or 4 mg nicotine as the resin in a chewing gum base.

Uses Nicotine replacement. When Nicorette is chewed, nicotine is slowly released into the mouth and is absorbed through the buccal mucosa. A proportion, by the swallowing of nicotine-containing saliva, reaches the stomach and intestine and any nicotine absorbed by this route is inactivated.

Indications: Nicorette is intended to help smokers who want to give up smoking, but experience great difficulty in doing so because of their nicotine dependence.

Dosage and administration *Adults:* The strength of gum to be used depends upon the smoking habits of the individual. It is recommended that patients beginning treatment should always start with Nicorette 2 mg to determine its acceptability. If more than 15 × 2 mg Nicorette per day are required, transfer to the 4 mg gum may be considered.

Nicorette should be chewed slowly, when there is an urge to smoke up to a maximum of 15 × 4 mg pieces per day; however the patient's individual need may be considerably less than this number. Most patients require about 10 pieces of 2 mg per day initially.

All available nicotine is released from a piece of gum after about 30 minutes chewing. Since effective absorption is through the buccal mucosa, the rate of chewing should be adjusted to minimise the swallowing and inactivation of nicotine contained in saliva.

After 3 months ad libitum dosage Nicorette should be gradually withdrawn.

Children: Not to be administered to children.

Contra-indications, warnings, etc Nicotine in any form is contra-indicated in pregnancy. Smokers who wear dentures may experience difficulty in chewing

Nicorette. Dependence is a rare side-effect and is both less harmful and easier to break than smoking dependence.

Precautions:

1. Swallowed nicotine may exacerbate symptoms in patients suffering from gastritis or peptic ulcer.

2. Nicotine's cardiovascular effects may be deleterious to patients with angina or a history of coronary artery disease. Nicorette presents a lesser hazard, however, than smoking which introduces carbon monoxide as an additional toxic factor.

Adverse effects: Nicorette in the recommended dose has not been found to cause any serious adverse effects. Nicotine from the gum may sometimes cause a slight irritation of the throat at the start of treatment, and may also cause increased salivation. Excessive swallowing of dissolved nicotine may, at first, cause hiccupping. Those with a tendency to indigestion may suffer initially from minor degrees of indigestion or heartburn if the 4 mg gum is used. Slower chewing and the use of the 2 mg gum (if necessary more frequently) will usually overcome this problem.

Excessive consumption of Nicorette by patients who have not been in the habit of inhaling tobacco smoke could possibly lead to nausea, faintness or headaches (as may be experienced by such patients if tobacco smoke is inhaled).

Overdosage: Overdosage of Nicorette can occur only if many pieces are chewed simultaneously. The fatal acute dose of nicotine in man is probably about 60 mg. Risk of overdosage with Nicorette is, however, small since nausea or vomiting usually occurs at an early stage.

Risk of poisoning by swallowing the gum is also small, since the release of nicotine from the gum is slow. Therefore very little nicotine is absorbed from the stomach or intestine and any that is will be inactivated in the liver. Nicotine is excreted in acid urine four times as rapidly as in alkaline urine.

Treatment of overdosage: In the event of overdosage vomiting should be induced with syrup of ipecacuanha or gastric lavage carried out (wide bore tube). A suspension of activated charcoal (Medicoal) should then be passed through the tube and left in the stomach. Artificial respiration with oxygen should be instituted if needed and continued for as long as necessary. Other therapy, including treatment of shock, is purely symptomatic.

Pharmaceutical precautions No special storage conditions are necessary. The preparation has a shelf life at room temperature of 2 years from the date of manufacture.

Legal category POM.

Package quantities Package of 105 pieces, in the form of 7 blister-packed strips each containing 15 pieces (2 mg or 4 mg).

Further information Nicorette should be chewed slowly. Sufficient nicotine may be released from the gum by chewing intermittently and leaving the gum under the lip or in the corner of the mouth between chews.

Nicorette is sugar-free.

Product licence numbers

2 mg: 0458/0020

4 mg: 0458/0021

*Trade Mark

Martindale Pharmaceuticals Limited

Chesham House
Chesham Close
Romford, Essex RM1 4JX



CUTISAN* OINTMENT CUTISAN* POWDER CUTISAN* SOLUTION

Presentation

1. White, water-miscible ointment containing triclocarban 2% w/w.
2. White dusting-powder containing triclocarban 1% w/w.
3. Clear, water-miscible solution containing triclocarban 1% w/w.

Uses Antibacterial for external use.

Indications: Acne, impetigo, boils, pyodermitis, infected wounds or burns, varicose ulcers, infected eczema, infected contact dermatitis, etc.

Dosage and administration For external use only.

Cutisan Ointment: Apply to affected area and massage gently.

Cutisan Powder: Sprinkle liberally on the affected area two or three times a day.

Cutisan Solution: Spread over the affected area with the help of the flattened end of the dropper/applicator.

Note: Cutisan should be applied well beyond the infected area – to prevent any spread of the infection.

Contra-indications, warnings, etc

Contra-indications: None.

Side-effects: Break-down products of triclocarban, formed from it by heating (e.g. by boiling soap solutions containing triclocarban or by autoclaving garments previously rinsed in a triclocarban solution), have been responsible for occasional methaemoglobinemia in infants.

Pharmaceutical requirements No special precautions.

Legal category GSL.

Package quantities *Cutisan Ointment:* Tubes of 30 g.

Cutisan Powder: Sprinkler drums of 80 g.

Cutisan Solution: Bottles with dropper/applicator of 45 ml.

Further information Cutisan Ointment is in general more suitable for less inflamed and less irritating skin lesions.

Cutisan is non-staining.

Product licence numbers

Cutisan Ointment 0123/5004

Cutisan Powder 0123/5005

Cutisan Solution 0123/5006

E.S.T.P.*

Ether Soluble Tar Paste

Presentation E.S.T.P. is a light tan-coloured, non

staining and emollient Ether Soluble Tar Paste containing:

Ether soluble tar distillate	1.5%
Zinc oxide BP	14.0%
Starch BP (Maize)	12.0%
Emollient base to	100%

Uses E.S.T.P. is indicated for the treatment of mild to moderate Eczema and Psoriasis and other skin conditions.

Dosage and administration Apply to the affected areas three or four times daily or at the discretion of the Physician

Contra-indications, warnings, etc Known sensitivity to tar extracts.

Pharmaceutical precautions Protect from heat.

Legal category P.

Package quantities E.S.T.P. is available in jars of 50g and 500g.

Further information Nil.

Product licence number 0542/5006

INOLAXINE* GRANULES

Presentation Orange-coloured granules containing Sterculia BPC 98%.

Uses Bulk-promoting agent, exerting its effects mainly by a hydrophilic action: it increases the bulk of the stools, alters their consistency, shortens their transit time and thus militates against the rise in intraluminal colonic pressure that is believed in the long term to be responsible for diverticular disease of the colon and possibly other disorders. Inolaxine is not absorbed and has no local or systemic action.

Indications: Diverticular disease of the colon in those patients not suited or improved by dietary changes.

Irritable bowel syndrome; ulcerative colitis and the spastic colon syndrome when watery stools are present; colostomy or ileostomy, to improve the consistency of the effluent.

Haemorrhoids – to treat or prevent any associated constipation, and after treatment to ensure smooth bowel action; similarly before and after rectal surgical procedures.

Anal fissure – prevention of recurrence.

Simple constipation associated with pregnancy, lack of bulk in the diet or colonic atony.

Bed-ridden or post-operative patients, to maintain bowel regularity and prevent straining at stool.

Dosage and administration *Adults:* 1–2 heaped teaspoonsful once or twice a day (maximum: 4 heaped teaspoonsful daily).

Children: Half the adult dose (maximum: 2 heaped

teaspoonful daily). It is best to start with 1 heaped teaspoonful a day ($\frac{1}{2}$ teaspoonful for children) and to gradually increase the dose until the desired effect on bowel action is secured. The dose should be swallowed (without chewing) with a drink of water, fruit juice, etc. or if preferred stirred into the drink and swallowed. If there is difficulty in swallowing solids the granules may be stirred into a $\frac{1}{4}$ glass of water, left for $\frac{1}{2}$ –1 hour and the resulting jelly eaten with a spoon.

Contra-indications, warnings, etc

Contra-indications: None.

Side-effects: Occasional flatulence and mild abdominal discomfort, which may be due to insufficient fluid intake.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantity 175 g.

Further information Inolaxine Granules do not contain any added sugar.

Product licence number 0123/0009.

MEDILAVE* GEL

Presentation Pale buff-coloured gel. Contains Benzocaine PhEur. 1.0% and Cetylpyridinium Chloride BP 0.01% in a specially formulated water-immiscible protective base.

Uses For the relief of pain from abrasions and ulcers of the gums, palate, cheek, tongue and lips, including soreness due to teething.

Dosage and administration Cover the affected area 3 to 4 times daily with a thin film as required, filling the depression in the ulcer, particularly before meals. Do not rub in.

Contra-indications, warnings, etc Not to be used in infants under 6 months of age. In cases of dental abrasion, care should be taken to remove the underlying cause of the lesion. Consult doctor or dentist if symptoms persist. Some individuals may be hypersensitive to Benzocaine. If so, cease treatment immediately.

Pharmaceutical precautions No special precautions required.

Legal category P.

Package quantities Tube of 10 g.

Further information Nil.

Product licence number 0156/0014.

MEDISED* SUSPENSION

Presentation Medised is a pleasant tasting, blackcurrant flavoured suspension containing 120 mg Paracetamol PhEur and 2.5 mg Promethazine Hydrochloride PhEur in each 5 ml.

Uses For the treatment of mild to moderate pain, including headache, toothache, sore throat, aches and pains. For the symptomatic relief of influenza, feverishness and feverish colds and chicken pox. For the reduction of nasal irritation and watery discharge.

Dosage and administration Medised Suspension

should be administered up to 4 times a day in the following doses

Children 3 months to 1 year: 5 ml.

1 year to 6 years: 10 ml.

6 years to 12 years: 20 ml.

Dosages should not be repeated more frequently than 4 hour intervals and no more than 4 doses should be taken in any 24 hour period. Not to be given to children under 3 months old except on the advice of a doctor.

If symptoms persist, dosage should not be continued for more than 3 days without consulting a doctor.

Contra-indications, warnings, etc Reports of adverse reactions to therapeutic doses of paracetamol are rare. However, overdose can be dangerous. A patient who takes an overdose may not show any signs of toxicity for the first three days, but may then succumb to liver damage. As little as 15 g of paracetamol has proved fatal in an adult. Medised will enhance the action of any sedative, hypnotic or other central nervous depressant. The consumption of alcohol should be avoided. This preparation may cause drowsiness – do not drive or operate machinery if affected. In the event of overdose, gastric lavage should be carried out. It has been found that the administration of 30–50 g activated charcoal, either alone or following emesis, will reduce the absorption of paracetamol. If necessary, haemodialysis should be considered along with other steps known to be effective in the treatment of paracetamol toxicity.

Pharmaceutical precautions Protect from light. Shake the bottle well.

Legal category P.

Package quantity Bottle of 100 ml.

Further information Nil.

Product licence number 0156/0013.

MILLOPHYLINE* TABLETS

MILLOPHYLINE* AMPOULES

MILLOPHYLINE* SUPPOSITORIES (ADULT)

MILLOPHYLINE* SUPPOSITORIES (PAEDIATRIC)

Presentation Active ingredient: Etamiphylline camsylate.

1. Red, sugar-coated tablets containing 100 mg.
2. Ampoules containing 700 mg/5 ml Water for injections.
3. Suppositories containing 500 mg.
4. Suppositories containing 200 mg.

Uses Millophylline has the following effects:

1. Relaxes smooth muscle, in particular of the bronchi, and of the coronary arteries.
2. Increases the amplitude of ventricular contraction, thus increasing cardiac output – without increasing the heart rate.
3. Increases the rate and depth of respiration by a stimulant action on the respiratory centre, being two to three times more effective in this respect than theophylline.
4. Miscellaneous: Mild diuretic action, some central stimulant action.

Indications: Bronchial asthma – prevention and treatment. Bronchospasm in chronic bronchitis, etc. Cheyne-Stokes respiration. Cardiac asthma, due to left ventricular failure. Congestive cardiac failure. Angina – prevention.

Coronary thrombosis – as part of the management. Status asthmaticus. Laryngeal stridor in children.

In various of the conditions named Millophyline is used as only one element in the treatment, or else as a substitute or alternative when remedies with a different mode of action have been tried and have failed.

Dosage and administration *Adults: Tablets – oral:* Normally 1–3 tablets three or four times daily after food. *Suppositories – Rectal (500 mg):* 1–2 daily. The insertion of a suppository at bedtime provides night-time prophylaxis against, for instance, asthmatic attacks, either bronchial or cardiac in origin.

Ampoules – Intramuscularly: 1 ampoule three to four times daily.

Intravenously: 2.5 ml (half the contents of one ampoule) diluted with 7.5 ml of water for injections, and injected slowly: to be repeated as required.

Children: Tablets – Oral: The doses indicated in the table below may be given up to three times a day after food.

Suppositories – Rectal (200 mg): The whole or a portion of a suppository to be inserted once or twice a day according to the table of individual doses given.

Ampoules – Intravenously or intramuscularly: A dilute solution, prepared as described for adults, to be injected (slowly in the case of intravenous injection), and of such a volume that it provides the quantity of Millophyline indicated in the table below.

	0–1 year	1–5 years	6–12 years
<i>Tablets</i>	–	100 mg (1 tablet)	100–200 mg (1–2 tablets)
<i>Suppositories</i>	–	50–100 mg	100–200 mg
<i>Intravenously, or intra- muscularly</i>	10–25 mg	25–50 mg	50–100 mg

Contra-indications, warnings, etc *Contra-indications:* The suppository form of administration should not be used when an inflammatory anal condition is present.

Side-effects: Occasional insomnia due to central stimulation, which is readily countered by the use of a suitable hypnotic. The gastric upset (from oral intake) and pain (from tissue irritation after parenteral administration) produced by theophylline and various of its derivatives are commonly absent in the case of Millophyline.

Intravenous administration should be performed slowly.

Overdosage: Treat as for theophylline derivatives. Treat symptomatically. Gastric lavage may be attempted for oral preparations, or enema for suppositories. Maintain electrolyte and fluid balance with intravenous fluids. Sedatives and oxygen may be required.

Pharmaceutical precautions None.

Legal category Tablets P.
Ampoules POM.
Suppositories P.

Package quantities

Tablets: 100 and 500.

Ampoules: Boxes of 6.

Suppositories (adult and paediatric): Boxes of 10.

Further information Millophyline has all the effects of theophylline but, unlike that substance, is soluble and

relatively non-irritant to the stomach and to the tissues when injected.

Product licence numbers

Millophyline Tablets	0123/5012
Millophyline Ampoules	0123/5009
Millophyline Suppositories (Adult)	0123/5010
Millophyline Suppositories (Paediatric)	0123/5011

MITOMYCIN C KYOWA*

Presentation Purple crystalline powder for intravenous injection containing Mitomycin C Kyowa 2 mg with 48 mg Sodium Chloride and Mitomycin C Kyowa 10 mg with 240 mg Sodium Chloride for dissolving in water for injections using the volume recommended for each strength.

Uses *Action:* Mitomycin C Kyowa is an antitumour antibiotic that is activated in the tissues to an alkylating agent which disrupts deoxyribonucleic acid (DNA) in cancer cells by forming a complex with DNA and, also acts by inhibiting division of cancer cells by interfering with the biosynthesis of DNA. In vivo, Mitomycin C Kyowa is rapidly cleared from the serum after intravenous administration. The time required to reduce the serum concentration by 50% after a 30 mg bolus injection is 17 minutes. After injection of 30 mg, 20 mg or 10 mg i.v., the maximal serum concentrations were 2.4 mcg/ml, 1.7 mcg/ml and 0.52 mcg/ml respectively. Clearance is affected primarily by metabolism in the liver, but metabolism occurs in other tissues as well. The rate of clearance is inversely proportional to the maximal serum concentration because, it is thought, of saturation of the degradative pathways. Approximately 10% of a dose of Mitomycin C Kyowa is excreted unchanged in the urine. Since metabolic pathways are saturated at relatively low doses, the percentage dose excreted in the urine increases with increasing the dose. In children, excretion of intravenously administered Mitomycin C Kyowa is similar to that in adults.

Indications: Antimitotic and Cytotoxic. Mitomycin C Kyowa is recommended for certain types of cancer, either in combination with other drugs or after primary therapy has failed. In particular, Mitomycin C Kyowa has been successfully used to improve subjective and objective symptoms in a wide range of neoplastic conditions including carcinomas of the stomach, pancreas, breast and uterus; adenocarcinoma of the lung; peritonitis carcinomatosa; colonic, bladder, rectal and skin cancer. In addition, Mitomycin C Kyowa may also be of some value in sarcomas, hepatic cancer, acute and chronic leukaemias and Hodgkin's disease.

Dosage and administration For systemic administration, Mitomycin C Kyowa should be given intravenously using great care to avoid extravasation. The usual dosage is in the range 4–10 mg (0.06–0.15 mg/kg) at 1–6 weekly intervals, depending on whether other drugs are given in combination and on bone marrow recovery. A total dosage ranging from 40–80 mg (0.58–1.2 mg/kg) is often required for satisfactory response to Mitomycin C Kyowa when used singly and in combination. A higher dosage may be used when Mitomycin C Kyowa is used alone.

For reconstitution, the contents of the 2 mg vial should be dissolved in 5 ml water for injections, or 20% dextrose solution, and those of the 10 mg vial in 10–20 ml of the same solvents and administered by intravenous injection.

The dose should be adjusted according to the age and condition of the patient.

For administration to specific tissues, Mitomycin C Kyowa can be given also into the pleural and peritoneal cavities, by the arterial route, directly into tumours.

Because of cumulative myelosuppression, patients should be fully re-evaluated after each course of Mitomycin C Kyowa and the dose reduced if the patient has experienced any toxic effects. Doses greater than 0.6 mg/kg have not been shown to be more effective and are more toxic than lower doses.

Treatment of superficial urinary bladder tumours: In the prevention of recurrent bladder tumours, the usual dose is the equivalent of 4–10 mg (0.06–0.15 mg/kg) potency of Mitomycin C Kyowa instilled into the bladder through a urethral catheter once or three times a week. In the treatment of bladder tumours, the usual dose is the equivalent of 10–40 mg (0.15–0.6 mg/kg) potency of Mitomycin C Kyowa instilled into the bladder either weekly or three times a week for a total of 20 doses. In either case, it should be dissolved in 20 ml–40 ml of water for injections before use. The dose should be adjusted in accordance with the age and condition of the patient.

Contra-indications, warnings, etc Mitomycin C Kyowa should be administered under the supervision of a physician experienced in cytotoxic cancer chemotherapy. Patients should be monitored closely during each course of treatment, paying particular attention to peripheral blood count including platelet count.

The principal toxicity of Mitomycin C Kyowa is bone marrow suppression, particularly thrombocytopenia and leucopenia. The nadir is usually around four weeks after treatment and toxicity is cumulative, with increasing risk after each course of treatment.

No repeat dosage should be given until leucocyte count has returned to 3.0×10^9 per l and platelet count to 90.0×10^9 per l. If disease progression continues after two courses of treatment, the drug should be stopped since the chances of response are then minimal.

Severe renal toxicity has occasionally been reported after treatment and renal function should be monitored before starting treatment and again after each course.

Nausea and vomiting are sometimes experienced immediately after treatment but these are usually mild and of short duration. Local ulceration and cellulitis may be caused by tissue extravasation during intravenous injection and utmost care should be taken in administration. In the event of extravasation following an intravenous injection of Mitomycin C Kyowa, it is recommended that 5 ml of Sodium Bicarbonate 8.4% solution is immediately infiltrated into the area where extravasation has occurred followed by an injection of 4 mg Dexamethasone. In addition, a systemic injection of 200 mg Vitamin B6 may be of some value in promoting the regrowth of tissues that have been damaged.

Mitomycin C Kyowa should not normally be administered to patients who are pregnant or to mothers who are breast feeding. Teratological changes have been noted in animal studies. The effect of Mitomycin C Kyowa on fertility is unknown. Mitomycin C Kyowa is contraindicated in patients who have demonstrated a hypersensitive or idiosyncratic reaction to it in the past.

The person administering the injection of Mitomycin C Kyowa should not allow the solution to come into contact with his or her skin.

Pharmaceutical precautions Store below 30°C.

Protect from light. Mitomycin C Kyowa remains stable for four years after manufacture at room temperature. After dissolving, it is preferable to use the solution within six hours. If it is necessary to store the solution, it should be kept at 4°C in the dark. If added to infusion fluids, the resultant solution should be used immediately.

Legal category POM.

Package quantities 2 mg and 10 mg vials for intravenous injection.

Further information Mitomycin C Kyowa vials are available to Hospitals only.

Product licence number 0123/5018

PARDALE* TABLETS

Presentation White bevelled-edge tablets, 11 mm diameter, DPL device on one side, breakline on the other.

Each tablet contains:

Paracetamol PhEur	400 mg
Codeine Phosphate PhEur	9 mg
Caffeine Monohydrate PhEur	10 mg

Uses Analgesic for the treatment of mild to moderate pain, including headache, migraine, neuralgia, toothache, sore throat, period pains, aches and pains. Symptomatic relief of rheumatic pain, influenza, feverishness and feverish colds.

Dosage and administration One or Two tablets, 3 or 4 times a day at no more than 4-hourly intervals. No more than 4 doses should be taken in a 24 hour period.

Not recommended for children.

Contra-indications, warnings, etc An overdose of paracetamol may cause hepatic necrosis. The codeine component may cause mild constipation.

Overdosage: In cases of overdose gastric lavage should be carried out. Administration of 30–50 g of activated charcoal may reduce the absorption of paracetamol. If necessary, haemodialysis should be carried out and other supportive measures taken which are known to be effective in the treatment of paracetamol toxicity.

Pharmaceutical precautions No special requirements.

Legal category P.

Package quantities Containers of 100 and 500 tablets.

Further information Nil.

Product licence number 0123/5015.

THEOSOL* SUPPOSITORIES

Presentation Cream coloured, torpedo-shaped suppositories containing 300 mg Anhydrous Theophylline PhEur.

Uses Theophylline relaxes smooth muscle and relieves bronchial spasm. Theosol suppositories are used in the treatment of bronchial asthma, bronchitis and associated conditions where bronchial spasm is present.

Dosage and administration **Adults:** One or Two suppositories daily, administered rectally.

Contra-indications, warnings, etc *Children:* Not to be used unless directed by a physician.

Theophylline stimulates the myocardium, reduces venous pressure and leads to an increase in cardiac output. Theosol should therefore be used with caution in patients suffering from cardiac disease. Bronchodilator effects may be enhanced by sympathomimetics and other xanthines.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities Pack of 12.

Further information Theosol suppositories have been designed to provide a stable theophylline preparation, giving a predictable dose response, which does not always occur with traditional products.

Product licence number 0156/0012.

**Trade Mark*

May & Baker Limited

Dagenham

Essex RM10 7XS

**M&B May & Baker**

ANTHISAN®

Presentation Anthisan is presented as:

Dark green, sugar-coated tablets containing 50 mg mepyramine maleate and marked 'Anthisan 50' in ivory print.

Uses Anthisan is a potent, rapidly acting antihistamine agent; it also possesses antipruritic properties and a local analgesic action. It is indicated in the treatment of allergic, anaphylactic and sensitisation reactions.

Dosage and administration *Adults – orally:* 100 mg three times daily, increased by steps of 50–100 mg daily up to a maximum of 1.0 g daily.

Children – orally: Up to 3 years, 12.5–25 mg three or four times daily.

From 3 to 7 years, 25–50 mg three or four times daily.

From 7 to 14 years, 25–75 mg three or four times daily.

Contra-indications, warnings, etc Anthisan may cause drowsiness and patients should not drive or operate machinery until the effect has been ascertained. Alcoholic drinks should be avoided.

Embryopathic effects have not been recorded but as with all medicines, Anthisan should not be given during pregnancy or lactation unless the physician considers it essential.

Side-effects: Drowsiness or fatigue may occur soon after the beginning of treatment, but this tends to disappear after a few days. Gastric upset may be avoided by ensuring that Anthisan is taken with food or a well sweetened drink. Dizziness or dry mouth occurs infrequently.

Treatment of overdosage: In the event of overdosage, vomiting should be induced by pharyngeal stimulation or with an emetic, followed by gastric lavage with warm sodium bicarbonate solution. Stimuli liable to provoke convulsions should be avoided, but if this complication should occur intramuscular paraldehyde should be given; sedatives which are liable to increase respiratory depression should be avoided. Other measures such as artificial respiration and oxygen may also be required and an antibiotic can be given as a prophylactic against pneumonia.

Pharmaceutical precautions Protect from light.

Legal category P.

Package quantities Containers of 500 tablets.

Further information Nil.

Product licence number
Tablets 50 mg 0012/5099

ASCABIOL®

Presentation Ascabiol is a mildly perfumed white emulsion containing 25% benzyl benzoate.

Uses Ascabiol is an efficient acaricide and is used in the treatment of scabies. It is also indicated in the treatment of pediculosis.

Dosage and administration *Scabies:* After a hot bath and drying, Ascabiol is applied to the whole body except the head and face. If the application is thorough, one treatment should suffice, but the possibility of failure is lessened if a second application is made within five days of the first.

Alternatively, Ascabiol can be applied to the whole body, except the head and face, on three occasions at 12-hourly intervals. The patient has a hot bath 12 hours after the last application and changes to clean clothes and sheets.

Pediculosis: The affected region is coated with Ascabiol followed by a wash 24 hours later with soap and water. In severe cases this procedure may need to be repeated two or three times. An examination should always be made a week after the last treatment to confirm disinfection.

Ascabiol can be diluted with an equal quantity of water for older children and with three parts of water for babies.

Contra-indications, warnings, etc Ascabiol causes little skin irritation but may cause a slight transient burning sensation; it is also irritating to the eyes. The eyes should therefore be protected if it is applied to the scalp.

If this preparation is accidentally taken by mouth, treatment should consist of gastric lavage or the administration of an emetic. An anticonvulsant should be given if necessary, otherwise treatment is symptomatic.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Bottle of 200 ml.

Further information Nil.

Product licence number 0012/5104.

AVOMINE®

Presentation Avomine is presented as white tablets, each containing 25 mg promethazine theoclate, indented 'Avomine' on one face and with a break line on the reverse.

Uses Long-acting anti-emetic, indicated for prevention and treatment of nausea and vomiting: including motion sickness, postoperative vomiting particularly following

fenestration operation; and nausea and vomiting arising from other causes including drug-induced vomiting, and vomiting associated with gastro-enteritis. Vertigo due to Ménière's syndrome, labyrinthitis and other causes.

Dosage and administration *Motion sickness:* Adults: For prevention on long journeys: one 25 mg tablet each evening at bedtime, starting the day before setting out. The duration of action is such that a second dose in 24 hours is not often necessary.

For prevention of motion sickness on short journeys: one 25 mg tablet one or two hours before travelling or as soon after as possible.

Treatment of motion sickness: One 25 mg tablet as soon as possible and repeated the same evening followed by a third tablet on the following evening.

Nausea and vomiting due to other causes: Adults: One 25 mg tablet at night is often sufficient, but two or more of the 25 mg tablets, or more frequent administration twice or three times daily of one 25 mg tablet, may be necessary for some patients. It is not often necessary to give more than four of the 25 mg Avomine tablets in 24 hours.

Children: In the above indications children over 10 years of age may be given the lower adult doses described above. Children between 5 and 10 years may be given half the adult dose.

Contra-indications, warnings, etc There are no absolute contra-indications to the use of Avomine tablets.

Precautions: Avomine may enhance the effect of any sedative or other central nervous system depressant. Avoid alcoholic drinks.

Patients taking Avomine for the first time should not be in control of vehicles or machinery until it is established that they are not hypersensitive to the central effects of the drug and do not suffer from disorientation, dizziness or confusion.

In nausea and vomiting of unknown origin, it is essential to establish the diagnosis before giving an anti-emetic, to ensure that a serious underlying condition is not masked.

There is inadequate evidence of safety of the drug in human pregnancy, but it has been in wide use for many years without apparent ill consequence; animal studies having shown no hazard.

Side-effects: Drowsiness may occur in some cases. It is minimised by giving dosage at bedtime.

Dizziness is uncommon and confusion or disorientation is rare in the dosage recommended.

Treatment of overdose: Induce vomiting, but bear in mind that anti-emetic action may counteract the effect of emetic drugs if absorption has taken place. Wash out stomach with warm bicarbonate solution, leaving some to precipitate insoluble promethazine base. Nurse in quiet, darkened room avoiding stimuli. If agitation, hallucinations or convulsions occur, avoid long-acting sedatives or hypnotics, the effects of which tend to be enhanced by promethazine. Despite its closely related chemical structure, chlorpromazine has been suggested for the hallucinated and disturbed patient. Administration of oxygen plus carbon dioxide may be indicated for respiratory depression and the use of artificial respiration. To prevent pneumonia the use of an antibiotic may be considered.

Pharmaceutical precautions Protect from light.

Legal category P.

Package quantities Containers of 10 and 250 × 25 mg tablets.

Further information Nil.

Product licence number 0012/5253.

BANISTYL*

Presentation Banistyl is presented as white, uncoated tablets containing the equivalent of 20 mg dimethothiazine base (as mesylate), indented 'Banistyl 20' on one face and with a break line on the reverse.

Uses Antihistamine and antipruritic, with less sedative effect than other antihistamine phenothiazine derivatives.

Indicated in all allergic disorders and sensitisation reactions that respond to antihistamine therapy, including hay fever and other forms of nasal allergy, urticaria and other allergic skin conditions. Also indicated for symptomatic relief of pruritus associated with allergic skin conditions or arising from other causes.

Dosage and administration Adults: 20 mg three times daily initially. Increase up to a total of 120 mg daily divided in three doses if necessary.

Children: 6–12 years: 10 mg twice daily.

12–15 years: 20 mg two or three times daily.

Contra-indications, warnings, etc Patients starting their first course of Banistyl should not be in charge of vehicles or machinery for the first few days, until it is established that they are not hypersensitive to the central effects of the drug and do not suffer from excessive drowsiness or mental confusion or disorientation. Avoid alcoholic drink.

Though no embryopathic effects have been reported, it is a sound medical principle to avoid prescribing any drug during pregnancy or lactation.

Side-effects and reactions reported are somnolence, which is infrequent and usually slight, and tending to diminish after the initial period of treatment or can be controlled by reducing the dose, dry mouth, nausea, epigastric pain, vertigo, diarrhoea and mild headache.

In the event of overdose, there is no specific antidote, so that treatment is symptomatic after gastric lavage to remove any residual drug left in the stomach. Warm sodium bicarbonate solution is used for gastric lavage and some should be left in the stomach to precipitate the insoluble dimethothiazine base and delay absorption. Should convulsions occur paraldehyde can be given, but the greatest care must be exercised in administering sedatives which may be given for central nervous system stimulation, and oxygen may be indicated. The administration of penicillin as a prophylactic against pneumonia may be considered advisable.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Containers of 50 × 20 mg tablets.

Further information Nil.

Product licence number 0012/5105.

BREVIDIL* E

Approved name: Suxethonium Bromide

Presentation Brevidil E is presented as an off-white crystalline powder for extemporaneous preparation of intravenous injections by the addition of appropriate volumes of Water for Injections BP.

Uses Brevidil E is an ultra-short-acting muscle relaxant of the depolarising type and is particularly indicated in electroconvulsive therapy where the ultra-short duration of its action and the subsequent rapid return of full muscular activity make it the relaxant of choice. Other uses include intubation, various endoscopies, orthopaedic manipulations and dental surgery.

Dosage and administration Brevidil E is administered by intravenous injection after the patient has been lightly anaesthetised. It should be noted that in very muscular or frail patients adjustment to the recommended dosage may be required.

Adults and children: 1–1.25 mg cation/kg body weight (1 mg cation equivalent to 1.5 mg total salt).

N.B. Full or fractional doses may be repeated as necessary without danger of cumulative effects, but once relaxation with apnoea has been achieved increased dosage does not affect the duration of action.

Contra-indications, warnings, etc The onset of relaxation is sometimes preceded by a short period of muscle fibrillation, the intensity of which is dependent on the speed of injection; however, this phenomenon provides a useful sign that the drug is exerting its action. Post-operative muscular pain and aching may also occur.

Brevidil E is contra-indicated with non-depolarising (competitive relaxants) and, should recovery be delayed, anticholinesterase agents, e.g. neostigmine, should not be used as these tend to enhance the relaxant effect.

Should recovery be delayed, as may happen in patients with low pseudo-cholinesterase levels, e.g. patients suffering from malnutrition or gross hepatic insufficiency, those exposed to organic phosphorus insecticides or those receiving concurrent treatment with non-depolarising (competitive) muscle relaxants, the patient should be given continuous artificial respiration with at least 30% oxygen in nitrous oxide until spontaneous respiration returns. In some cases the infusion of fresh blood may be useful.

N.B. It is of paramount importance, when using Brevidil E, as with all muscle relaxants, that the apparatus necessary for laryngoscopy and artificial respiration must be immediately to hand.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Box of 10 × 150 mg ampoules (150 mg total salt equivalent to 100 mg cation).

Further information Brevidil E, in the dry state, retains full activity on storage.

As alkaline solutions of suxethonium salts begin to lose activity within five minutes of preparation, it is inadvisable to mix Brevidil E with soluble barbiturates in the same solution.

Product licence number 0012/5081.

BREVIDIL* M

Approved name: Suxamethonium Bromide

Presentation Brevidil M is presented as a cream, amorphous powder for extemporaneous preparation of intravenous injections or continuous intravenous infusion by the addition of appropriate amounts of Water for Injections BP, or normal saline or 5% dextrose.

Uses Brevidil M is a short-acting muscle relaxant of the depolarising type particularly indicated in surgical, anaesthetic and other procedures where a brief period of muscle relaxation is required, e.g. intubation, endoscopies, manipulations and electro-convulsive therapy.

Dosage and administration Brevidil M is administered after anaesthesia has been induced, by intravenous injection.

Adults: 0.5–1 mg cation/kg body weight (1 mg cation equivalent to 1.67 mg total salt).

Children: Newborn 1–2 mg cation/kg followed by supplements of 0.25–0.5 mg.

Older 1 mg cation/kg followed by supplements of one-third original dose.

By continuous intravenous infusion:

Adults: 0.1% solution in normal saline or 5% dextrose: 0.05–0.1 mg cation/kg/minute.

Contra-indications, warnings, etc Muscle pains similar in nature to those occurring after strenuous exercise may occur in the immediate post-operative period and persist for several days. Muscles of the chest, abdomen, shoulder girdle, trunk and neck are sometimes also affected; however, these pains may be minimised by giving a small dose of a non-depolarising relaxant just prior to the injection of suxamethonium.

Suxamethonium causes a rise in intra-ocular pressure; it therefore should not be used in ocular surgery while the globe is incised. It is also contra-indicated in severe liver disease, in burned patients, advanced myasthenia gravis and in patients with myotonic rigidity which renders inflation of the lungs impossible. It should also be noted that streptomycin, neomycin, polymyxin, kanamycin, with suxamethonium, result in prolonged response as does the administration of anticholinesterase eye drops, e.g. ecothiopate. There is some evidence that diazepam antagonises the action of suxamethonium.

Should recovery be delayed, as may happen in dual block or in a patient with a very low or atypical pseudo-cholinesterase activity, the treatment depends on correct diagnosis which is aided by the use of a peripheral nerve stimulator and observation of finger movements, otherwise the only effective treatment is prolonged ventilation.

Dual block: This occurs in patients who have received at least 1 g of suxamethonium by infusion. The peripheral nerve stimulator will show whether the block is polarising or non-depolarising in nature. In the former case only ventilation is effective; with the latter, 10 mg of edrophonium, a short-acting anti-cholinesterase drug, may be given intravenously and if this produces an observable improvement a longer-acting anticholinesterase drug may be given, e.g. neostigmine.

Low pseudo-cholinesterase levels: Prolonged ventilation should be effected; however, a dual block may have developed during treatment. A test should therefore be made with the peripheral nerve stimulator and, should non-depolarisation be detected, anticholinesterase agents should be given as above.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Box of 10 × 67 mg ampoules (67 mg total salt equivalent to 40 mg cation).

Further information Breviril M in the dry state retains full activity on storage.

Product licence number 0012/5085.

BROLENE* EYE DROPS

Presentation Brolene Eye Drops are a colourless solution containing 0.1% propamidine isethionate in a sterile (aqueous) vehicle, the resultant solution being isotonic with lachrymal secretion.

Uses Propamidine is a member of the aromatic diamidine group of compounds which possess powerful bacteriostatic properties against a wide range of organisms.

These diamidines exert rapid and intense antibacterial action against pyogenic cocci, antibiotic-resistant staphylococci and some Gram-negative bacilli, the activity of the diamidines being retained in the presence of organic matter such as pus and lachrymal secretion.

Brolene Eye Drops are for the treatment of eye infections such as acute and chronic conjunctivitis, and for the prevention of infection resulting from minor injuries and lesions to the eye caused by foreign bodies, etc. Useful for the initial treatment and prophylaxis of ophthalmia neonatorum; and as a lubricant for contact lenses.

Dosage and administration Brolene Eye Drops should be instilled into the infected eye at the rate of 1 or 2 drops four times a day for not more than a week. If the condition has not significantly improved at the end of a week's treatment, medical advice should be obtained.

Contra-indications, warnings, etc The drops should be discarded 14 days after first opening the flap of the outer cardboard for domiciliary use, or, when used under hospital conditions, seven days after opening.

If no improvement is observed within seven days, medical advice should be obtained and a different antibacterial preparation used where necessary.

There is always the possibility, although rare, of a sensitisation reaction resulting from the use of Brolene Eye Drops; in such an event, treatment should be discontinued immediately.

Pharmaceutical precautions Protect from light. Store in a cool place.

Legal category P.

Package quantities Plastic dropper bottle of 10 ml.

Further information Nil.

Product licence number 0012/5087.

BROLENE* EYE OINTMENT

Presentation Brolene Eye Ointment is a deep yellow, smooth ointment containing 0.15% dibromopropamidine isethionate in Eye Ointment Basis BP.

Uses Dibromopropamidine is a member of the aromatic diamidine group of compounds which possess powerful

bacteriostatic properties against a wide range of organisms.

These diamidines exert rapid and intense antibacterial action against pyogenic cocci, antibiotic-resistant staphylococci and some Gram-negative bacilli, the activity of the diamidines being retained in the presence of organic matter such as pus and lachrymal secretion.

Brolene Eye Ointment is particularly suitable for the treatment of eyelid infections, such as blepharitis, and for the treatment of minor injuries to the eyes, particularly for night-time application. A useful indication is to relieve sticky eyes, very commonly experienced with babies.

Dosage and administration Before application it is advisable where practicable, to cleanse the affected eye or eyes with warm water or saline which has previously been boiled. Brolene Eye Ointment should be applied to the eyelids or conjunctival sacs two or three times daily for not more than one week.

Contra-indications, warnings, etc If no improvement is observed within seven days, medical advice should be obtained and a different antibacterial preparation used where necessary.

There is always the possibility, although rare, of a sensitisation reaction resulting from the use of Brolene preparations; in such an event, treatment should be discontinued immediately.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Collapsible tube of 5 g.

Further information Nil.

Product licence number 0012/5086.

CONRAY*

Presentation Ampoules or vials containing colourless sterile solutions of varying strengths of meglumine and/or sodium iothalamate.

Conray 280: Meglumine lothalamate Injection 60% w/v containing 280 mg iodine in combined form per ml.

Conray 325: Sodium lothalamate Injection 54% w/v containing 325 mg iodine in combined form per ml.

Conray 420: Sodium lothalamate Injection 70% w/v containing 420 mg iodine in combined form per ml.

Cardio-Conray: Injection of Meglumine lothalamate 52% w/v and Sodium lothalamate 26% w/v. It contains 400 mg iodine in combined form per ml.

Uses X-ray contrast media for the opacification of the vascular and renal systems – do not normally possess any pharmacological action.

Dosage and administration See table on following page.

Contra-indications, warnings, etc For cerebral arteriography, Conray 280 should be used; Cardio-Conray, Conray 325 and 420 should not be employed in this procedure and are not recommended in any peripheral arteriography.

Conray preparations must never be injected into the subarachnoid space.

Since the cause of severe reactions to iodinated water-soluble contrast media are unknown and preliminary

testing is unreliable as an indication that a patient will react unfavourably, the only other safeguards are physical examination and a careful evaluation of the patient's history to screen out subjects known to suffer from allergy or severe cardiovascular disease, plus the provision of facilities for resuscitation.

Side-effects associated with the use of Conray media in intravenous urography have been minor and infrequent. Among those which have been occasionally reported are nausea, vomiting, dizziness and urticaria.

In cerebral arteriography, the most common (and

normally the only) side-effect is facial heat of varying but usually slight degree.

In angiocardiology or aortography, after the rapid injection of the medium, patients commonly experience a wave of moderate warmth, often associated with flushing passing over the body.

Other transient reactions reported with these media are nausea, occasional vomiting, hypotension, headache and a metallic taste.

Pharmaceutical precautions Protect from light.

Procedure	Conray 280	Conray 325	Conray 420	Cardio-Conray
Intravenous urography	<i>Adults:</i> 40–80 ml. As for Conray 280. In the absence of preliminary dehydration 40–100 ml may be used. <i>Infants and children:</i> Under 12 kg: 2 ml/kg body weight. Over 12 kg: 1.5 ml/kg body weight (with a minimum of 24 ml). Over 10 years of age: Lower range of adult dosage.		40 ml is usually adequate but the schedule for Conray 280 can be used with safety in adults.	
Femoral and other peripheral arteriographies.	15–20 ml injected into the femoral or iliac artery will provide excellent visualisation of the arterial tree of the leg. A similar or smaller dose is indicated for smaller arteries.	Do not use		
Cerebral angiography (carotid and vertebral)	Average adult dose is 6–10 ml for each injection. Exceptionally, up to 10 injections of 8 ml each have been made into the carotid artery.	Do not use		
Abdominal aortography (direct puncture or retrograde catheterisation).	<i>Adults:</i> 20–30 ml.	<i>Adults:</i> 20–30 ml.	<i>Adults:</i> 20–30 ml.	<i>Adults:</i> 20–30 ml.
Thoracic aortography (including arch aortography)	Often adequate in children: 0.5–1 ml per kg body weight. May be used as a test dose in positioning catheter tip.	<i>Adults and children:</i> 0.5–1 ml per kg body weight. The usual volume employed in the adult is 20–40 ml. Cardio-Conray is specifically designed for this type of procedure.		
Intravenous aortography	—	—	<i>Adults and children:</i> 1 ml per kg body weight. In adults 80–100 ml or more per injection is often used. Frequently this amount is subdivided equally and given by rapid simultaneous bilateral injection.	Conray 420 is generally preferable.
Angiocardio-graphy	May be used as test dose in positioning catheter tip. Volumes of up to 40 ml have been used for this purpose prior to the diagnostic dose of more concentrated medium.		Cardio-Conray is the product of choice for this procedure. <i>Adults and children over 14 years of age:</i> 20 to 50 ml per injection. <i>Small children and infants:</i> 0.5–1.0 ml per kg body weight with a minimum of 3 ml. Multiple injections may be required and the above doses may be repeated with confidence but 3 ml per kg body weight should not be exceeded.	
Splenography portal venography	<i>Adults:</i> 20–40 ml.	<i>Adults:</i> 20–40 ml.	<i>Adults:</i> 20–40 ml.	—
Femoral venography and/or inferior vena cavography	<i>Adults:</i> 20–60 ml.	<i>Adults:</i> 20–60 ml.	<i>Adults:</i> 20–60 ml.	—

Legal category POM.

Package quantities *Conray 280:* Box of 10 × 20 ml ampoules. Box of 10 × 50 ml bottles.

Conray 325: Box of 10 × 20 ml ampoules. Box of 10 × 50 ml bottles.

Conray 420: Box of 10 × 20 ml ampoules. Box of 10 × 50 ml bottles.

Cardio-Conray: Box of 10 × 20 ml ampoules. Box of 10 × 50 ml bottles.

Further Information Nil.

Product licence numbers

Conray 280 0012/5033

Conray 325 0012/5034

Conray 420 0012/5035

Cardio-Conray 0012/5038

DIAGINOL* VISCOUS

Presentation Ampoules containing a yellowish-brown, sterile solution of sodium acetrizate 40% w/v with the addition of dextran to increase the viscosity.

Uses An X-ray contrast medium, primarily indicated for use in hysterosalpingography. There is no theoretical reason why Diaginol Viscous should not be used in direct cholangiography, urethrography, the visualisation of sinuses, injection into the vas deferens and for other radiographic procedures in which this type of contrast agent is indicated.

Dosage and administration About 10 ml are usually required for hysterosalpingography and this should be administered slowly via a syringe and a suitable cannula.

Diaginol Viscous may be used for children at the surgeon's discretion.

Contra-indications, warnings, etc Diaginol Viscous may be injected at any time during the menstrual cycle, but some workers recommend that the investigation should be made 9–14 days from the beginning of the patient's last menstrual period, as this time is considered the least likely for intravasation or disturbance of a very early pregnancy to occur.

The medium is well tolerated in the majority of patients, but some degree of pain is occasionally complained of, although it may be difficult to distinguish that due to instrumentation and that due to the medium. Some degree of discomfort may be experienced when the medium enters the pelvic peritoneal cavity.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Ampoules of 15 ml.

Further information Nil.

Product licence number 0012/5002.

EPI-C

Presentation White, creamy dispersion of barium sulphate 70% w/w (150% w/v) in 2 litre plastic containers.

Uses For the opacification of the colon by double (air) or single contrast barium enema. Barium sulphate is not absorbed and is excreted via the rectum. Neither does it possess any pharmacological action.

Dosage and administration Epi-C dispersion is administered rectally as an enema. It should be diluted with an equal volume of water. The Epi-C dispersion *always* being added to the water. A typical amount for an enema is 300 ml Epi-C dispersion added to 300 ml water. One ml of foam control preparation should be added to the mixture immediately before use. For double contrast enema, air is introduced into the rectum after partial evacuation of the barium mixture, thus allowing the mucosa of the colon to be visualised. No children's dosage recommended as such investigations in children are rare and specialised. The dosage will therefore be decided by the radiologist to suit the special requirements in each case.

Preparation of the patient: Meticulous cleansing of the colon is an essential preliminary to achieving good diagnostic accuracy in barium enema examinations, especially in the double contrast technique. If the patient's condition permits, this usually involves a low residue diet with high fluid intake for two days, and laxatives for one or two days prior to the examination. A high colonic washout is performed on the day of the procedure. During the examination, smooth muscle relaxants such as glucagon or hyoscine n-butyl bromide may be administered intravenously to provide colon relaxation and to reduce discomfort.

Contra-indications, warnings, etc As barium sulphate causes peritoneal adhesions if there is a defect in the bowel wall allowing leakage into the peritoneal cavity barium enemas are contra-indicated: (a) if there is any possibility of perforation, (b) in acute dilatation in inflammatory bowel disease, and (c) within 48 hours of sigmoidoscopic biopsy.

Precautions: Use in pregnancy. Barium enema examinations should not be carried out in pregnant women unless considered by the clinician to be absolutely essential. In women of child-bearing age, the 'ten-day' rule should be observed.

Side-effects: No serious adverse effects are likely. Some patients may suffer from constipation.

Treatment of overdose: Epi-C dispersion is non-toxic and overdose is most unlikely.

Pharmaceutical precautions Store at room temperature. Do not allow to freeze. Shake well before use.

Legal category P.

Package quantities 2 litre plastic containers.

Further information Nil.

Product licence number 4135/0002.

FLAGYL* AND FLAGYL-S* SUSPENSION

Presentation Tablets containing 200 mg and 400 mg metronidazole. The 200 mg tablets are white, uncoated, indented 'Flagyl 200' on the face with a break-line on the reverse. The 400 mg tablets are yellow, uncoated, indented 'Flagyl 400' on the face with a break-line on the reverse.

Suspension: Buff-coloured, each 5 ml containing 320 mg benzoylmetronidazole, equivalent to 200 mg metronidazole.

Suppositories containing 500 mg and 1.0 gram metronidazole.

Injection (for intravenous infusion) 0.5 per cent w/v in

100 ml bottles or VIAFLEX containers (500 mg metronidazole per 100 ml) and 20 ml ampoules (100 mg metronidazole per 20 ml).

Uses Flagyl is indicated in the treatment of infections in which anaerobic bacteria have been identified or are suspected pathogens. Flagyl is active against a wide range of pathogenic micro-organisms notably *Trichomonas vaginalis*, *Entamoeba histolytica*, *Giardia lamblia*, *Balantidium coli* and other species of bacteroides, fusobacteria, eubacteria, clostridia and anaerobic cocci.

It is indicated in the treatment of:

1. Urogenital trichomoniasis in the female (trichomonal vaginitis) and in the male.
2. Non-specific vaginitis.
3. All forms of amoebiasis (intestinal and extra-intestinal disease and that of symptomless cyst passers).
4. Giardiasis.
5. Acute ulcerative gingivitis.
6. Anaerobically-infected leg ulcers and pressure sores.

7. Acute dental infections (e.g. acute pericoronitis and acute apical infections).

8. Septicaemia, bacteraemia, brain abscess, necrotising pneumonia, osteomyelitis, puerperal sepsis, pelvic abscess, pelvic cellulitis, peritonitis and post-operative wound infections from which one or more pathogenic anaerobes have been isolated.

9. And in the prevention of post-operative infections due to anaerobic bacteria, particularly species of bacteroides and anaerobic streptococci.

Dosage and administration Flagyl tablets should be swallowed without chewing with half a tumbler of water. It is recommended that the tablets be taken during or after a meal, and the suspension at least one hour before a meal. Oral medication is used for all the indications listed in the following table. Dosage (oral, intravenous, rectal) for anaerobic infections is listed separately. Each 5 ml suspension contains the equivalent of 200 mg metronidazole; if dosages less than 200 mg equivalent of metronidazole are prescribed, the suspension can be diluted with Syrup BP.

The diluted suspension has a shelf life of 14 days.

ANAEROBIC INFECTIONS

Treatment of Anaerobic Infections: Treatment for seven days should be satisfactory for most patients but, depending on the clinical and bacteriological assessments, the physician might decide to prolong treatment.

A. Oral medication

The tablets or suspension may be given alone or concurrently with other bacteriologically appropriate antibacterial agents:

Adults and Children over 10 years – 400 mg orally three times daily.

Children and Infants – 7.5 mg per kg bodyweight three times daily.

Prevention of Anaerobic Infections

Adults:

1. In gynaecological surgery 1.0 g orally as a single dose followed, if possible, by 200 mg three times daily during or after meals until pre-operative withholding of solids and liquids by mouth becomes necessary; oral medication with 200 mg three times daily should be resumed as soon as possible after operation for up to seven days.

2. In elective colonic surgery three regimes have been used successfully, namely:

- (a) 200 mg orally six-hourly with kanamycin (1.0 g orally six-hourly) for three days before surgery (without further medication).
- (b) 400 mg orally eight-hourly with phthalylsulphathiazole (2.5 g orally six-hourly) for four days before surgery (without further medication).
- (c) 1.0 g orally as a single dose and 200 mg orally eight-hourly during the 24-hour period before pre-operative starvation followed by 1.0 g rectally (by suppository) at eight-hourly intervals, starting two hours before surgery, until oral medication (200–400 mg three times daily) can be given to complete a seven-day course; if rectal medication is necessary, after the third post-operative day, the frequency of administration should be reduced to 12-hourly.

Children:

Age in years	Metronidazole orally (8-hourly for 48 hours)	Neomycin orally (6-hourly for 3 days)
<i>Pre-operative medication</i>		
5 to 10	100 mg	500 mg
1 to 5	5 mg per kg bodyweight	250 mg
Under 1	5 mg per kg bodyweight	125 mg
<i>Post-operative medication</i>		
<i>Flagyl per rectum or via colostomy (8-hourly for 48 hours)</i>		
5 to 10	500 mg suppository	250 mg and
1 to 5	One-half of a 500 mg suppository (250 mg)	125 mg
Under 1	One-quarter of a 500 mg suppository (125 mg)	suppositories can be prepared by melting 500 mg suppositories and pouring into 1.0 g or 500 mg suppository moulds respectively.

B. Rectal medication

1. **Treatment of anaerobic infections:** Adults and children over 10 years: One gram suppository inserted into the rectum eight-hourly for three days. Oral medication with 400 mg three times daily should be substituted as soon as this becomes feasible. If rectal medication must be continued for more than three days, the suppositories should be inserted at 12-hourly intervals.

Children (5 to 10 years): As for adults but with 500 mg suppositories and oral medication with 7.5 mg per kg bodyweight three times daily.

Infants and children under 5 years: As for children of 5 to 10 years but with appropriate reduction in dosage of suppositories (one half of a 500 mg suppository for 1 to 5 years and one quarter of a 500 mg suppository for under 1 year).

2. Prevention of Anaerobic Infections:

- (a) In appendicectomy: Adults and children over 10 years: One gram suppository inserted into the rectum two hours before surgery and repeated at

Dosage is given in terms of metronidazole or metronidazole equivalent

	Duration of dosage in days	Adults and children over 10 years	Children		
			7 to 10 years	3 to 7 years	1 to 3 years
<i>Urogenital trichomoniasis</i> Where re-infection is likely, the consort should receive a similar course of treatment concurrently.	7	200 mg three times daily	100 mg three times daily	100 mg twice daily	50 mg three times daily
	or 2	800 mg in the morning and 1,200 mg in the evening			
	or 1	2.0 g as a single dose			
<i>Non-specific vaginitis</i>	7	400 mg twice daily			
	1	2.0 g as a single dose			
<i>Amoebiasis</i>					
(a) Invasive intestinal disease in susceptible subjects	5	800 mg three times daily	400 mg three times daily	200 mg four times daily	200 mg three times daily
(b) Intestinal disease in less susceptible subjects and 'chronic' amoebic hepatitis	5–10				
(c) Amoebic liver abscess also other forms of extra-intestinal amoebiasis	5	400 mg three times daily	200 mg three times daily	100 mg four times daily	100 mg three times daily
(d) Symptomless cyst passers	5–10	400–800 mg three times daily	200–400 mg three times daily	100–200 mg four times daily	100–200 mg three times daily
<i>Giardiasis</i>	3	2.0 g once daily	1.0 g once daily	600–800 mg once daily	500 mg once daily
<i>Acute ulcerative gingivitis</i>	3	200 mg three times daily	100 mg three times daily	100 mg twice daily	50 mg three times daily
<i>Acute dental infections</i>	3–7	200 mg three times daily			
<i>Leg ulcers and pressure sores</i>	7	400 mg three times daily			
<i>Anaerobic infections (general)</i>		See data sheet text			

† Immature children and babies weighing less than 10 kg should receive proportionately smaller dosages.

eight-hourly intervals until oral medication (200 to 400 mg three times daily) can be given to complete a seven day course. If rectal medication is necessary after the third post-operative day, the frequency of administration should be reduced to 12-hourly.

Children (5 to 10 years): 500 mg suppositories administered as for adults until oral medication (3.7 to 7.5 mg per kg bodyweight three times daily) become possible.

(b) Pre-operative medication for elective colonic surgery. See under 'Oral Medication'.

C. Intravenous medication

Intravenous medication can be used in patients with severe anaerobic infections for whom oral or rectal medication is not possible or is contra-indicated; it is particularly useful in emergencies and is indicated in patients needing surgery who:

- have or are believed to have anaerobic sepsis such as septicaemia, peritonitis, subphrenic or pelvic abscesses.
- at operation show signs of established or impending anaerobic sepsis.

– undergo operations in which contamination occurs with anaerobes from the gastro-intestinal or female genital tracts or the oropharynx.

In patients maintained on intravenous fluids, Flagyl injection may be diluted with appropriate volumes of normal saline, dextrose-saline, dextrose 5 per cent w/v or potassium chloride injections (20 mmol and 40 mmol).

1. **Treatment:** Adults and children over 10 years: 100 ml by intravenous infusion eight-hourly. The injection should be infused intravenously at the rate of 5 ml per minute but may be administered alone or concurrently (but separately) with other appropriate anti-bacterial agents in parenteral dosage forms. Oral medication with 400 mg three times daily may be substituted as soon as this becomes feasible.

Children under 10 years: As for adults but the intravenous dose is based on 1.5 ml (7.5 mg metronidazole) per kg bodyweight and the oral dose on 7.5 mg per kg bodyweight.

2. **Prevention:** Adults and children over 10 years: 100 ml by intravenous infusion immediately before, during or after operation, followed by the same dose eight-hourly until oral medication (200 to 400 mg three times daily) can be given to complete a seven-day course.

Children under 10 years: As for adults but the intravenous dose is based on 1.5 ml (7.5 mg metronidazole) per kg bodyweight and the oral dose on 3.7 to 7.5 mg per kg bodyweight.

Use in pregnancy: Animal studies have shown no hazard.

Pregnant women tolerate metronidazole well and no adverse effect on their offspring has been reported. As with all medicines, Flagyl should not be given during pregnancy or during lactation unless the physician considers it essential; in these circumstances the short, high-dosage regimes are not recommended.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to metronidazole.

Precautions: The recommended dosages, frequencies of administration and duration of medication have been found effective and well tolerated in nearly all cases. However, regular clinical and biological surveillance are advised if administration of Flagyl for more than 10 days is considered to be necessary.

In the absence of microbiological diagnosis of the cause(s) of infection in a patient who is to be treated for urogenital trichomoniasis, the prescriber should bear in mind the possibility that an accompanying gonococcal infection might persist in a symptomless state after *Trichomonas vaginalis* has been eliminated.

Clinicians who contemplate continuous therapy, for the relief of chronic conditions, for periods longer than those recommended are advised to consider the possible therapeutic benefit against the risks of peripheral neuropathy.

Available evidence suggests that patients with limited degrees of renal functional impairment need no alteration in recommended dosage. Metronidazole is readily removed from the plasma by haemodialysis and patients should be dosed immediately following this procedure.

Patients should be advised not to take alcoholic drinks during metronidazole therapy.

Some potentiation of anticoagulant therapy has been reported when metronidazole has been used with certain oral anticoagulants. Dosage of the latter may require adjustment. No interactions have been reported with

parenteral anticoagulants of the heparin type. However, anticoagulant activity should be routinely monitored with these products. Metronidazole has no direct activity against aerobic or facultative anaerobic bacteria.

Warnings and adverse effects: Serious adverse reactions occur very rarely with standard recommended regimens. There have been occasional reports of an unpleasant taste in the mouth, furred tongue, nausea, vomiting, gastro-intestinal disturbance, and of urticaria and angioedema. Anaphylaxis may occur rarely.

Drowsiness, dizziness, headache, ataxia, skin rashes, pruritus, inco-ordination of movement and darkening of the urine (due to a metronidazole metabolite) have been reported but very rarely.

During intensive and/or prolonged metronidazole therapy, a few instances of peripheral neuropathy have been reported, but in most cases the reaction disappeared after treatment was stopped or when dosage was reduced. A moderate leucopenia has been reported in some patients but the white cell count has always returned to normal before or after treatment has been completed.

Transient epileptiform seizures have been reported in a few patients undergoing intensive, high-dosage metronidazole radiosensitisation therapy (this use does not appear in the clinical indications but it is known that the product is being tried for such a purpose in a few well-known specialised centres).

Treatment of overdose: Uneventful recovery has followed attempts at suicide with quantities of 30 and 60 × 200 mg tablets.

There is no specific treatment for gross overdose of Flagyl.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Containers of 21 and 250 × 200 mg tablets. Containers of 100 × 400 mg tablets.

Bottles of 50 and 125 ml suspension (benzoylmetronidazole).

Containers of 10 × 500 mg and 10 × 1.0 gram suppositories.

Boxes of 10 × 100 ml bottles injection 0.5 per cent w/v.

Boxes of 48 × 100 ml injection 0.5% w/v in VIAFLEX containers.

Carton of 10 × 20 ml ampoules 0.5 per cent w/v.

Further information Metronidazole has no useful direct activity against aerobic and facultatively anaerobic bacteria.

Flagyl Injection does not contain a preservative; the 100 ml bottle is not, therefore, intended as a 'multi-dose'.

Product licence numbers

Tablets 200 mg	0012/5256
Tablets 400 mg	0012/0084
Suppositories 500 mg	0012/0113
Suppositories 1.0 g	0012/0114
Injection 100 ml	0012/0107
Injection 20 ml	0012/0125
Suspension	0012/0131

FLAGYL COMPAK®

Presentation Flagyl Compak is a combined treatment pack containing: 21 × 200 mg Flagyl (metronidazole)

Tablets, 14 × 100,000 units nystatin vaginal inserts, 1 vaginal insert applicator.

The 200 mg metronidazole tablets are white, uncoated, indented 'Flagyl 200' on the face with a break line on the reverse.

The 100,000 units nystatin vaginal inserts are yellowish cream, almond shaped, indented 'M & B' on one face.

Uses Flagyl is active against a wide range of pathogenic micro-organisms. However, it is its potent trichomonocidal action which is of relevance in this presentation.

Nystatin is a fungistatic and fungicidal antibiotic which is active topically against *Candida albicans*.

Flagyl Compak is indicated in the treatment of vaginitis where a mixed trichomonal/candidal infection is diagnosed or suspected. Presenting symptoms may include vaginal discharge, pruritus vulvae and dyspareunia.

Dosage and administration One Flagyl Tablet to be swallowed whole, with half a glassful of water during or after meals, three times daily for seven days.

Concurrently, one nystatin vaginal insert to be moistened and introduced high into the vagina night and morning for seven days. Some physicians may prefer to instruct patients to use one insert nightly, before retiring, for fourteen nights. Full patient instructions for use of the applicator are included in each Compak.

This product is not recommended for girls under 10 years of age.

Where cross infection with *Trichomonas vaginalis* is confirmed or suspected the male consort should be treated concurrently with one Flagyl tablet by mouth three times daily for seven days.

Contra-indications, warnings, etc

Contra-indications and precautions: There are no absolute contra-indications to the use of Flagyl or nystatin; but in the absence of microbiological diagnosis of the cause(s) of the patient's infection prescribers should bear in mind the possibility that an accompanying gonococcal infection might persist in a symptomless state after *Trichomonas vaginalis* and/or *Candida albicans* have been eliminated.

As with other drugs, alcohol should be avoided during treatment with Flagyl.

Side-effects and adverse reactions: Flagyl is remarkably well tolerated and no serious adverse reaction has been encountered. There have been occasional reports of an unpleasant taste in the mouth, furred tongue, nausea, vomiting (very rarely) and gastro-intestinal disturbance. Drowsiness, headache, skin rashes and pruritus have been reported, but very rarely.

No adverse effects due to the use of nystatin vaginal inserts have been reported.

Treatment of overdosage: There is no specific treatment for gross overdosage of Flagyl, but early gastric lavage is recommended. Uneventful recovery has followed attempts at suicide with quantities of 30 and 60 × 200 mg tablets.

Nystatin is not absorbed.

Pharmaceutical precautions Protect from light. Flagyl Compak should be stored in a cool place.

As nystatin loses potency slowly on storage, the vaginal inserts should be used within 18 months of the date of manufacture.

Legal category POM.

Package quantities Combined treatment pack containing: 21 × 200 mg Flagyl Tablets, 14 × 100,000 units

nystatin vaginal inserts, 1 vaginal insert applicator, full instructions for the patient.

Further information There is no evidence of resistance to either Flagyl or nystatin.

Pregnant women tolerate metronidazole well and no adverse effect on their offspring has been reported. Neither has any such effect been reported due to the use of nystatin vaginal inserts. As with all medicines Flagyl Compak should not be given during pregnancy or lactation unless the physician considers it essential.

Product licence number 0012/5091.

FLAXEDIL*

Presentation Colourless injection solution containing gallamine triethiodide 4% w/v.

Uses Non-depolarising (competitive-blocking) muscle relaxant having a duration of action of 20–30 minutes. Flaxedil is used as a relaxant in surgery and to give suitable conditions for intubation. It is also given to potentiate the muscle-relaxant properties of halothane and to protect against the bradycardia it causes. Flaxedil is employed to aid the management of certain convulsive states and as a diagnostic agent for myasthenia gravis.

Dosage and administration Flaxedil is administered intravenously after the patient has been anaesthetised. Dosage must be adjusted to individual requirements, the nature of the general anaesthetic used, and the duration of the operation. Some anaesthetists recommend that a test dose of 20 mg should be given before anaesthesia is induced to exclude sensitivity.

As a guide the average adult requires 80–120 mg of Flaxedil for the provision of adequate muscular relaxation. Supplementary doses of 20–40 mg are given as required. Where no suitable vein is available, Flaxedil may be given intramuscularly with or without hyaluronidase. For children a dosage of 1.5 mg per kg should be given intravenously. In suspected myasthenia gravis a dosage of 0.025 mg per kg may be used as a diagnostic procedure.

Contra-indications, warnings, etc Flaxedil is contra-indicated in patients suffering from myasthenia gravis (except for diagnosis). Since gallamine is excreted by the kidneys extra care is necessary in its use in patients with renal dysfunction. In operative obstetrics, because gallamine passes rapidly through the placental barrier, it should be used with care until after delivery of the foetus. Flaxedil should only be used when facilities for securing an effective airway and providing controlled respiration with adequate oxygen are available. The action of muscle relaxants is enhanced by the antibiotics, amikacin, gentamycin, kanamycin, neomycin, streptomycin, polymyxin, tetracycline and by potent anaesthetics such as halothane.

Muscular relaxation with Flaxedil is singularly free from side-effects, other than tachycardia which occurs in the majority of patients and which is associated with its vagolytic action. Ill effects of this have not been noted, but care is advised in its use in patients with heart conditions. Anaphylactic reactions have been reported occasionally.

Overdosage with Flaxedil is an unlikely event. If it is necessary to reverse the effects of Flaxedil rapidly, the antagonist neostigmine methylsulphate should be injected intravenously in a dosage of 1 mg initially followed

by increments of 0.5 mg until the respiratory exchange is adequate. The use of neostigmine must always be preceded by the intravenous injection of atropine sulphate 0.5–1 mg. No patient who has received neostigmine should be left alone until all risk of excessive bradycardia and of recrudescence of muscular paralysis has passed.

Pharmaceutical precautions Protect from light.

Flaxedil is compatible with solutions of thiopentone sodium, but it is important to add the Flaxedil to the thiopentone solution, not vice versa. Flaxedil is incompatible with pethidine hydrochloride solutions.

Legal category POM.

Package quantities Boxes of 10 × 2 ml ampoules.

Further information Nil.

Product licence number 0012/5077.

GAROIN*

Presentation White, uncoated tablets indented 'Garoin' on one face with a break line on the reverse. Each tablet contains 50 mg phenobarbitone sodium and 100 mg phenytoin sodium.

Uses Phenobarbitone sodium is a long-acting barbiturate with sedative, hypnotic and anticonvulsant actions. Phenytoin sodium is an anticonvulsant with little or no hypnotic action.

Garoin is indicated in the treatment of major epilepsy, psychomotor seizures and some cases of petit mal.

Dosage and administration The dosage of Garoin must be adjusted individually. For adults it is advisable to commence treatment with 1 tablet three times daily, increasing to 2 tablets three times a day if necessary.

For children over 6 years of age, the daily dosage may be up to 4 tablets given in divided doses; for younger children the dosage should be proportionately reduced.

A more rapid effect is achieved if the tablets are taken on an empty stomach, but if this causes gastric upset they should be taken after meals with a draught of water.

Patients already receiving treatment with phenobarbitone should be transferred to Garoin gradually, the introduction of the latter and withdrawal of phenobarbitone being overlapped. If treatment with Garoin is effective and produces cessation of fits, dosage must be continued for a minimum of three years, and may then be gradually reduced during the following two years.

Garoin must be administered with persistence and perseverance if the best results are to be achieved. The patient or the patient's relatives should be supplied with carefully written instructions and the patient must be carefully watched for toxic reactions.

Contra-indications, warnings, etc Garoin is contra-indicated in patients with acute intermittent porphyria and those who have a natural or acquired idiosyncrasy to barbiturates. It should be used with caution in patients receiving thyroid replacement therapy. The effects of phenytoin are enhanced by substances which reduce its metabolism in the liver or impair hepatic function, and diminished by substances which induce hepatic enzyme activity.

There is some evidence that anticonvulsant medicines cause foetal abnormalities (Lowe *et al.*, *Lancet*, 1973, i, 9; Loughnan *et al.*, *Lancet*, 1973, i, 70) and care is needed in their use during the early months of pregnancy. The physician must consider the hazards to both mother

and foetus associated with the withdrawal of anticonvulsant therapy and those of continuing therapy with the possibility of inducing congenital malformations.

Side-effects which accompany the administration of Garoin may be due to either phenobarbitone, phenytoin or both. Untoward effects due to phenobarbitone in therapeutic dosage are rare, but mental depression may be encountered after prolonged administration. Phenytoin is usually well tolerated, but dizziness, gastric irritation and mental confusion may occur. Phenytoin may also give rise to tenderness and hyperplasia of the gums, and to hirsutism, especially in young females.

The treatment of acute overdosage is similar to that used for acute barbiturate toxicity. This involves gastric lavage, or the use of an emetic if the patient is not comatose, artificial respiration and the administration of oxygen. Physiotherapy and antibiotics should be given to prevent bronchopneumonia, and correction of disordered fluid and/or electrolyte balance is indicated. Where facilities are available forced diuresis or haemodialysis should be undertaken.

Pharmaceutical precautions Store in a dry place.

Legal category POM.

Package quantities Container of 100 tablets.

Further information Nil.

Product licence number 0012/5078.

HALOTHANE – M&B*

Presentation Halothane is an almost colourless liquid with a distinctive, pleasant odour.

Uses Halothane is a general anaesthetic used in inhalation anaesthesia. It is of particular value:

1. When cautery or diathermy is to be used.
2. In giving a pleasant and rapid induction particularly in children.
3. As it suppresses secretions from the salivary, bronchial and gastric glands.
4. In maintaining the required plane of anaesthesia which is easily reversed.
5. Since relaxation is adequate for most operations and respiration is readily controlled.
6. Since recovery is rapid and nausea and vomiting are rare.
7. As it is suitable for most types of surgery.
8. As it can be given with a very high percentage of oxygen when this is indicated.

Dosage and administration *The technique of halothane anaesthesia:*

1. *Pre-medication:* A small dose of pethidine with or without the addition of promethazine will produce satisfactory sedation in most patients and will reduce the tendency to tachypnoea. Atropine in an appropriate dose should be administered to all patients.

2. *Induction:* This is most conveniently carried out with a sleep dose of thiopentone sodium, to allow the application of a face mask. A gas flow of 8 litres/minute should be administered, of which at least 30% should be oxygen, and then the Halothane should slowly be introduced. Administration should start at 0.5% and be increased by a further 0.5% every few breaths until the inspired gases contain 3% Halothane. Intubation can be carried out after five minutes' inhalation of 3% Halothane in a carrier gas flow of 8 litres/minute or before exposure

to Halothane if an intubating dose of suxamethonium is given. If intubation is performed before exposing the patient to Halothane, the introduction of Halothane must still be stepwise.

3. Maintenance: At a gas flow of 8 litres/minute, Halothane concentrations of between 0.5% and 1.5% are usually adequate. At a 2 litres/minute gas flow with the vaporiser out of circuit (VOC) a concentration of 2–2.5% fed into the absorber circuit will suffice. A low resistance vaporiser may be placed within the circle (VIC), but in this case controlled or assisted ventilation must not be used. A vaporiser for VIC use must not be capable of delivering a concentration greater than 3%.

4. Recovery: This is usually rapid and uneventful. If the Halothane is withdrawn as skin closure starts, reflexes will have returned by the time the dressings are in place. Shivering is occasionally seen during recovery if there is a marked temperature differential between the theatre and the ward. This is readily controlled by the administration of a small dose of chlorpromazine, but supplementary oxygen may be required for a few minutes.

Methods of administration: Halothane is a potent anaesthetic and should, wherever possible, be administered via a specially calibrated and temperature-compensated vaporiser. A number of such vaporisers are now available.

Halothane can also be administered from the ordinary bottle vaporiser of a Boyle's machine, but the scale should be extended to allow fine adjustment in the concentration of Halothane delivered.

Open-drop anaesthesia with Halothane is not generally recommended; however, a few drops carefully applied to the mask may smooth the subsequent administration of ether.

Draw-over machines and inhalers can be satisfactorily used with Halothane, but if air is the carrier gas, supplementary oxygen or assisted respiration may be necessary to maintain full oxygenation.

Contra-indications, warnings, etc Whilst no absolute contra-indication to Halothane anaesthesia exists, particular care should be exercised in the following conditions:

1. In obstetrics – uterine relaxation and post-partum haemorrhage may result.
2. In neurosurgery – a rise in CSF pressure has been recorded, the effects of which may be mitigated by the use of moderate hyperventilation.
3. When Injection of Adrenaline is used concurrently – cardiac arrhythmias may occur.
4. In multiple anaesthetics and infectious hepatitis – the possibility that multiple exposure to Halothane and/or concomitant infectious hepatitis may cause liver failure. Unexplained pyrexia or jaundice occurring after an administration of Halothane should be regarded as a contra-indication to further Halothane anaesthesia until such time as the relationship between post-anaesthetic jaundice and Halothane has been elucidated. Multiple anaesthetics with any anaesthetic agent are more prone to be followed by hepatic damage than a single exposure. There is some evidence that a second exposure to Halothane within four weeks is undesirable and should be avoided.

The use of beta adrenergic blocking agents during Halothane anaesthesia is at the discretion of the anaesthetist.

Muscle relaxants: All commonly used muscle relaxants may be used in conjunction with Halothane, but, as

Halothane potentiates the actions of gallamine and *d*-tubocurarine, the doses of these muscle relaxants must be reduced. The association of *d*-tubocurarine with Halothane may lead to a marked fall in blood pressure.

Ganglion blocking agents: Potentiation occurs between Halothane and the standard hypotensive agents such as pentolinium, pempidine and trimetaphan. These drugs must be used in reduced dosage when administered in conjunction with Halothane.

Vaporiser: Halothane must not be used in the EMO ether vaporiser as it attacks the metal; a vaporiser specially constructed for Halothane should be used.

Pharmaceutical precautions Store in a dark place below 25°C. Keep well closed. The vaporiser should be drained at regular intervals. Any discoloured Halothane should be discarded.

Legal category P.

Package quantities Bottle of 250 ml.

Further information Nil.

Product licence number 0012/0095.

HEXABRIX* ▼

Presentation Ampoules and bottles of a sterile solution of meglumine ioxaglate 39.30% w/v and sodium ioxaglate 19.65% w/v containing 320 mg iodine in combined form per ml.

Uses X-ray contrast medium for the opacification of the vascular system, urinary tract, joints and female genital tract.

Dosage and administration See accompanying table. For ease of injection it may be found helpful to warm Hexabrix to near body temperature.

Procedure

Hysterosalping-ography

Femoral and other peripheral arteriographies

Cerebral angiography (carotid and vertebral)

Angio-cardiography

Dosage and administration

About 10 ml are usually required, administered by slow injection into the uterine cervical canal via a syringe or suitable cannula.

15–20 ml injected into the femoral or iliac artery will provide excellent visualisation of the arterial tree of the leg. A similar or smaller dose is indicated for smaller arteries.

Average adult dose: 6–8 ml for each injection. Up to 10 injections each of 8 ml may be required.

Multiple small test injections may be used for positioning catheter tip.

Adults and children over 14 years: 30–50 ml per injection.

Children (14 years and under) and infants:

1–1.5 ml per kg bodyweight.

Multiple injections may be required. Total dosage should not normally exceed 4 ml per kg bodyweight. In exceptional circumstances, this total dose may be exceeded according to the clinical condition.

<i>Abdominal aortography (direct puncture or catheterisation)</i>	Adults: 20–30 ml. Up to 50 ml may be used particularly if films of the legs are also taken following the same injection.
<i>Thoracic aortography (including arch aortography)</i>	Adults and children: 0.5–1 ml per kg bodyweight up to 40 ml per injection. This may be repeated if necessary. Total dosage should not normally exceed 4 ml per kg bodyweight.
<i>Pulmonary angiography</i>	Adults: 20–40 ml Children: 0.5–1 ml per kg bodyweight. Special care should be exercised in patients with pulmonary arterial hypertension.
<i>Coronary arteriography</i>	Adults: 3–8 ml per injection, depending on size of artery. Several injections are usually given for complete demonstration, particularly in the left coronary artery.
<i>Intravenous aortography</i>	Adults and children: 1–1.5 ml per kg bodyweight. In adults 100 ml is often used; frequently this amount is sub-divided equally and given by simultaneous rapid bilateral injection.
<i>Femoral venography and/or inferior vena cavography</i>	Adults: 25–50 ml.
<i>Leg phlebography</i>	20–50 ml injected into a vein in the foot. The contrast medium may be diluted with Water for Injections, before injection, to a concentration of 220 mg iodine equivalent per ml.
<i>Intravenous urography</i>	Adults: 20–80 ml. 60–100 ml may be used provided that the patient is not dehydrated. Children: Under 12 kg – 2 ml per kg bodyweight. Over 12 kg – 1.5 ml per kg bodyweight (with a minimum of 24 ml). Over 10 years of age – lower range of adult dosage. Patients with severe renal disease or diabetes should be well hydrated. Particular care is necessary in these patients as temporary deterioration in renal function has been reported.
<i>Splenography</i>	Adults: 20–40 ml by splenic puncture.
<i>portal venography</i>	
<i>Knee arthrography (double contrast)</i>	By injection into the knee joint. Adults: 4.5 ml together with injections of air before and after the positive contrast medium.

Contra-indications, warnings, etc Hexabrix must never be injected by the subarachnoid or epidural route. It is definitely contra-indicated for myelography.

Precautions: Since the causes of severe reactions to

iodinated water-soluble contrast media are unknown and preliminary testing is unreliable as an indication that a patient will react unfavourably, the only other safeguards are physical examination and a careful evaluation of the patient's history to screen out subjects known to suffer from allergy, asthma, or severe cardiovascular disease. The provision of facilities for resuscitation and the training of staff members in their prompt use is mandatory.

A positive history of allergy, asthma or of untoward reactions during previous similar investigations does not necessarily contra-indicate the use of the contrast agent, but it emphasises the need for extra caution, for a sensitivity-test dose before the definitive injection, possibly steroid cover, and for even greater than usual preparedness to deal promptly with any reaction that might occur.

Extra caution should be exercised in carrying out radiographic procedures with contrast media in patients with severe systemic disease, asthma, and in allergic subjects. In patients with advanced renal disease and inadequate renal function as reflected by a raised blood urea, and in diabetics, the normally rapid excretion of the contrast medium may be markedly impaired. Even in patients with kidney disease substantial deterioration of renal function is minimised if the patient is well hydrated. Urine output must be carefully checked in these patients after the procedure.

Patients with hepatorenal insufficiency should not be examined unless the possibility of benefit clearly outweighs the additional risk. Re-examination should be delayed for five to seven days.

Special care should be exercised when Hexabrix is injected into the right heart or pulmonary artery in patients with pulmonary arterial hypertension. Right heart angiography is probably best avoided in patients with pulmonary arterial hypertension.

Special care should be exercised in patients being treated with a calcium ion antagonist (eg verapamil) and who are to undergo coronary angiography; in such circumstances, a few instances of serious arrhythmias have been reported.

Patients with MYELOMATOSIS, and to a lesser degree, DIABETES, show poor tolerance of all intravenous radio-diagnostic compounds, the use of which should be avoided unless the possibility of benefit clearly outweighs the risk. These patients must be particularly well hydrated should intravascular iodinated injections be necessary and urine output carefully monitored.

All organic iodine contrast media interfere with tests of thyroid function. If required, such diagnostic tests should be undertaken before procedures with Hexabrix or a few weeks after the procedures.

Use in pregnancy: There is no evidence as to the drug safety in human pregnancy, nor is there evidence in animal work that it is free from hazard. Before administration of Hexabrix to women during pregnancy the benefit to the patients should be carefully weighed against the possible risk to the foetus. The ten-day rule in women of child-bearing age should be observed.

Sensitivity testing: Hypersensitivity to Hexabrix has been very rare but may be tested for by any of the standard techniques. It is doubtful, however, whether routine sensitivity testing is justified, providing careful enquiry has been made concerning a history of allergy or of untoward reactions on any previous occasion. A 'negative' sensitivity test-dose does not imply that the patient will tolerate a larger volume.

Resuscitation: It is essential to have at hand injections of adrenaline, a vasopressor, an anti-histaminic and hydrocortisone, together with appropriate sterile syringes, needles etc. Means for administering oxygen under positive pressure and maintaining an adequate air-way should always be available.

Because of the possibility, remote though it may be, of a delayed reaction to the contrast agent, the patient should never be left unsupervised for the thirty minutes immediately after the injection.

Warnings and adverse effects: In cerebral arteriography, the only frequent side-effect is facial heat, usually of mild degree. In femoral and iliac arteriography a warm feeling is usually experienced and very rarely slight pain may be felt but leg movement and/or vocal protests are unusual.

After the rapid injection of Hexabrix for angiocardiology or aortography, patients may experience a wave of mild warmth, associated with flushing passing over the body. Slight coughing may occur after right heart pulmonary artery injections. Other transient reactions reported rarely are nausea, vomiting, hypotension, headache and a metallic taste.

A few ventricular extrasystoles are common after any rapid intraventricular injection and the injection flow should not exceed 12 ml/sec in the adult ventricle. Ventricular fibrillation may occur very infrequently after intra-cardiac or intra-coronary injection and a DC defibrillator and other equipment necessary for defibrillation must always be available during these studies.

Following intracardiac, ascending aortic or coronary artery injection, the QRST complex of the ECG may be altered briefly. After prolonged cardiac catheterisation (with or without injection of a contrast medium), 5 to 10 per cent of patients may develop some degree of shivering or shock.

In intravenous urography, nausea, vomiting, dizziness and urticaria have been reported occasionally but have been of little consequence.

Toxicity and treatment of overdosage: In laboratory animals, the main signs of toxicity are convulsions, pulmonary congestion and oedema, respiratory depression, prostration, darkening of the eyes and hypersalivation; it is most unlikely that such toxic signs would occur in man, as it would be necessary to inject far greater doses than the maximum of those recommended. In man, overdosage as such should not arise but, since the causes of severe reactions to iodinated water-soluble contrast media are unknown, the information detailed under *Precautions and resuscitation* should be carefully studied.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Box of 10 x 20 ml ampoules.
Box of 10 x 50 ml bottles.

Further information Nil.

Product licence number 0012/0135

INTRAVAL* SODIUM

Presentation Intraval Sodium is presented as ampoules or bottles of Thiopentone Sodium BP.

It is supplied in ampoules of 0.5 g and bottles of 2.5 g for extemporaneous preparation of 2.5% solutions, and in ampoules of 0.5 g and 1.0 g and bottles of 5 g for extemporaneous preparation of 5.0% solution.

Uses Administered intravenously Intraval Sodium produces general anaesthesia of short duration; also used rectally.

Intraval Sodium is indicated for the induction of general anaesthesia; for general anaesthesia of short duration with or without the addition of a muscle relaxant; for the control of convulsive states. It is administered rectally for the induction of basal anaesthesia.

Dosage and administration Intraval Sodium is administered usually as a 2.5% solution, but a 5% solution is sometimes used. A 2.5% solution is advised for all elderly and bad-risk patients. The injection may be given through any superficial vein, but the most commonly used is the median cephalic at the elbow. Any other vein may be employed if the elbow site is inconvenient to the surgeon, so that the veins of the dorsum of the foot or back of the hand should be considered. Varicose veins should be avoided because of the sluggish state of blood flow in them.

Definite dosage cannot be stated for every case. The response of each patient must be observed and the dose regulated according to the onset of unconsciousness. Fractional administration is advised rather than the single-dose method, as this gives close control and greater flexibility of the anaesthetic and helps to prevent overdosage.

Most patients will require not more than 0.5 g, otherwise recovery will be prolonged and possibly complicated. The patient should in all cases be premedicated with atropine and if necessary with an analgesic or tranquilliser, although the latter will increase materially the post-operative time. If chlorpromazine (Largactil) or promethazine (Phenergan) is used for pre-medication the amount of Intraval Sodium required for induction should be reduced.

For induction: Inject 2-3 ml of the 5% or twice this volume of the 2.5% solution in 10-15 seconds, then pause for 30 seconds to 1 minute to observe the effect of the drug, depending on the state of the patient's circulation. Usually there is loss of consciousness and some relaxation. A further quantity of the solution may then be given if indicated, otherwise anaesthesia should be maintained by an appropriate inhalation agent.

For minor operations: Induction is as described above and additional quantities of the anaesthetic solution are given as required to maintain anaesthesia at a level adequate to obtund pain reflexes. The level of anaesthesia is best judged by the depth of respiration; surgical anaesthesia is usually present when respiration is depressed. It cannot be too strongly emphasised that the airway must be kept open with the patient breathing an adequate concentration of oxygen. In these circumstances the depressed respiration is not dangerous and the patient should remain a good colour with the skin warm, pink and dry.

Intravenous anaesthesia is not recommended for the maintenance of unconsciousness in lengthy procedures, so that for these, after induction, it should always be supplemented by the chosen inhalation agent.

Intraval Sodium may be employed rectally in the form of a solution for producing narcosis in 10-12 minutes. When given as a solution, it is usual to calculate dosage on the basis of 1 g per 23 kg body weight, which quantity is dissolved in 25 ml of water and instilled through a rectal catheter.

Children: Intraval Sodium is suitable for use in children as well as adults.

Contra-indications, warnings, etc There are few absolute contra-indications to the use of Intraval Sodium, but porphyria is generally considered to be completely restrictive.

There are, however, a number of relative contra-indications demanding extra care with regard to both dosage and rate of administration. In all these instances the 2.5% or a weaker solution is strongly recommended. The following is a list of such conditions: hypovolaemia, severe haemorrhage, burns, dehydration; severe anaemia; cardiovascular disease; status asthmaticus; severe liver disease; myasthenia gravis, and muscular dystrophies; adrenocortical insufficiency even when controlled by cortisone; cachexia and severe toxæmia; raised intracranial pressure; raised blood urea; raised plasma potassium; metabolic disorders, e.g. thyrotoxicosis, myxoedema, diabetes.

In obstetrics, Intraval Sodium has been considered hazardous to the foetus, but it is now generally considered that small induction doses, e.g. 250 mg, are permissible.

Reduced doses are required in the elderly and in patients heavily pre-medicated with narcotics and other central depressants. On the other hand, those addicted to drugs are difficult subjects to anaesthetise with normal thiopentone dosage and it is advised that supplementary analgesic agents and relaxants be given as necessary.

The jaw drops rapidly after starting the injection and must be supported, since it is imperative to keep the airway open. The patient should always be in a recumbent position to avoid cerebral anaemia. If Intraval Sodium is used in dental work a mouth prop is inserted before injection is commenced. The throat must be properly packed to prevent access of blood, etc. to the larynx and the dose employed should not exceed 0.25 g, otherwise recovery will be delayed. Facilities for intubation and administration of oxygen under positive pressure must always be available.

To prevent accidental intra-arterial injection the site of administration must be palpated carefully and after insertion of the needle a little blood should be drawn into the syringe to observe its colour. Intra-arterial injection produces severe arterial spasm with intense burning pain in the hand and fingers. The patient can sometimes warn the anaesthetist of this before losing consciousness. In the event of such accident, inject procaine hydrochloride directly into the artery and perform a stellate ganglion block. Early anticoagulant therapy is advisable.

Coughing, sneezing or laryngeal spasm may occur during induction. Extravasation causes pain and possible tissue necrosis. Thrombophlebitis may result from the use of 5% solution. Skin rashes, fever, arthralgia and weakness are rare side-effects. Respiratory depression during thiopentone anaesthesia must be treated by artificial ventilation with oxygen, as also cardiac arrhythmia associated with anoxia or hypercarbia. A fall in blood pressure is often noted initially, while overdose may lead to circulatory failure.

Apnoea or serious respiratory depression must be treated by controlled respiration with oxygen. Cardiovascular collapse requires immediate lowering of the head of the table; if the blood pressure fails to rise a pressor agent such as mephentermine or a plasma expander should be given. If the heart stops immediate massage should be given.

Pharmaceutical precautions Aqueous solutions of thiopentone sodium are strongly alkaline; a 2.5% solution has a pH about 10.5. The solution is incompatible with acids, acidic salts and oxidising agents. Solutions decompose on standing giving cloudiness, precipitation or crystallisation; any such solution must not be used.

Solutions should be freshly prepared and used within 24 hours.

Legal category POM.

Package quantities For the preparation of a 2.5% solution: Ampoules of 0.5 g in boxes of 10 and 25. Multidose container of 2.5 g.

For the preparation of a 5% solution: Ampoules of 0.5 g and 1 g in boxes of 10 and 25. Multidose container of 5 g.

Further information Nil.

Product licence number 0012/5043.

LARGACTIL*

Presentation White, sugar-coated tablets containing 10 mg, 25 mg, 50 mg and 100 mg chlorpromazine hydrochloride, printed in black 'Largactil 10', '25', '50' and '100' respectively.

Pale straw-coloured injection solution 1%, ampoules of 5 ml.

Pale straw-coloured injection solution 2.5%, ampoules of 1 ml and 2 ml.

Syrup coloured brown, each 5 ml containing 25 mg chlorpromazine hydrochloride.

Forté suspension coloured orange, each 5 ml containing 145 mg chlorpromazine embonate equivalent to 100 mg chlorpromazine hydrochloride.

Cream-coloured suppositories each containing 100 mg chlorpromazine base.

Uses Largactil has marked activity affecting both the autonomic and central nervous systems. It has a powerful, peripheral anti-adrenaline action but relatively limited antihistamine activity.

It has a marked psycho-corrective action. Other central effects of the drug include the suppression of psychomotor overactivity and the induction of a state of mental calm and tranquillity. Largactil also enhances the effects of some central nervous depressants, including most hypnotics, analgesics and anaesthetics, thus substantially reducing the amount of these agents required. Largactil is indicated in the following:

1. Psychiatry:

- As a neuroleptic and sedative: in schizophrenia, in other psychoses, including the manic or hypomanic phases of manic-depressive psychosis; as an adjunct to ECT.
- Agitation accompanying depression.
- Disturbances induced by drugs such as LSD, mescaline and psilocybin.
- In psychoneuroses, as a sedative in anxiety and tension states and in anorexia nervosa.
- Behaviour disturbances resulting from organic brain disease and in subnormality and in psychopaths.

2. General medicine:

- In the management of terminal illness, to enhance the effect of analgesics and to control nausea and vomiting.
- In the control of the intractable hiccup.

- (c) In eclampsia and pre-eclampsia.
- (d) In behaviour disturbances resulting from organic brain disease and in subnormality.
- (e) Treatment of anxiety states.

3. Anaesthetics:

- (a) As a routine anti-emetic before operation, or as required during the post-operative period.
- (b) In association with pethidine, with or without atropinising drugs.
- (c) To enhance or facilitate anaesthesia with minimal amounts of the usual anaesthetic agents, used immediately before or during operation.
- (d) To facilitate the induction of hypothermia and to prevent shivering.

Dosage and administration Dosage varies with the individual and the purpose for which the drug is used, so that the following dosages are only for general guidance with regard to possible effectiveness and good tolerance. Initial dosages should be low, with increments at frequent, regular intervals until the desired response is obtained. Dosage intervals are usually six to eight hours, but in some patients the 24-hour requirement may be conveniently administered in a single bedtime dose. Whenever possible the oral route of administration should be used, patients who are unable or refuse to swallow tablets should receive the equivalent dose of Largactil Syrup or Largactil Forte Suspension (under no circumstances should Largactil Tablets be crushed).

It may be essential to give the drug parenterally in the initial stages of treatment in psychiatric cases. Injectable solutions of Largactil are irritant, but the deep intramuscular route is moderately well tolerated for short periods. Subcutaneous injection is absolutely contra-indicated.

When it is impossible or undesirable to administer Largactil orally or parenterally the rectal route may be used. Each Largactil Suppository contains 100 mg chlorpromazine base and has an effect comparable with that of 40–50 mg by mouth, or 20–25 mg intramuscularly.

Adults: Oral: The initial dosage for ambulant patients is 25 mg three times daily, increased by 25 mg daily to an effective but tolerable level, after which maintenance dosage should be established in the range of 75–300 mg per day.

Bed patients may start treatment with double the above doses. Patients with psychoses may require much larger doses than indicated above, the 24-hour requirement of some may be 1,000 mg.

Parenteral: A single intramuscular injection of 25–50 mg followed by oral therapy will suffice in many cases, but the intramuscular dose may be repeated if required at six- to eight-hour intervals. As soon as possible the treatment should be transferred to oral administration, using the parenteral route to supplement the oral dosage when required.

Rectal: One 100 mg suppository is given as required; it may be repeated at intervals of six to eight hours. The onset of action is slower and duration of effect more prolonged than with oral administration.

Children: Over 5 years of age, one-third to one-half of the adult dosage may be given; below this age the dose is 5–10 mg. These doses may be repeated three times a day as required. For the control of severe symptoms the same doses may be injected by the intramuscular route; alternatively, a suppository (100 mg), or a portion thereof, may be used if necessary.

Contra-indications, warnings, etc Largactil is contra-indicated in cases of coma due to direct central nervous depressants such as alcohol, barbiturates and opiates; its use for minor ailments should be avoided in patients with known liver dysfunction.

It should be used with caution (1) where a low leucocyte count is known to exist and in patients receiving drugs known to cause leucopenia; and (2) in the presence of an acute infection unrelated to the condition for which Largactil is indicated.

It may be advisable to modify or restrict the use of Largactil in patients with existing tachycardia or cardiac insufficiency; careful dosage adjustment may be necessary if other drugs likely to cause postural hypotension are being taken.

During the initiation of Largactil therapy it is advisable that certain activities should be suspended for some days, e.g. the driving of vehicles or operating of machinery, until it is evident that any undue drowsiness has either subsided or not appeared.

Since Largactil may mask conditions such as intestinal obstruction, it is important to establish accurate diagnosis before the drug is used to relieve severe vomiting.

If Largactil is employed in labour it should be withheld until labour is established and the cervix dilated 3–4 cm.

Largactil is usually well tolerated, but drowsiness, which rapidly disappears, may occur at the start of treatment with dry mouth, nasal stuffiness and other atropine-like effects occurring in some. Insomnia and mild agitation are rare side-effects.

As with all drugs, Largactil should not be given during pregnancy or lactation unless the physician considers it essential.

Patients treated parenterally may develop postural hypotension with tachycardia during the initiation of treatment. Pain at the site of injection followed by nodule formation may occur. With high dosage, body temperature may fall while in some there is a paradoxical rise in temperature without apparent underlying cause.

Liver function: Jaundice, usually transient, occurs in a very small percentage of patients taking chlorpromazine. A premonitory sign may be a sudden onset of fever after one to three weeks of treatment followed by the development of jaundice. Chlorpromazine jaundice has the biochemical and other characteristics of obstructive jaundice and is associated with obstruction of the canaliculi by bile thrombi; the frequent presence of an accompanying eosinophilia indicates the allergic nature of this phenomenon. Treatment should be withheld on the development of jaundice.

Blood picture: No changes in the red cell count or haemoglobin percentage have been observed, but a raised ESR may be noted. Leucocytosis or leucopenia have variously been reported; agranulocytosis may occur in sensitive patients.

Skin and eyes: Contact skin sensitisation is a serious but fortunately rare complication in those frequently handling preparations of chlorpromazine; the greatest care must be taken to avoid contact of the drug with the skin. Skin rashes of various kinds may also be seen in patients treated with the drug. Patients on high dosage may develop photosensitivity in sunny weather.

Ocular changes and the development of a metallic greyish-mauve coloration of exposed skin have been noted in some individuals, mainly females, who have received chlorpromazine continuously for long periods (four to eight years) in a daily dosage range from 500 mg

to 1.5 g or more. The reactions become less intense when the drug is withheld.

Parkinsonism: Patients receiving continuous chlorpromazine may develop a parkinsonian-like syndrome which responds to withdrawal of the drug or concurrent administration of an anti-parkinsonian drug.

Treatment of overdosage: In the absence of a specific antidote, should include gastric lavage; countering of acute hypotension by the adoption of a supine or head-down position, a plasma expander and use with care, as Largactil may reverse the normal response, of phenylephrine or possibly of noradrenaline by intravenous drip infusion; the conservative symptomatic treatment of central nervous depression as advocated for acute barbiturate toxicity, including physiotherapy and antibiotics to prevent bronchopneumonia. Haemodialysis is ineffective. Body temperature should be allowed to recover naturally unless it falls below 30°C, at which level cardiac arrhythmias may occur. A special watch should be kept for the development of intestinal and bladder distension.

Pharmaceutical precautions Protect from light. Largactil Injection Solutions, on exposure to light, rapidly develop a pink or yellow coloration; any such solution should be discarded. Largactil Injection Solutions have a pH of 5.0–6.5; they are incompatible with benzylpenicillin potassium, pentobarbitone sodium and phenobarbitone sodium. Largactil Forte Suspension and Syrup may be diluted, if required, with simple syrup (without preservatives).

Legal category POM.

Package quantities Tablets 10 mg and 25 mg: Containers of 500. 50 mg and 100 mg: Containers of 50 and 500.

Injection Solution 1%: Box of 10 × 5 ml ampoules.

Injection Solution 2.5%: Box of 10 × 1 ml ampoules.

Injection Solution 2.5%: Boxes of 10 × 2 ml ampoules.

Syrup: Bottles of 125 ml, 1 litre and 2 litres.

Forte Suspension: Bottle of 1 litre.

Suppositories: Boxes of 5 and 50.

Further information Nil.

Product licence numbers

Tablets 10 mg	0012/5108
Tablets 25 mg	0012/5109
Tablets 50 mg	0012/5110
Tablets 100 mg	0012/5111
Injection Solution 1%	0012/5082
Injection Solution 2.5%	0012/5308
Syrup	0012/5083
Forte Suspension	0012/5001
Suppositories	0012/5084

LIPIODOL* ULTRA FLUID

Presentation Lipiodol Ultra Fluid is a pale-yellow oil which is a sterile iodine addition product of the ethyl esters of the fatty acids of poppyseed oil, containing approximately 38% w/v organically combined iodine.

Uses An X-ray contrast medium for use in certain radiological investigations where it is desirable to outline a viscus or other structure with directly instilled radio-opaque material. From most sites in the body it is slowly

absorbed, but from the peritoneal cavity (after hysterosalpingography) absorption is relatively rapid.

On account of its low viscosity Lipiodol Ultra Fluid is suitable for introduction into narrow channels and may therefore be used in ducts and sinuses.

Dosage and administration The medium should be administered via a suitable syringe and cannula, the volume to be administered depending on the technique being carried out.

Lipiodol Ultra Fluid may be used for children at the surgeon's discretion.

Contra-indications, warnings, etc Care should be taken in those subjects presenting a history of previous allergic manifestations or of thyroid dysfunction. The injection of the medium into certain fistulae should be conducted with great care in order to avoid penetration of vascular channels and the possibility of oil embolism. The medium is therefore contra-indicated in cases of recent haemorrhage.

Lipiodol Ultra Fluid is unsuitable for bronchography as it would rapidly fill the bronchioles and the alveoli.

Iodine idiosyncrasy – it is strongly recommended that the patient be tested before the administration of Lipiodol Ultra Fluid in other than small amounts.

Iodism occurs more frequently with Lipiodol than with water-soluble organic iodine derivatives.

Pharmaceutical precautions Protect from light. If the product becomes opaque or dark amber in colour it should not be used.

Legal category P.

Package quantities Ampoule of 10 ml.

Further information Lipiodol Ultra Fluid has been shown to dissolve polystyrene; for this reason disposable syringes made from this material must not be used to administer this preparation.

Product licence number 0012/5061.

M&B* ANTISEPTIC CREAM

Presentation M&B Antiseptic Cream is a smooth, white cream of the oil-in-water type containing 0.15% w/w propamidine isethionate.

Uses Propamidine isethionate is a powerful antibacterial agent which is highly active against pathogenic, streptococci and staphylococci, including penicillin-resistant strains, and has some activity against a number of Gram-negative bacilli. Its antibacterial action is not inhibited by pus, blood or *p*-aminobenzoic acid. In addition, it has useful activity against species of pathogenic fungi. M & B Antiseptic Cream may be used as a first-aid treatment for minor burns, scalds, abrasions and other open injuries, and their routine treatment.

Dosage and administration The lesion should be cleansed with normal saline or detergent solution (although some workers avoid preliminary cleansing in the case of burns) and M & B Antiseptic Cream is spread on gauze or on a sterile dressing (for burns) which is applied to the lesion. The number and frequency of re-applications of the cream are determined mainly by the amount of discharge. When infection has been eliminated, subsequent treatment will depend on the extent and severity of the injury. Small areas may be left to epithelialise naturally under the serum scab.

Contra-indications, warnings, etc Prolonged use may interfere with healing.

There is always the possibility, although rare, of a sensitisation reaction occurring; in such an event, treatment should be discontinued immediately.

Pharmaceutical precautions Nil.

Legal category GSL.

Package quantities Tube of 25 g.

Further information Nil.

Product licence number 0012/5270.

MYOCRISIN*

Presentation Ampoules containing injection solutions of varying strengths of sodium aurothiomalate. The solutions are pale yellow.

Uses Active Progressive Rheumatoid Arthritis (including Stills Disease).

Dosage and administration Myocrisin is administered by deep intramuscular injection, followed by gentle massage of the area.

Adults:

1. Remission Induction. Injections of 1 mg, 5 mg, and 10 mg at weekly intervals followed by 20–50 mg per week until remission occurs or a total of 1 gram has been given. Remission should occur around the 400–500 mg level.

2. Maintenance. 20–50 mg every 2–4 weeks should be administered according to response.

Children: (Stills Disease). The dosage is based on body weight. Therapy should be initiated with small weekly doses (1 mg/kg) up to a maximum weekly dose of:

Body weight under 20 kg	10 mg
Body weight 20–50 kg	20 mg
Body weight over 50 kg	30 mg

Treatment should be continued for six months. Response can be expected at the 300–500 mg level. If patients respond, maintenance therapy should be continued with the dosage administered over the previous 2–4 weeks for 1–5 years.

Contra-indications, warnings, etc Pregnancy. In patients with gross renal or hepatic disease, a history of blood dyscrasias, exfoliative dermatitis or systemic lupus erythematosus.

The absolute contra-indications should be positively excluded before considering gold therapy. Myocrisin should be administered with extra caution in the elderly and in patients with a history of urticaria, eczema or colitis. Extra caution should also be exercised if phenylbutazone or oxyphenbutazone are administered concurrently.

Before starting treatment and again before each injection, the urine should be tested for protein, the skin inspected for rash and a full blood count performed, including a numerical platelet count (not an estimate) and the readings plotted. Blood dyscrasias are most likely to occur when between 400 mg and 1 gram of gold have been given, or between the 10th and 20th week of treatment, but can also occur with as little as 40 mg or after only 2–4 weeks of therapy.

The presence of albuminuria, pruritus or rash, or an eosinophilia, are indications of developing toxicity; the Myocrisin should be withheld for one or two weeks until

all signs have disappeared when the course may be restarted on a smaller dosage.

A complaint of sore throat, glossitis, buccal ulceration and/or easy bruising or bleeding, demands an immediate blood count, followed, if indicated by appropriate treatment for agranulocytosis and/or thrombocytopenia. Every patient treated with Myocrisin should be warned, both in writing and verbally, to report immediately the appearance of pruritus, metallic taste, sore throat or tongue, buccal ulceration or easy bruising, purpura, epistaxis, bleeding gums, menorrhagia or diarrhoea.

Diffuse unilateral or bilateral pulmonary fibrosis very rarely occurs. This progressive condition usually responds to drug withdrawal and steroid therapy – annual chest X-ray is recommended and attention should be paid to unexplained breathlessness and dry cough.

Side-effects may be largely avoided by the indicated careful titration of dosage. Minor reactions, usually manifest as skin rashes, are the most frequent and commonly benign, but as such reactions may be the forerunners of severe gold toxicity they must never be treated lightly. Significant skin complications are almost exclusively pruritic.

Treatment of overdosage: Minor side-effects resolve spontaneously on withdrawal of Myocrisin. Symptomatic treatment of pruritus with antihistamines may be helpful. Major skin lesions and serious blood dyscrasias demand hospital admission when dimercaprol or penicillamine may be used to enhance gold excretion. Fresh blood and/or platelet transfusions, corticosteroids and androgenic steroids may be required in the management of severe blood dyscrasias.

Pharmaceutical precautions Protect from light. Discoloured solutions should not be used.

Legal category POM.

Package quantities Boxes of 10 × 1 mg, 5 mg, 10 mg, 20 mg and 50 mg ampoules.

Further information Some rheumatologists provide their patients with a 'gold card' on which is recorded the amount of gold salt injected and results of laboratory tests, at the same time issuing a proforma for further treatment to the general practitioner responsible for the management of the patient. These are valuable aids in the early detection, and so reduce the incidence of toxic reactions.

Product licence numbers

Injection 0.2%	0012/5116
Injection 1%	0012/5115
Injection 2%	0012/5114
Injection 4%	0012/5113
Injection 10%	0012/5006

NEULACTIL*

Presentation Neulactil tablets contain 2.5, 10 or 25 mg pericyazine. They are yellow, uncoated and embossed 'Neulactil', 'Neulactil 10' or 'Neulactil 25' respectively on one face with a break line on the reverse.

Neulactil Forte Syrup is brown and contains 10 mg pericyazine in each 5 ml.

Uses The cardiovascular and antihistaminic effects of pericyazine are similar to those of chlorpromazine, but it has a stronger antiserotonin effect and a powerful central sedative action. It exerts a specific action as an inhibitor of aggression and impulsiveness, thus modifying dis-

turbed behaviour such as occurs in mental subnormality and senile dementia or the schizophrenic patient during a disturbed phase.

Children with behaviour disorders or showing aggressive disturbed behaviour may respond well to Neulactil. It has been used with success to control outbursts of violent behaviour in the aggressive psychopath. Other uses include the treatment of severe cases of anxiety and tension states or as a maintenance psycho-sedative for discharged hospital patients.

Dosage and administration In all cases, dosage should be progressively increased until the most effective level is reached, after which dosage should be adjusted to maintain control of symptoms.

General practice: Mild to moderate conditions.

Adults: The initial daily dose is 15–30 mg divided into two portions, with the larger dose being given in the evening.

Geriatric: The starting dose is 10 mg per day, being increased as necessary – dosage should be divided and the larger portion given in the evening.

Hospital practice: Adult patients with moderate to severe conditions.

Oral: Initial dosage is 75 mg per day in divided doses. The dosage should be increased by 25 mg weekly until an optimum effect is achieved.

Geriatric: The initial dosage is 30 mg per day, but once tolerance has been established this may be increased steadily until the disturbed behaviour is controlled.

Children: The initial daily dosage should be 0.5 mg per year of age. In older children (16 years) the dose should not exceed 30 mg in 24 hours with a daily maintenance dose of 1 mg per year of age. Dosage up to 75 mg per day is permissible in hospitals.

Contra-indications, warnings, etc If Neulactil is prescribed in conjunction with other centrally acting drugs the usual dose of these compounds should be reduced by at least half whilst the new treatment is being gradually introduced. Subsequent doses of either should be determined by the patient's response.

There have been a few isolated reports to the effect that some children and geriatric patients are hypersensitive to the hypotensive effects of Neulactil. Such effects usually develop within the first two days of treatment and, when they occur, treatment should be discontinued.

The use of Neulactil should be modified or restricted in patients with existing tachycardia, cardiac insufficiency or any circulatory disturbance.

Activities such as the control of vehicles or machinery should not be undertaken until it is evident that any transient soporific effect has subsided.

No embryopathic effects have been recorded, but as with all drugs Neulactil should not be given during pregnancy or lactation unless the physician considers it essential.

Experience indicates that it is unlikely to give rise to photosensitisation or to cholestatic jaundice.

The following side-effects have been occasionally observed:

1. Initial drowsiness, which usually wears off within a few days.
2. Postural hypotension and tachycardia sometimes associated with fainting attacks, especially in children and geriatric patients.

3. Extrapyramidal effects such as tremor, muscular restlessness, mild hypertonus and other symptoms associated with high dosage.

4. Autonomic disturbances such as sweating and sialorrhoea.

Careful adjustment of dosage by giving the larger portion in the evening will lessen these effects.

As there is no specific antidote, patients should be carefully nursed and treated symptomatically after gastric lavage to remove any drug still present in the stomach. An anti-parkinsonian agent and a pressor amine (other than adrenaline) should be available. Haemodialysis has not proved an effective treatment of these cases.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Containers of 500 × 2.5 mg and 10 mg tablets and of 50 × 25 mg tablets.

Forte syrup (10 mg per 5 ml) in bottles of 1 litre.

Further information Nil.

Tablets 2.5 mg	0012/5276
Tablets 10 mg	0012/5277
Tablets 25 mg	0012/5278
Forte Syrup	0012/5016

NIVAQUINE*

Presentation White tablets, each containing 200 mg chloroquine sulphate (equivalent to 150 mg chloroquine base), embossed Nivaquine 200 on one face, with a break line on the reverse.

A red syrup, containing 68 mg chloroquine sulphate (equivalent to 50 mg chloroquine base), in each 5 ml.

Uses Nivaquine is a 4-aminoquinoline compound which has a high degree of activity against the asexual erythrocytic forms of all species of malaria parasites. It is indicated for the suppression and clinical cure of all forms of malaria and, in addition, produces radical cure of falciparum malaria.

Nivaquine also exerts a beneficial effect in certain collagen diseases and protects against the effects of solar radiation. It is employed in the treatment of rheumatoid arthritis, juvenile rheumatoid arthritis, discoid and systemic lupus erythematosus and skin conditions aggravated by sunlight.

Nivaquine is also active against *Entamoeba histolytica* and *Giardia lamblia* and when Flagyl (metronidazole) is not available it may be used in hepatic amoebiasis and giardiasis.

Dosage and administration **Adults:** Rheumatoid arthritis: 1 × 200 mg tablet daily.

Lupus erythematosus: 1 × 200 mg tablet daily until maximum improvement is obtained, followed by a smaller maintenance dose.

Light sensitive skin eruptions: 1 or 2 × 200 mg tablets daily during the period of maximum light exposure.

Children's dosage: 3 mg/kg bodyweight daily.

Treatment should be discontinued if no improvement has occurred after six months.

Suppression of malaria: **Adults:** 2 × 200 mg tablets in a single dose, on the same day each week during exposure.

Children: 5 mg/kg (as chloroquine base) at weekly intervals.

This may be conveniently administered as Nivaquine syrup according to the following schedule:

1-2 years	1 × 5 ml spoonful
3-4 years	1½ × 5 ml spoonfuls
5-7 years	2 × 5 ml spoonfuls
8-10 years	3 × 5 ml spoonfuls
11-12 years	4 × 5 ml spoonfuls

It is advisable to start taking Nivaquine two weeks before entering an endemic area and to continue for six weeks after leaving.

Treatment of malaria: Adults and children over 10 years: for partially immune subjects a single dose of 4 × 200 mg tablets will provide a safe and effective course of treatment.

In non-immune subjects treatment should consist of 4 × 200 mg tablets in one dose, followed by 2 × 200 mg tablets after six hours and then 2 × 200 mg tablets daily for the next two days.

The above dosage is intended as a guide in the treatment of *P. falciparum* malaria; due to variation in strain sensitivity it may sometimes be necessary to increase the dosage up to 14 tablets (2,100 mg base) given over a period of five days.

Infants and children under 10 years: In partially immune subjects, the child should be given the number of 5 ml spoonfuls of Nivaquine Syrup equal to its age next birthday. The syrup or the equivalent dosage in tablets may be given as a single dose or divided into two with six hours between doses.

In non-immune subjects the dosage given above should be regarded as the first dose. This should be followed by a second dose, half the size of the first after six hours. This second dose should then be repeated once on each of the next two days.

In the above schemes tablets can be substituted for the syrup if desired (3 × 5 ml spoonfuls of Nivaquine Syrup are equivalent to 1 × 200 mg tablets).

Contra-indications, warnings, etc Nivaquine is generally contra-indicated in pregnancy. However, clinicians may decide to administer Nivaquine to pregnant women for the prevention or treatment of malaria. There is evidence that high doses throughout pregnancy can give rise to foetal cochlear damage.

Caution is advised in cases of porphyria, hepatic or renal disease, severe gastro-intestinal, neurological and blood disorders and in patients receiving anticoagulant therapy.

Retinopathy: Irreversible retinal damage may occur with prolonged treatment. Ophthalmological examination should always be carried out before and regularly (3-6 monthly intervals) during treatment. Retinal damage is particularly likely to occur if treatment has been given for longer than one year, or if the total dosage has exceeded 1.6 g/kg bodyweight. These precautions also apply to patients receiving chloroquine continuously at weekly intervals as a prophylactic against malarial attack for more than three years.

Nivaquine has a temporary effect on visual accommodation and patients should be warned regarding driving or operating machinery. Bone marrow depression, including aplastic anaemia, occurs rarely. Full blood counts should therefore be carried out regularly during extended treatment.

The more common side-effects include gastro-intestinal disturbances, headache and skin eruptions. Depigmentation or loss of hair may also occur. Corneal opacities and visual disturbances may occur, apart from

retinal damage. These usually disappear on cessation of treatment.

Treatment of overdosage: Prompt measures will be required to counteract the depressant effect of the drug on the respiratory and cardiovascular systems. Vomiting should be induced or gastric lavage carried out as soon as possible followed by appropriate resuscitative measures, such as tracheal intubation with artificial respiration and the administration of vasopressor agents or intravenous fluids. Intravenous ½ molar sodium lactate solution has been used to counteract the quinidine-like action of chloroquine on the myocardium. The administration of enteric-coated ammonium chloride tablets 0.5 g every eight hours to promote excretion of the drug is also recommended.

Pharmaceutical precautions Nivaquine Syrup should be protected from light.

Legal category POM. When supplied for prevention of malaria in a container specifically labelled for that purpose P.

Package quantities Containers of 100 tablets and 125 ml bottle of syrup.

Further information Nil.

Product licence numbers

Tablets 0012/5260

Syrup 0012/5020

NOZINAN®

Presentation Colourless injection solution 2.5% methotrimeprazine hydrochloride in ampoules of 1 ml.

Uses Management of the terminally ill patient. Methotrimeprazine resembles chlorpromazine and promethazine in the pattern of its pharmacology. It possesses anti-emetic, anti-histamine and anti-adrenaline activity and exhibits a strong sedative effect.

Nozinan potentiates the action of other central nervous system depressants but may be given in conjunction with appropriately modified doses of narcotic analgesics in the management of severe pain. Nozinan does not significantly depress respiration and is particularly useful where pulmonary reserve is low.

Nozinan is indicated in the management of terminal pain and accompanying restlessness or distress.

Dosage and administration Dosage varies with the condition and the individual response of the patient.

The usual dose for adults is 12.5-25 mg (0.5-1 ml) by the intramuscular, or after dilution with an equal volume of normal saline by the intravenous route; in cases of severe agitation up to 50 mg (2 ml) may be used, repeated every six to eight hours. Methotrimeprazine may induce postural hypotension requiring close observation of the patient.

Contra-indications, warnings, etc There are no absolute contra-indications to the use of Nozinan in terminal care.

Precautions: The hypotensive effects of Nozinan should be taken into account when it is administered to patients with cardiac disease and the elderly or debilitated. Patients receiving Nozinan should not drive or operate machinery. The safety of methotrimeprazine in pregnancy has not been established.

Side effects: Somnolence and asthenia are frequent side

effects. Dry mouth is encountered less frequently. Hypotension may occur, especially in the elderly patient. A raised ESR may occasionally be encountered and agranulocytosis has been reported as have photosensitivity and allergic skin reactions.

Parkinsonian-like reactions may occur in patients receiving prolonged high dosage. Jaundice is a rare side-effect.

Treatment of overdosage should include countering acute hypotension by the adoption of either a supine or head-down position, and possibly the use of phenylephrine or noradrenaline by intravenous drip infusion; the active symptomatic treatment of central nervous depression is not usually required. Haemodialysis is ineffective. Body temperature should be allowed to recover naturally unless it falls below about 29.4°C at which level cardiac arrhythmias may develop. A special watch should be kept for intestinal and urinary bladder distension.

Pharmaceutical precautions Protect from light. Nozinan Injection Solution, on exposure to light, rapidly develops a pink or yellow colouration and any such solution should be discarded. Nozinan Injection Solution is incompatible with alkaline solutions.

Legal category POM.

Package quantities Injection Solution 2.5%, Box of 10 × 1 ml ampoules.

Further information Nil.

Product licence number 0012/5007.

OCUSERT®

Presentation Ocuser Pilocarpine therapeutic systems are elliptically-shaped units designed to release pilocarpine continuously following placement into the upper or lower conjunctival sac. The systems consist of a core reservoir of pilocarpine surrounded by a membrane which controls the drug's diffusion from the system into the tear fluid. Two systems are available, Pilo-20 and Pilo-40, which release 20 and 40 mcg per hour, respectively, for one week. The Pilo-20 system is 5.7 × 13.4 mm across its axis, 0.3 mm thick, and contains 5 mg pilocarpine, the Pilo-40 system is 5.5 × 13 mm on its axis, 0.5 mm thick, and contains 11 mg pilocarpine. Except for the opaque white margin, the systems are clear.

Uses The Ocuser pilocarpine system is indicated for control of elevated intra-ocular pressure in glaucoma in pilocarpine-responsive patients.

Dosage and administration *Initiation of therapy:* The Ocuser Pilo-20 system will usually control a patient previously controlled by 1 per cent or 2 per cent pilocarpine eye drops; a patient who has used higher strengths of pilocarpine eye drops may require the Pilo-40. However, there is no direct correlation between the two strengths of Ocuser and the strength of pilocarpine eye drops necessary to achieve the required reduction of pressure. The Ocuser systems reduce the amount of pilocarpine necessary to achieve adequate reduction of intra-ocular pressure; therapy may be started therefore with the Ocuser Pilo-20 system irrespective of the strength of pilocarpine eye drops used previously by the patient. If the pressure is satisfactorily reduced with the Ocuser Pilo-20 system the patient should continue its use, replacing each unit every seven days; if greater reduction of intra-ocular pressure is required, the patient

should be transferred to the Pilo-40 system. Depending on the patient's age, family history, and disease status, the ophthalmologist may elect to begin therapy with the Pilo-40 system.

Concomitant therapy: Where necessary, adrenaline or timolol eye drops or a diuretic of the carbonic anhydrase inhibitor type may be used concurrently with Ocuser systems. The release rate of pilocarpine from the Ocuser systems is not influenced by the beta adrenoceptor antagonist, by carbonic anhydrase inhibitors, adrenaline eye drops, fluorescein, or local anaesthetics, antibiotics or anti-inflammatory steroid eye drops.

Placement and removal of the Ocuser systems: Patient instructions for the placement of the Ocuser systems in the eye and their removal are included in each package. It is strongly recommended that the patient's ability to manage the placement and removal of the system be reviewed at the first patient visit after initiation of therapy.

Since pilocarpine-induced myopia from the Ocuser systems may occur during the first few hours of therapy, the patient should be advised to place the system into the conjunctival sac at bedtime. By morning the induced myopia is at a stable level.

Handling precautions: Patients should be instructed to wash their hands thoroughly with soap and water before touching or manipulating the Ocuser systems. If a displaced unit contacts unclean surfaces, rinsing with cool tap water before replacing is advisable. Biologically contaminated units should be discarded and replaced with fresh ones.

Retention in the eye: During the initial adaptation period, the Ocuser unit may slip out of the conjunctival sac on to the cheek. The patient is usually aware of such movement and can replace the unit without difficulty.

In those patients in whom retention of the Ocuser unit is a problem, placement in the upper conjunctival sac is often more acceptable. The Ocuser unit can be manipulated from the lower to the upper conjunctival sac by a gentle digital massage through the lid, a technique readily learned by the patient. For best retention, the unit should be moved before sleep to the upper conjunctival sac. Should the unit slip out of the conjunctival sac during sleep, its ocular hypotensive effect continues for a period of time comparable to that following instillation of eye drops. The patient should be instructed to check for the presence of the Ocuser unit before sleep and on rising.

Contra-indications, warnings, etc Ocuser systems are contra-indicated where pupillary constriction is undesirable, such as glaucomas associated with acute inflammatory disease of the anterior segment of the eye, and glaucomas occurring or persisting after extracapsular cataract extraction where posterior synechiae may occur.

Ocuser systems should not be used in patients with acute infectious conjunctivitis or keratitis except on specialist advice. Damaged or deformed systems should not be placed or retained in the eye. Systems believed to be associated with an unexpected increase in drug action should be removed and replaced with new systems.

The safety of Ocuser systems in patients with retinal detachment or with filtration blebs has not been established. Although eye drops have been used effectively in conjunction with the Ocuser systems, systemic reactions consistent with an increased rate of absorption from the eye of an autonomic drug, such as adrenaline, have been observed. In rare instances, reactions of this type can be severe. The conjunctival erythema and oedema associ-

ated with adrenaline eye drops are not substantially altered by concomitant use of an Ocusert system. The use of pilocarpine eye drops should be considered when intense miosis is desired in certain ocular conditions.

Ciliary spasm is encountered with pilocarpine usage but is not a contra-indication to continued therapy unless the induced myopia is debilitating to the patient. Irritation from pilocarpine has been frequently encountered and may require cessation of therapy depending on the judgement of the doctor. True allergic reactions are uncommon but require discontinuation of therapy if they occur.

Although withdrawal of the peripheral iris from the anterior chamber angle by miosis may reduce the tendency for narrow angle closure, miotics can occasionally precipitate angle closure by increasing the resistance to aqueous flow from posterior to anterior chamber. Miotic agents may also cause retinal detachment; thus, care should be exercised with all miotic therapy especially in young myopic patients.

Some patients may notice signs of conjunctival irritation, including mild erythema with or without a slight increase in mucous secretion when they first use Ocusert systems. These signs tend to lessen or disappear after the first week of therapy. In rare instances a sudden increase in pilocarpine effects has been reported.

Pharmaceutical precautions Store in a refrigerator at 2° to 8°C, i.e. not in the freezer compartment.

Legal category POM.

Package quantities Ocusert Pilo-20 or Ocusert Pilo-40 systems are available in containers of eight individual sterile systems.

Further information The decrease in intra-ocular pressure obtained with both the Pilo-20 and Pilo-40 systems is fully established within 1½ or 2 hours after placement in the conjunctival sac and is maintained for 24 hours a day for seven days. Intra-ocular pressure reduction with Ocusert systems for an entire week is achieved with either 3.4 mg or 6.7 mg pilocarpine (20 mcg or 40 mcg times 24 × 7, respectively), as compared with 28 mg of pilocarpine administered as a 2 per cent ophthalmic solution four times a day.

Ocusert systems may be used in association with contact lenses.

Product licence numbers

Pilo-20 0012/0118

Pilo-40 0012/0119

ORUDIS®

Presentation Capsules each containing 50 mg ketoprofen, bicoloured (opaque green/opaque purple) with each half printed 'Orudis 50' in white. Capsules each containing 100 mg ketoprofen (flesh opaque) printed 'Orudis 100' in black.

Suppositories each containing 100 mg ketoprofen.

Uses Orudis is a potent non-steroidal anti-inflammatory analgesic agent and a strong inhibitor of prostaglandin synthetase.

Orudis is recommended in the management of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, acute articular and periarticular disorders (bursitis, capsulitis, synovitis, tendinitis), fibrositis, cervical spondylitis, low back pain (strain, lumbago, sciatica, fibrositis), painful musculo-skeletal conditions and dysmenorrhoea.

Orudis reduces joint pain and inflammation, and facilitates increase in mobility and functional independence. As with other non-steroidal anti-inflammatory agents, it does not cure the underlying disease.

Dosage and administration Orudis is administered orally and/or rectally; to limit occurrence of gastrointestinal disturbance, capsules should always be taken with food (milk, meals).

Oral dosage is 50–100 mg twice daily, depending on patient weight and on severity of symptoms; medication should be taken early in the morning and late at night.

Rectal dosage is one suppository (100 mg) late at night supplemented as required with Orudis capsules during daytime.

If adverse effects (see below) develop on 100 mg orally twice daily, morning dosage, and if necessary night-time dosage also, should be reduced for several days to 50 mg night and morning, and then increased slowly, as tolerated; some patients are adequately controlled with oral night-time only treatment (100–200 mg).

Orudis suppositories are especially appropriate for controlling overnight symptoms (severity of night and morning pain; duration and severity of morning stiffness). Suppositories administered late at night provide more consistent effective control of overnight symptoms than oral medication.

Best results are obtained by titrating dosage to suit each patient; start with a low dosage in mild chronic disease and a high dosage in acute severe disease. Some patients derive greater benefit by treatment with capsules only; some with a combined capsule/suppository regimen; and others with a higher dosage at night-time than at early morning. Where patients require a maximum oral dosage initially, an attempt should be made to reduce this dosage for maintenance since lower dosage might be better tolerated for purposes of *long-term* treatment. Paediatric dosage not established.

Contra-indications, warnings, etc Active peptic ulceration; a history of recurrent peptic ulceration or chronic dyspepsia; disease in children (safety/dosage during long-term treatment has not been established).

Suppositories should not be used following recent proctitis or in association with haemorrhoids.

Ketoprofen should not be given to patients sensitive to aspirin or other non-steroidal anti-inflammatory agents known to inhibit prostaglandin synthetase. Severe bronchospasm might be precipitated in these subjects, and in patients suffering from, or with a history of, bronchial asthma or allergic disease.

Precautions *Pregnancy and lactation:* Embryopathic effects have not been recorded with this drug but it is recommended to avoid medication during pregnancy and lactation.

Plasma protein-binding drugs: Orudis is highly protein-bound. Concomitant use of other protein-binding drugs, e.g. anticoagulants, sulphonamides, hydantoins, might necessitate modification of dosage in order to avoid increased levels of such drugs resulting from competition for plasma protein-binding sites.

Warning and adverse effects: Gastro-intestinal intolerance may occur and, very rarely, gastro-intestinal haemorrhage. Orudis capsules should always be prescribed 'To be taken together with food'.

Adverse effects, frequently transient, include indigestion, dyspepsia, flatulence, heartburn, abdominal dis-

comfort, nausea and, very rarely, skin rashes. Bronchospasm might be precipitated in patients suffering from or with a history of bronchial asthma or allergy. Use of suppositories is sometimes associated with change in stool consistency, mostly of mild softening. In a study of 64 patients treated for up to six months with one suppository each night (supplemented during daytime with 'Orudis' capsules), local intolerance to suppositories sufficiently severe to discontinue treatment occurred in only four subjects.

Pharmaceutical precautions Store in a dry place, below 25°C.

Legal category POM.

Package quantities Orudis 50: Containers of 100 × 50 mg and 500 × 50 mg capsules.

Orudis 100: Containers of 100 × 100 mg capsules.

Blister pack of 7 × 100 mg suppositories.

Further information Nil.

Product licence numbers

50 mg capsules 0012/0122

100 mg capsules 0012/0133

100 mg suppositories 0012/0109

ORUVAIL ▼

Presentation Transparent pink capsules with opaque purple cap (each half printed 'Oruvail' in white), holding white pellets. Each capsule contains 100 mg Ketoprofen in a pH sensitive controlled release delivery system.

Uses Oruvail is a potent non-steroidal anti-inflammatory analgesic agent and a strong inhibitor of prostaglandin synthetase.

Oruvail is recommended in the management of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, acute articular and periarticular disorders (bursitis, capsulitis, synovitis, tendinitis), fibrositis, cervical spondylitis, low back pain (strain, lumbago, sciatica, fibrositis), painful musculo-skeletal conditions and dysmenorrhoea.

Oruvail reduces joint pain and inflammation, and facilitates increase in mobility and functional independence. As with other non-steroidal anti-inflammatory agents, it does not cure the underlying disease.

Dosage and administration Oruvail is administered orally, usually with food.

Dosage is one or two capsules (100–200 mg.) once daily, depending on patient weight and on severity of symptoms.

Paediatric dosage not established.

Contra-indications, warnings, etc Active peptic ulceration; a history of recurrent peptic ulceration or chronic dyspepsia.

Ketoprofen should not be given to patients sensitive to aspirin or other non-steroidal anti-inflammatory agents known to inhibit prostaglandin synthetase. Severe bronchospasm might be precipitated in these patients and in those suffering from, or with a history of bronchial asthma or allergic disease.

Precautions: Pregnancy and lactation: embryopathic effects have not been recorded with this drug but it is recommended to avoid medication during pregnancy and lactation.

Plasma protein-binding drugs: Oruvail is highly protein-bound. Concomitant use of other protein-binding

drugs, eg anticoagulants, sulphonamides, hydantoins, might necessitate modification of dosage in order to avoid increased levels of such drugs resulting from competition for plasma-protein-binding sites.

Warning and adverse effects: Gastro-intestinal intolerance may occur and very rarely, gastro-intestinal haemorrhage. Oruvail capsules should always be prescribed 'To be taken with food'.

Adverse effects, frequently transient, include, indigestion, dyspepsia, flatulence, heartburn, abdominal discomfort, nausea and, very rarely, skin rashes. Bronchospasm might be precipitated in patients suffering from or with a history of bronchial asthma or allergy.

Pharmaceutical precautions Store in a dry place, below 25°C.

Legal category POM.

Package quantities Containers of 100 capsules.

Further information Nil.

Product licence number 0012/0143.

PATENT BLUE V

Presentation A deep blue sterile, isotonic solution containing 2.5% of Patent Blue V (Colour Index Number 42051).

Uses Colours the lymph vessels so that they can then be injected with an X-ray contrast medium.

Dosage and administration Two ml of Patent Blue V Injection Solution is diluted with an equal volume of sterile normal saline (an alternative method advocates dilution with 1% lignocaine hydrochloride solution) and 0.5 ml of the diluted dye is injected into the subcutaneous tissue of each interdigital web space. When the lower extremities are being examined, 1 ml is also injected below the tip of each malleolus. The lymphatics should then be visible through the skin and it is important that there should be no accidental spillage of the dye.

Patent Blue V may be used for children at the surgeon's discretion.

Contra-indications, warnings, etc Before administration it is essential to enquire if there is a previous history of allergy or intolerance. In such circumstances it is advisable to administer a corticosteroid or antihistamine pre-medication.

It would also seem prudent to test for hypersensitivity by injecting a very small volume of the solution and waiting a few moments to ascertain if there is a reaction.

Patent Blue V Solution can provoke allergic reactions of varying degrees of severity. These reactions are rare and can be rapidly controlled with a corticosteroid. They occur immediately or a few minutes after injection of the dye.

Nausea, hypotension and generalised muscle tremors have also been reported; laryngeal spasm, if it occurs, requires the use of a muscle relaxant and intubation. Rare but more serious allergic reactions include circulatory failure with a state of shock, dyspnoea and oedema of the glottis.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Box of 5 × 2 ml ampoules.

Further information After injection of the dye a bluish coloration of the skin occurs, which normally disappears within 24–48 hours. More persistent coloration, which should not be confused with cyanosis, may occasionally be seen in cases of lymphatic stasis or circulatory disorder; this persistence may be avoided by using the minimum quantity of dye. An area of blue coloration can persist around the injection site for eight to ten days.

Product licence number 0012/5068.

PHENERGAN*

Presentation Phenergan is presented as:

Blue, sugar-coated tablets containing 10 mg promethazine hydrochloride, marked M & B in reddish-brown print.

Blue, sugar-coated tablets containing 25 mg promethazine hydrochloride, marked 'Phenergan 25' in reddish-brown print.

An orange-coloured elixir containing 5 mg promethazine hydrochloride per 5 ml.

A colourless injection solution containing 2.5% w/v promethazine hydrochloride.

Uses Potent long-acting antihistamine with additional, anti-emetic and sedative/calming effects. Indicated in symptomatic treatment of allergic conditions of the respiratory tract and skin; sensitisation reactions to drugs or foreign proteins; anaphylactic reactions.

For sedation, hypnosis and insomnia, and minor emotional disturbances in adults and children.

For pre-medication for its sedative/calming effect, anti-emetic action, antisialogogue effect and to enhance the effects of anaesthetics.

In obstetrics.

As a paediatric sedative.

In Parkinson's syndrome and drug-induced parkinsonism.

Dosage and administration *Adults: Oral administration:* Initial dose one 25 mg tablet at night – may be increased to two or three 25 mg tablets at night if necessary. In allergic conditions more frequent administration twice or three times daily may be necessary, starting with one or two 10 mg tablets and increasing as required.

Parenteral administration: The usual adult dose is 25–50 mg by deep intramuscular injection or, in emergency, by slow intravenous injection after dilution of 2.5% solution to 10 times its volume with Water for Injections. Maximum parenteral dose 100 mg.

Children: They may be treated more conveniently by the elixir containing 5 mg per 5 ml.

As an antihistamine in allergy:

Infants from 6 months to 1 year	5–10 mg
Children of 1–5 years	5–15 mg
Children of 5–10 years	10–25 mg

In cases where two doses in 24 hours are required the lower amount stated should be given.

As a hypnotic/sedative:

Infants from 6 months to 1 year	10 mg
Children 1–5 years	15–20 mg
Children 5–10 years	20–25 mg

Given as a single night-time dose.

Parenteral: Half the oral dose, i.e. 6.25–12.5 mg for children from 5 to 10 years may be given by deep intramuscular injection.

Contra-indications, warnings, etc Ambulant patients receiving Phenergan for the first time should not be in control of vehicles or machinery for the first few days until it is established that they are not hypersensitive to the central nervous effects of the drug and do not suffer from disorientation, confusion or dizziness. Avoid alcoholic drink.

Cross-sensitivity with other phenothiazine derivatives, such as chlorpromazine, is possible.

Somnolence is minimised by giving all or the major part of the dose at night.

Dizziness, disorientation, slight headache, twitching and jerking of the limbs at night, ataxia, nightmares and hallucinations on high doses have occasionally been reported. Solar dermatitis following oral administration has been reported in a few patients with a history of subacute rheumatism and eczema.

Phenergan will enhance the action of any sedative, hypnotic or other central nervous depressant.

No embryopathic effects have been recorded, but as with all drugs Phenergan should not be given during pregnancy or lactation unless the physician considers it essential.

In the event of overdosage, treatment is symptomatic, the main symptoms being muscular twitching, convulsions, coma, restlessness and irritability, mental confusion and possibly hallucinations. Induce vomiting, but anti-emetic action may counteract emetics if absorbed. Wash out stomach with warm sodium bicarbonate solution, leaving some in the stomach to precipitate insoluble promethazine base and delay absorption.

Nurse in quiet darkened room, avoiding stimuli to prevent convulsions.

Avoid long-acting sedatives or hypnotics for convulsions and restlessness as Phenergan will enhance their reactions, including any tendency to cause respiratory depression.

Despite its close chemical relationship, Largactil (chlorpromazine) has been suggested for restlessness, irritability, and hallucinations caused by Phenergan. Oxygen plus carbon dioxide may be necessary for respiratory depression, as may artificial respiration.

The administration of an antibiotic to prevent pneumonia should be considered.

Pharmaceutical precautions Protect from light. Solutions of Phenergan are incompatible with alkaline substances, which precipitate the insoluble promethazine base.

Legal category Tablets, Elixir, P. Injection solution: POM.

Package quantities Containers of 50 and 500 of both strength tablets.

Injection Solution 2.5%: Boxes of 10 × 1 ml and 10 × 2 ml ampoules.

Elixir: Bottles of 125 ml and 2 litres.

Further information Nil.

Product licence numbers

Tablets 10 mg	0012/5285
Tablets 25 mg	0012/5286
Elixir	0012/5025
Injection	0012/5054

PHENERGAN* COMPOUND EXPECTORANT LINCTUS

Presentation Phenergan Compound Expectorant Linctus is presented as a straw-coloured linctus containing in each 5 ml:

Promethazine hydrochloride	5 mg
Ipecacuanha Liquid Extract BP	0.01 ml
Potassium guaiacolsulphonate	45.0 mg
Citric acid	65.0 mg

in a strawberry-flavoured vehicle.

Uses Cough linctus combining the antihistamine, anti-emetic, central sedative, local analgesic and anticholinergic actions of promethazine with the expectorant and mucolytic actions of ipecacuanha, potassium guaiacolsulphonate and citric acid.

Indicated for the symptomatic relief of nasal and bronchial congestion associated with coughs, colds and allied conditions of the respiratory tract.

Dosage and administration Phenergan Compound Expectorant Linctus should be administered two or three times daily in the following doses:

Up to 5 years	2.5 ml
5-10 years	2.5-5 ml
Over 10 years	5-10 ml
Adults	5-10 ml

Small infants should be treated under medical supervision only.

The linctus may be diluted with simple Syrup BP for the lower doses recommended above.

Contra-indications, warnings, etc Apart from drowsiness, it is possible that a patient may prove hypersensitive to the central effects of promethazine and suffer from confusion or disorientation. It is therefore recommended that adults should not be in charge of vehicles or machinery during the first few days of taking the linctus, until it is established that their response has not been adversely affected. Avoid alcoholic drink.

It should be borne in mind that the promethazine in the linctus may tend to enhance the effects of any sedative, hypnotic or other central depressant drug given concurrently. Slight drowsiness may occur in some patients and this can usually be avoided by reducing the dosage.

No embryopathic effects have been recorded, but as with all drugs Phenergan Compound Expectorant Linctus should not be given during pregnancy or lactation unless the physician considers it essential.

In the event of gross overdose, the ipecacuanha content will probably cause vomiting. If this does not occur, vomiting should be induced or gastric lavage should be carried out.

Further treatment is symptomatic according to the individual responses to the various constituents of the linctus.

Pharmaceutical precautions Protect from light.

Legal category P.

Package quantities Bottles of 125 ml and 2 litres.

Further information Nil.

Product licence number 0012/0093.

PHENERGAN* CREAM

Presentation Phenergan Cream is a white or off-white

cream containing 2% w/w promethazine base and 0.15% w/w dibromopropamide isethionate.

Uses Local antihistamine and local analgesic properties of promethazine are combined with the antibacterial action of dibromopropamide isethionate. Indicated in early treatment of first and second degree burns and scalds in which it limits local reaction of erythema, blistering and oedema, relieves pain and prevents infection. For early application to insect bites and stings, particularly where there is a risk of secondary infection.

Dosage and administration In burns and scalds the cream is applied direct. Minor lesions and those on exposed parts may require no covering or only such as is necessary for their protection; for lesions on other parts of the body a gauze dressing and bandage may be indicated which should not be disturbed more often than necessary. Prolonged use of the cream for the treatment of burns or scalds is not indicated, since the antihistamine and local analgesic actions of promethazine are only effective and useful for the first few days; this applies also to insect bites and stings.

Contra-indications, warnings, etc Prolonged use and repeated applications may interfere with healing, and the period of applications should be restricted to three or four days.

Topical application of promethazine may occasionally give rise to a skin sensitisation reaction which may take the form of photosensitivity; exposure to bright sunlight should, therefore, be avoided.

Phenergan Cream is not suitable for application to eczematous skin, and should be applied sparingly and with caution where the skin is extensively broken or denuded.

It is possible that if very large areas of the skin are liberally covered with the cream, sufficient promethazine might be absorbed to cause drowsiness in an individual particularly sensitive to the central effects of the drug, but this is not likely to occur unless several ounces of the cream have been used.

Phenergan Cream may stain clothing, bed linen, etc. and the stains may only become evident after laundering.

Pharmaceutical precautions Protect from light.

Legal category P.

Package quantities Tube of 25 g.

Further information Nil.

Product licence number 0012/5029.

PHENSEDYL* COUGH LINCTUS

Presentation Phensedyl Cough Linctus is presented as an orange-brown linctus, each 5 ml containing:

Promethazine hydrochloride	3.6 mg
Codeine phosphate	9.0 mg
Ephedrine hydrochloride	7.2 mg

Uses Combines central sedative, antihistamine, anti-emetic, anticholinergic and local analgesic actions of promethazine hydrochloride with the antitussive action of codeine, and bronchodilator action of ephedrine, which also counteracts any excessive sedation.

Indicated for symptomatic relief of unproductive cough, including post-influenza cough, cough due to pharyngitis and associated with bronchospasm, the

spasms of whooping cough, cough due to smoking and other forms of irritation, cough which disturbs sleep.

Dosage and administration *Adults and children over 10 years:* 5–10 ml two to three times daily.

Children of 5–10 years: 2.5–5 ml two or three times daily.

Children 2–5 years: 2.5 ml two or three times daily.

Contra-indications, warnings, etc Because of ephedrine content do not use with monoamine oxidase inhibitors. Certain patients may be hypersensitive to the central effects of promethazine and suffer excessive drowsiness or disorientation or mental confusion. It is therefore recommended that those taking Phensedyl for the first time should not be in charge of vehicles or machinery for the first few days until it is established that their response has not been adversely affected. Avoid alcoholic drink. Promethazine may enhance the effects of sedatives, hypnotics or other central depressant drugs given concurrently. Phensedyl may cause slight drowsiness which is usually transitory.

No embryopathic effects have been recorded, but as with all drugs Phensedyl should not be given during pregnancy or lactation unless the physician considers it essential.

In the event of overdosage, after inducing vomiting or washing out the stomach treatment is symptomatic.

Pharmaceutical precautions Protect from light.

Legal category P. MDA. Inv.

Package quantities Bottles of 125 ml and 2 litres.

Further information Nil.

Product licence number 0012/5023.

PHYTODERMINE* DUSTING POWDER

Presentation Phytodermine Dusting Powder is a fine, cream-coloured powder containing methyl hydroxybenzoate 5% and salicylic acid 5%.

Uses Phytodermine Dusting Powder is a fungicidal preparation which is indicated for the treatment of fungal infections of the skin, particularly where they involve the flexures and extremities including *Tinea interdigitalis* (athlete's foot), tropical epidermophytosis (Dhobie itch) and 'prickly heat'.

Dosage and administration A small quantity of the dusting powder should be applied to the affected area morning and evening after washing. The powder may also be used as a prophylactic after bathing.

Contra-indications, warnings, etc There are no known contra-indications and no side-effects have been reported with this preparation.

If this preparation is accidentally taken by mouth, gastric lavage should be carried out, followed by appropriate treatment as dictated by the symptoms.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Polythene bottle of 50 g.

Further information Nil.

Product licence number 0012/5030.

SECADREX ▼

Presentation Secadrex tablets are white, round, slightly biconvex, and film-coated, imprinted 'SECADREX' on one face; each contains the equivalent of 200 mg acebutolol (in the form of the hydrochloride) and 12.5 mg hydrochlorothiazide.

Uses Mild and moderate hypertension.

Dosage and administration One Secadrex tablet once daily, usually in the morning, is sufficient in most patients. If response is inadequate, dosage may be increased to two Secadrex tablets once daily. Two Secadrex tablets may be particularly suitable in moderately severe hypertension when satisfactory control of arterial blood pressure cannot be obtained with either a beta-blocker or a diuretic used alone.

Contra-indications, warnings, etc

- Cardiogenic shock is an absolute contra-indication to beta-blockade and caution is required in patients with blood pressures of the order of 100/60 or below.
- Heart block. Administration of any beta-adrenoceptor blocking agent is considered inadvisable (except perhaps in first degree block).
- Severe kidney and liver failure.
- Hypersensitivity to hydrochlorothiazide.
- Secadrex tablets should not be used with verapamil or within several days of verapamil therapy (and vice-versa).
- Insulin-dependent diabetes. Use in non-insulin dependent diabetics may be inadvisable since thiazide diuretics may cause further impairment of glucose tolerance.
- Gout or hyperuricaemia.

Precautions: An increase in airways resistance may be provoked in asthmatic patients. Whilst the use of Secadrex tablets is not contra-indicated in patients with obstructive airways disease, care should be exercised when they are used in such subjects.

Caution should be exercised:

- If Secadrex tablets are administered in the presence of bradycardia (depending on the circumstances).
- If Secadrex tablets are to be prescribed with a catecholamine-depleting drug, such as reserpine.
- In the presence of signs of heart failure, since acebutolol has a slight but acceptable cardio-depressant action.
- In anaesthesia: some anaesthetists prefer to discontinue therapy 48 hours before anaesthesia, others do not consider this essential. Withdrawal should be made gradually. Thiazides may increase responsiveness to tubocurarine.

If Secadrex tablets and clonidine are given concurrently, the clonidine should not be discontinued until several days after the withdrawal of the beta-blocker (see also prescribing information on clonidine).

All patients receiving hydrochlorothiazide therapy (as in Secadrex tablets) should be monitored periodically for clinical signs of fluid or electrolyte imbalance, hypokalaemia, hyponatraemia and hypochloreaemic alkalosis. Hypokalaemia can sensitise or exaggerate the response of the heart to the toxic effects of digitalis (eg increased ventricular irritability).

With the low dose of hydrochlorothiazide present in Secadrex tablets the possibility of significant imbalance becomes less likely.

As with all medicines, Secadrex tablets should not be given during pregnancy or during lactation unless the physician considers it essential.

Side effects: No serious side-effects have been reported with Secadrex treatment. The most common, i.e. those related to beta-blockade – hypotension, bradycardia, gastro-intestinal effects and depression have been met with infrequently, and usually do not require interruption or withdrawal or therapy.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenoceptor antagonists. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuation of the drug should be considered if any such reaction is not explicable. Cessation of treatment with a beta-blocker should be gradual.

Skin rashes and photosensitivity due to hydrochlorothiazide have been reported as have blood dyscrasias including thrombocytopenia but these are rare.

Drug interactions: Tricyclic antidepressants and MAO inhibitors should not be used concurrently with Secadrex tablets. Lithium should generally not be given to patients receiving diuretics since the risk of lithium toxicity is very high in such patients.

Pharmaceutical precautions Store in a cool, dry place.

Legal category POM.

Package quantities Calendar (blister) pack of 28 (2 × 14) tablets.

Further information Secadrex is an effective anti-hypertensive agent, which combines Sactal, a cardio-selective beta-adrenoceptor antagonist with partial agonist activity and hydrochlorothiazide, an effective and acceptable diuretic/antihypertensive agent. The combination of these two medicaments in a single tablet may facilitate the management of hypertension and improve patient compliance.

Treatment of overdosage In the rare event of excessive bradycardia or hypotension, 1 mg, atropine sulphate administered intravenously should be given without delay. If this proves insufficient, it should be followed by a slow intravenous injection of isoprenaline (5 mcg per minute) with constant monitoring until a response occurs. In cases of severe poisoning with beta-adrenoceptor antagonists the injection of 10 mg glucagon intravenously has produced rapid improvement. If bradycardia becomes severe electrical pacing may be necessary.

Product licence number 0012/0137.

SECTRAL*

Presentation Sactal capsules each containing the equivalent of 100 mg acebutolol (in the form of the hydrochloride). The capsules are bi-coloured (opaque buff/opaque white) each half printed 'SECTRAL 100' in black.

Sactal 200 capsules each containing the equivalent of 200 mg acebutolol (in the form of the hydrochloride). The capsules are bi-coloured (opaque buff/opaque pink) each half printed 'SECTRAL 200' in black.

Sactal 400 tablets each containing the equivalent of 400 mg acebutolol (in the form of the hydrochloride). The tablets are off white, varnished.

Sactal injection – ampoules of 2 ml of an 0.5 per cent

w/v injection of acebutolol (as hydrochloride), each ml containing the equivalent of 5 mg acebutolol.

Uses *Mode of action:* Sactal is a beta adrenoceptor antagonist which is cardioselective, i.e. acts preferentially on beta-1 adrenergic receptors in the heart. Its principal effects are to reduce heart rate especially on exercise and to lower blood pressure in hypertensive subjects. Sactal and its equally active metabolite, diacetolol have anti-arrhythmic activity, the combined plasma half-life of the active drug and metabolite being 7–10 hours. Both have partial agonist activity (PAA) also known as intrinsic sympathomimetic activity (ISA). This property ensures that some degree of stimulation of beta receptors is maintained. Under conditions of rest this tends to balance the negative chronotropic and negative inotropic effects. Sactal blocks the effects of excessive catecholamine stimulation resulting from stress.

Sactal is indicated in the following conditions:

1. The management of all grades of hypertension.
2. The management of angina pectoris.
3. The control of tachyarrhythmias.

Dosage and administration 1. *Hypertension:* Initial dosage of 400 mg orally once daily at breakfast or 200 mg orally twice daily. If response is not adequate within two weeks, dosage may be increased up to 400 mg orally twice daily; in some patients 1,200 mg orally daily, given as 800 mg at breakfast and 400 mg in the evening, may be required. A further reduction in blood pressure may be obtained by the concurrent administration of a thiazide diuretic or other anti-hypertensive agent (except rauwolfia and its alkaloids).

2. *Angina pectoris:* Initial dosage of 400 mg orally once daily at breakfast or 200 mg twice daily. In severe forms up to 300 mg three times daily may be required; up to 1,200 mg daily has been used.

3. *Cardiac arrhythmias*

- (a) In severe cases intravenous Sactal may be used, the dosage and rate of administration being dependent upon clinical response. Initially 25 mg should be administered preferably over a period of 3–5 minutes. This dose may be followed, if required, by a further 25 mg slow intravenous injection or infusion, preferably over an hour or more, with careful monitoring of blood pressure and heart rate. Response may be delayed for 10 minutes or even longer, hence the reason for the relatively slow administration of Sactal after the first 25 mg has been given. The more benign arrhythmias usually respond to 5–15 mg intravenously with an effect lasting 30–50 minutes; concomitant oral administration is advisable (see below).
- (b) When given orally an initial dose of 200 mg is recommended and may take up to three hours for maximal anti-arrhythmic effect to become apparent. Thereafter 100 mg–200 mg twice or three times daily is usually needed but may be increased as required if response is not obtained at lower dosage. When an acute arrhythmia has responded to intravenous Sactal, 200 mg should be given by mouth, concurrent with reduction in intravenous infusion (if used) over a period of 60–90 minutes. Thereafter oral treatment should be continued with appropriate doses twice or three times daily.

Contra-indications, warnings, etc Cardiogenic shock is an absolute contra-indication and caution is required in patients with blood pressures of the order of

100/60 mm Hg or below. Sectral is also contra-indicated in patients with atrioventricular block, marked bradycardia and uncontrolled heart failure. Sectral should not be used with verapamil or within several days of verapamil therapy (and vice-versa).

Renal impairment is not a contraindication to the use of Sectral which has both renal and non-renal excretory pathways. Some caution should be exercised when administering high doses to patients with severe renal failure as cumulation could possibly occur in these circumstances. Caution should be exercised in patients with obstructive airways disease and particularly if Sectral is to be administered intravenously in asthmatic subjects. Bronchospasm is usually at least partially reversible by the use of a suitable agonist.

In patients with labile and insulin-dependent diabetes the dosage of the hypoglycaemic agent may need to be reduced.

Cross reactions due to displacement of other drugs from plasma protein binding sites are unlikely due to the low degree of plasma protein binding exhibited by acebutolol and diacetolol. If a beta adrenoceptor antagonist is used concurrently with clonidine the latter should not be withdrawn until several days after the former is discontinued.

Sectral therapy should be brought to the attention of the anaesthetist prior to general anaesthesia. If treatment is continued, special care should be taken when using anaesthetic agents such as ether, cyclopropane and trichlorethylene.

As with all medicines, Sectral should not be given during the first trimester of pregnancy unless the physician considers it essential.

Beta-blockers administered in late pregnancy may give rise to bradycardia of the foetus. Animal studies have shown no teratogenic hazard.

Side-effects: Sectral possesses antihypertensive effects but these are unlikely to be noted in normotensive subjects. Those common to beta-blockade—bradycardia, gastrointestinal effects, cold extremities and lethargy have been met with infrequently. The low lipid solubility and lack of cumulation in CNS tissues of acebutolol and its active metabolite reduces the likelihood of sleep disturbances, depression or other central effects and such occurrences are rare.

There have been reports of skin rashes and/or dry eyes associated with the use of beta adrenoceptor blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuation of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta blocker should be gradual.

Treatment of overdose: In the rare event of excessive bradycardia or hypotension, 1 mg atropine sulphate administered intravenously should be given without delay. If this is insufficient it should be followed by a slow intravenous injection of isoprenaline (5 mcg per minute) with constant monitoring until a response occurs. In severe cases of self poisoning with circulatory collapse unresponsive to atropine and catecholamines the intravenous injection of glucagon 10–20 mg may produce a dramatic improvement. Cardiac pacing may be employed if bradycardia becomes severe.

Pharmaceutical precautions Sectral capsules should be stored in a dry place below 25°C.

Legal category POM.

Package quantities Capsules 100 mg: containers of 100 and 500.

Capsules 200 mg ('Sectral 200'): containers of 100.

Tablets 400 mg ('Sectral 400'): foil pack of 28 (2 × 14).

0.5% Injection Solution: Boxes of 10 × 2 ml ampoules.

Further information Sectral 400 tablets are available as a calendar pack containing 28 tablets for ease of use in once daily therapy for hypertension.

Product licence numbers

100 mg Capsules	0012/0100
200 mg Capsules ('Sectral 200')	0012/0101
400 mg Tablets ('Sectral 400')	0012/0124
Injection Solution	0012/0102

SONERYL®

Presentation Pink tablets each containing 100 mg butobarbitone, with the name 'Soneryl' indented on one face and a break line on the reverse.

Uses Soneryl is a barbiturate with a medium duration of action. It is a powerful hypnotic and is indicated for severe, intractable insomnia. Sleep is usually induced within 30–40 minutes and lasts for six to ten hours.

Dosage and administration One or two tablets at bedtime; may be increased to 3 or 4 in obstinate cases. These doses may be modified at the physician's discretion, but it is advisable not to exceed 6 tablets in 24 hours.

Contra-indications, warnings, etc

Contra-indications: Porphyria is an absolute contra-indication to the use of Soneryl. Patients with uncontrolled pain, or those with a history of alcohol or drug abuse should not be given Soneryl.

Soneryl should not be used in children, young adults, the elderly and the debilitated.

Pregnancy. Soneryl should not be administered during pregnancy or breast feeding.

Precautions: Reduced dosage should be used in patients with renal or hepatic failure.

Drug interactions: Barbiturates cause the induction of liver enzymes and this may affect the availability and blood concentrations of drugs given concurrently that are metabolised in the liver. These include the following: coumarin-type anticoagulants, synthetic steroids (including oral contraceptives), phenytoin, griseofulvin, rifampicin, phenothiazines such as chlorpromazine and tricyclic antidepressants.

Warnings and adverse effects: Drowsiness, sedation. Unsteadiness, vertigo and inco-ordination are common adverse effects.

Performance and alertness may be impaired during the first week of administration. Patients should be warned of the possible hazard when driving or operating machinery.

These effects may be potentiated by alcohol. Other adverse reactions may include a 'hangover' effect, paradoxical excitement, confusion, memory defects and skin rashes in patients who may be sensitive to this type of drug.

Treatment of overdose: Soneryl overdose should be treated by gastric lavage, artificial respiration with the administration of oxygen, maintenance of fluid balance and with an antibiotic to prevent pneumonia. Metaraminol may be used to treat hypotension, but if this is

unsuccessful, blood volume expanders or intravenous hydrocortisone should be given.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Containers of 500 tablets.

Further information Barbiturates have a high addiction potential. Long-term use or use of high dosage for short periods may lead to tolerance and subsequently to physical and psychological dependence. Symptoms of dependence include confusion, defective judgement and loss of emotional control. Withdrawal symptoms occur after long-term normal use (and particularly after abuse) on rapid cessation of barbiturate treatment. Symptoms include nightmares, irritability and insomnia and in severe cases, tremors, delirium, convulsions and death. Withdrawal symptoms have been reported in neonates after barbiturate treatment during pregnancy and labour.

Product licence number 0012/5262.

STEMETIL*

Presentation Stemetil tablets are white, uncoated, indented on the face with name and strength; reverse is plain (break line for 25 mg tablet). They contain 5 mg or 25 mg prochlorperazine maleate.

Stemetil 1.25% Solution – pale straw-coloured solution containing 12.5 mg prochlorperazine mesylate per ml in ampoules of 1 ml and 2 ml.

Stemetil Suppositories – cream-coloured suppositories containing base equivalent to 5 mg and 25 mg of maleate.

Stemetil Syrup (greenish-blue) contains 5 mg prochlorperazine mesylate in each 5 ml.

Uses Stemetil is effective for the treatment of vertigo due to Ménière's syndrome, labyrinthitis and other causes, for nausea and vomiting from whatever cause, including terminal cases. It may also be used for migraine, whether actuated by stress, allergy or endocrine disturbances; as an adjunct to the short-term management of anxiety, e.g. tension, uneasiness, nervousness, conversion or phobic reactions and obsessive reactions, schizophrenia, particularly in the chronic stage; acute mania. Maintenance treatment of the discharged mental patient.

Dosage and administration *Vertigo and Ménière's syndrome. Adults:* 1 × 5 mg tablets three times daily, increasing if necessary to a total of 6 × 5 mg tablets daily. After several weeks, dosage may be reduced gradually to 2 or 1 × 5 mg tablet daily.

Children: See Tables 1 and 2.

Children

Table 1

Age in years		Total daily dosage
1–5	$\frac{1}{2}$ × 5 ml spoonful syrup twice daily	5 mg
6–12	1 × 5 ml spoonful syrup two or three times daily	10–15 mg
13–16	use lower adult range	15–20 mg

Where necessary, 5 mg suppositories may be given in the following amounts:

Table 2

Age in years	5 mg suppositories	Total daily intake not to exceed
1–2	$\frac{1}{2}$ once or twice daily	7.5 mg
2–5	$\frac{1}{2}$ twice or three times daily	10 mg
5–12	$\frac{1}{2}$ thrice daily or 1 twice daily	15 mg

Nausea and vomiting: Adults: Prevention – 1 or 2 × 5 mg tablets two or three times daily.

Treatment – 4 × 5 mg tablets at once, followed, if necessary, by 2 × 5 mg tablets two hours later. If vomiting prevents oral ingestion, treatment may be started with 1 × 25 mg suppository or a deep intramuscular injection of 1 ml (12.5 mg) solution, followed, if required, by normal oral medication six hours later.

Children: See Tables 1 and 2.

Migraine: Adults: Prevention – 1 × 5 mg tablet three or four times daily. In cases associated with emotional disturbances, 1–2 × 5 mg tablets or a 25 mg suppository given some hours before the event and repeated, if necessary, may prevent the attack.

Treatment – 4 × 5 mg tablets at once followed, if required, by 2 × 5 mg tablets two hours later. In an established attack, if the patient is unable to retain tablets, a 25 mg suppository or a deep intramuscular injection of 1 ml (12.5 mg) solution should be used. The acute attack in some patients responds better to the concurrent administration of Stemetil and ergotamine.

Children: See Tables 1 and 2.

Minor mental and emotional disturbances: Adults: 3–4 × 5 mg tablets per day, increasing, if necessary, to a maximum of 8 × 5 mg tablets per day.

Schizophrenia and other psychotic disturbances: The usual effective daily adult oral dosage is of the order of 75–100 mg, but patients vary widely in response. The following schedule is suggested:

Starting dose of 12.5 mg twice daily for seven days, the daily amount being subsequently increased by 12.5 mg at four to seven day intervals until a satisfactory response is obtained.

After some weeks at this effective level, an attempt should be made to reduce the dosage. Total daily amounts as small as 50 mg, or even 25 mg, have sometimes been found adequate.

When oral administration is not practicable, a 25 mg suppository or a deep intramuscular injection of 12.5–25 mg (1–2 ml) of solution, twice or thrice daily, should be used until oral treatment becomes possible.

Contra-indications, warnings, etc No embryopathic effects have been recorded, but as with all drugs Stemetil should not be given during pregnancy or lactation unless the physician considers it essential.

It should be remembered that the anti-emetic action of Stemetil, by suppressing important symptoms, may render the assessment of such conditions as cerebral irritation or intestinal obstruction uncertain, so that an exact diagnosis should be made before the drug is administered.

At dosage levels up to 40 mg per day, which are recommended for the treatment of conditions encountered in general medical practice, Stemetil has been found to be remarkably free from side-effects. Slight transient drowsiness may occur in some patients during

the early stages of treatment, but it is rarely of an order to warrant reduction of dosage or withdrawal of the drug; however patients should not drive or operate machinery until the effect has been ascertained. Mild skin reactions have been reported and initially dryness of the mouth can occur.

In the much higher dosages employed in psychoses, parkinsonism, akathisia and acute dystonias have been reported. This last may appear in several forms including trismus, tongue protrusion, athetoid movements or spasm of the spinal muscles. These extra-pyramidal disturbances are reversible and can readily be controlled by the concurrent administration of an anti-parkinsonian drug such as promethazine hydrochloride (Phenergan).

In the event of overdose with Stemetil the major symptoms to be expected are those of extrapyramidal disorder, and these may be accompanied by either restlessness and agitation or central nervous depression.

Treatment is essentially symptomatic and supportive. Gastric lavage is helpful, particularly when carried out early. Particular attention must be directed to maintaining a clear airway, since this may be threatened by the extrapyramidal muscle dystonias. If hypotension is present strict attention to ventilation and posturing of the patient will often secure the desired effect, but failing this, consideration should be given to the administration of noradrenaline by intravenous drip infusion, alternatively the intra-muscular administration of metaraminol, or other suitable pressor agents. Adrenaline should not be used. As with other phenothiazine derivatives, haemodialysis is of no value.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Tablets 5 mg in containers of 25, 250 and 1,000.

Tablets 25 mg in containers of 50 and 500.

Injection solution of 1.25% in boxes of 10 × 1 ml and 2 ml ampoules.

Syrup presentation of 5 mg per 5 ml in bottles of 125 ml.

Suppositories of 5 mg and 25 mg in boxes of 5.

Further information Nil.

Product licence numbers

Tablets 5 mg	0012/5263
Tablets 25 mg	0012/5316
Injection	0012/5008
Suppositories 5 mg	0012/5117
Suppositories 25 mg	0012/5013
Syrup	0012/5022

STREPTOTRIAD*

Presentation Streptotriad is presented as pink tablets, with the name 'Streptotriad' embossed on one face and a break line on the reverse face. Each tablet contains:

Streptomycin (as sulphate)	65 mg
Sulphadiazine	100 mg
Sulphadimidine	100 mg
Sulphathiazole	100 mg

Uses Streptotriad is active against many strains of Shigellae which cause bacillary dysentery. The action of streptomycin is localised to the gut and the additional use of sulphonamides which are absorbed ensures activity within the wall and the lumen of the gut. The use

of three different derivatives to make up the total sulphonamide content greatly reduces the risk of crystalluria. Streptotriad is indicated for the treatment and prevention of non-specific diarrhoeas, including the so-called 'travellers' diarrhoea', and of bacillary dysentery.

Dosage and administration Streptotriad is administered orally.

Treatment: For adults the dosage is 2 tablets three times daily.

For children of 12 years and over, 1½ tablets three times daily.

For children of 7–11 years, 1 tablet three times daily.

For children of 3–6 years, ½ tablet four times daily.

For children of 1–2 years, ¼ tablet three times daily.

Treatment should be continued until the diarrhoea ceases; it is unlikely to be needed after the fourth day.

Prevention: For short-term prophylaxis in adults at risk, 1 or 2 tablets are given twice daily.

For children the dosage should be about half that recommended for treatment.

Contra-indications, warnings, etc Side-effects are unlikely with the recommended dosages of Streptotriad, but in susceptible persons the side-effects common to all sulphonamides could occur. These include nausea, vomiting, cyanosis, headache, depression, mental confusion and pyrexia, more rarely rashes, blood dyscrasias and crystalluria, and very rarely hepatitis and nephrosis. With oral streptomycin side-effects are very unlikely, as the compound is not appreciably absorbed from the gastro-intestinal tract.

Streptotriad should not be used in individuals who are known to be sensitive to sulphonamides and/or streptomycin, or in the presence of renal insufficiency or jaundice. Streptotriad should not be given to an infant within a week of full-term birth or within a month of premature birth, because of the risk of occurrence of kernicterus, and it should be given to infants under 6 months of age only if truly indicated. Streptotriad should not be administered to pregnant women shortly before term. An adequate fluid intake should be ensured, especially if the patient is dehydrated. Care should be taken in dispensing Streptotriad, as repeated handling of streptomycin can result in skin sensitisation.

As with all drugs, Streptotriad should not be given during pregnancy or lactation unless the physician considers it essential.

In the event of overdose an emetic should be administered and gastric lavage carried out. Continuous forced fluids should be given and the urine should be rendered alkaline to reduce the risk of crystalluria and to increase the rate of excretion. Otherwise treatment should be symptomatic.

Pharmaceutical precautions Store in a cool dark place.

Legal category POM.

Package quantities Containers of 50 tablets.

Further information Nil.

Product licence number 0012/5294.

SULPHADIAZINE INJECTION

Presentation Sulphadiazine Injection is presented in the form of a colourless 27.2% solution of Sulphadiazine

Sodium, each 4 ml ampoule of which contains the equivalent of 1 g of sulphadiazine.

Uses Sulphadiazine Sodium has a bacteriostatic action on a wide range of Gram-negative and Gram-positive micro-organisms and is indicated in the treatment of infection with pneumococci, β -haemolytic streptococci, *Haemophilus influenzae* and other sulphonamide-sensitive organisms.

Dosage and administration Sulphadiazine Sodium is administered parenterally. Because of the alkalinity of the solution Sulphadiazine Injection should preferably be given intravenously, diluted to 5% or 10% with Water for Injections, or added to an appropriate volume of saline for infusion. It may also be administered by deep intramuscular injection of the undiluted solution.

The average dose, when associated with or immediately followed by oral administration, is 2 g for adults, 1 g for children between 3 and 15 years of age and 0.5 g for children under 3 years. Higher doses may be given when parenteral therapy alone is used in the treatment of severe acute infections.

Contra-indications, warnings, etc Sulphadiazine Sodium Solution must never be given subcutaneously or intrathecally, as its high alkalinity can lead to necrosis. When the intramuscular route is used, the injection must be given deeply, with care to avoid contact with the subcutaneous tissues. Sulphadiazine Injection should not be given to patients who are known to be sensitive to sulphonamides or to those with jaundice or renal insufficiency. It should not be administered to infants under the age of 6 months or to pregnant women shortly before term. A high fluid intake should be maintained, such as 5–6 pints in 24 hours, and the urinary output should be not less than half that amount. In addition the urine should be rendered alkaline.

In susceptible individuals the side-effects common to all sulphonamides could occur with Sulphadiazine Injection. These include nausea, vomiting, cyanosis, headache, depression, mental confusion and pyrexia, more rarely rashes, blood dyscrasias and crystalluria, and very rarely hepatitis and nephrosis. If crystalluria should occur and be followed by haematuria or oliguria, Sulphadiazine should be withdrawn and copious amounts of fluid given, by drip infusion if necessary. Heat should be applied to the loins, and if the condition persists, cystoscopy should be carried out and a ureteric catheter passed, followed by irrigation with warm 2.5% sodium bicarbonate solution. Ureteric catheters should be left in position for 24–48 hours or until urinary function is restored.

No embryopathic effects have been recorded but as with all drugs Sulphadiazine Injection should not be given during pregnancy or lactation unless the physician considers it essential.

In the event of overdosage, continuous forced fluids may be necessary and the urine should be rendered alkaline. Otherwise treatment is symptomatic.

Pharmaceutical precautions Protect from light. Incompatible with acids, laevulose, iron salts and salts of heavy metals.

Legal category POM.

Package quantities Box of 10 $\times$ 4 ml ampoules.

Further information Nil.

Product licence number 0012/5057.

SURMONTIL*

Presentation Surmontil Tablets are compression-coated, white, each containing the equivalent of 10 mg or 25 mg trimipramine (as maleate). The face is indented with the name and strength; the reverse is plain. Surmontil Capsules (body white opaque with green cap, printed 'M & B SU50'), each contain the equivalent of 50 mg trimipramine (as maleate).

Uses Surmontil has a potent antidepressant action similar to that of other tricyclic antidepressants. It also possesses a pronounced sedative action. It is, therefore, indicated in the treatment of depressive illness, especially where sleep disturbance, anxiety or agitation is a presenting symptom. Sleep disturbance is controlled within 24 hours and true antidepressant action follows within 7–10 days.

Dosage and administration *Adults:* Mild/moderate depression in general practice. The recommended dosage is 50–75 mg orally given two hours before bedtime, the larger dose (75 mg) being preferable for those patients with more marked sleep disturbance. Treatment should be continued for at least three weeks.

Moderate/severe depression (patients under psychiatric supervision): Initial dosage – 75 mg orally per day. This is best given as a single dose late in the evening or as 25 mg midday and 50 mg late in the evening. Dosage should then be increased as necessary until the optimal therapeutic level is reached, usually 150–300 mg per day. Treatment at this dosage should be continued for four to six weeks, dosage then being reduced to a maintenance level, usually within the range of 75–150 mg per day, for two to three months.

Giving most of the total daily dosage at night induces a rapid return to normal sleep, reduces the need for night-time sedation and minimises daytime drowsiness.

Elderly: Initially 10–25 mg three times a day. The initial dose should be increased with caution under close supervision. Half the normal maintenance dose may be sufficient to produce a satisfactory clinical response.

Cyclothymic patients with recurrent depression may require maintenance therapy for up to one year or even longer.

Surmontil is not recommended for use in children.

Contra-indications, warnings, etc Recent myocardial infarction. Any degree of heart block or other cardiac arrhythmia. Mania, severe liver disease. During breast feeding.

The elderly are particularly liable to experience adverse reactions, especially agitation, confusion and postural hypotension (see Dosage).

Treatment should be avoided, if possible, in patients with narrow angle glaucoma, symptoms suggestive of prostatic hypertrophy and a history of epilepsy.

Patients posing a high suicidal risk require close initial supervision. The central nervous depressant action of alcohol is potentiated by Surmontil.

Anaesthetics given during tricyclic antidepressant therapy may increase the risk of arrhythmias and hypotension. If surgery is necessary, the anaesthetist should be made aware that a patient is being so treated.

Trimipramine should not be given concurrently with, or within 2 weeks of cessation of therapy with monoamine oxidase inhibitors. The anti-hypertensive effect of guanethidine, debrisoquine, bethanidine and possibly clonidine may be decreased by trimipramine.

It would be advisable to review all anti-hypertensive therapy during treatment with tricyclic anti-depressants. Trimipramine should not be given with sympathomimetic agents such as adrenaline, ephedrine, isoprenaline, noradrenaline, phenylephrine and phenylpropanolamine.

Barbiturates may increase the rate of metabolism of Surmontil.

Surmontil should be administered with care in patients receiving therapy for hyperthyroidism.

Use in pregnancy: Do not use during pregnancy, especially during the first and last trimester, unless there are compelling reasons. There is no evidence as to drug safety in human pregnancy nor is there evidence from animal work that it is free from hazard.

Patients should be monitored closely during the initial stages of treatment, as improvement may not occur during the first 2–4 weeks. Trimipramine may initially impair alertness. Patients should be warned of the possible hazard when driving or operating machinery. Cardiac arrhythmias and severe hypotension are likely to occur with high dosage or in deliberate overdosage. They may also occur in patients with pre-existing heart disease taking normal dosage. It may be advisable to monitor liver function in patients on long-term treatment with Surmontil.

Side-effects are similar to those of other tricyclic anti-depressants; they are usually more evident during the first few days of treatment and are invariably controlled by modification of dosage. Drowsiness may occur, but this is minimised by giving the total daily dosage at night. Atropine-like side effects including dry mouth, disturbances of accommodation, tachycardia, constipation and hesitancy of micturition are common early in treatment, but usually lessen. Other adverse effects including sweating, postural hypotension, tremor and skin rashes.

Interference with sexual function may occur.

Serious adverse effects are rare; the following have been reported: depression of the bone marrow including agranulocytosis, cholestatic jaundice, hypomania, convulsions and peripheral neuropathy. Psychotic manifestations, including mania and paranoid delusions, may be exacerbated during treatment with tricyclic anti-depressants. Withdrawal symptoms may occur on abrupt cessation of therapy and include insomnia, irritability and excessive perspiration. Adverse effects such as withdrawal symptoms, respiratory depression and agitation have been reported in neonates whose mothers had taken trimipramine during the last trimester of pregnancy.

Acute overdosage may be accompanied by hypotensive collapse, convulsions and coma. Provided coma is not present, gastric lavage should be carried out without delay even although some time may have passed since the drug was ingested. Patients in coma should have an endotracheal tube passed before gastric lavage is started. Absorption of trimipramine is slow but, as cardiac effects may appear soon after the drug is absorbed, a saline purge should be given. Electrocardiography monitoring is essential.

It is important to treat acidosis as soon as it appears with, for example, 20 ml per kg of M/6 sodium lactate injection by slow intravenous injection. Intubation is necessary and the patient should be ventilated before convulsions develop; convulsions should be treated with diazepam administered intravenously.

Ventricular tachycardia or fibrillation should be treated by electrical defibrillation; if supraventricular tachycardia develops, pyridostigmine bromide 1 mg (adults) intra-

venously or propranolol 1 mg (adults) intravenously should be administered at intervals as required.

Treatment should be continued for at least three days even if the patient appears to have recovered.

Pharmaceutical precautions Protect from light. Surmontil capsules should be stored in a dry place below 25°C.

Legal category POM.

Package quantities Tablets: Compression-coated – 10 mg in container of 50, and 25 mg in containers of 50 and 500. Capsules: 50 mg in containers of 50 and 500.

Further information Nil.

Product licence numbers

Tablets 10 mg	0012/5296
Tablets 25 mg	0012/5297
Capsules 50 mg	0012/5298

SVC*

Presentation SVC is presented in the form of effervescent vaginal tablets which are elongated, white and indented 'SVC' on one face. Each vaginal tablet contains 250 mg acetarsol with the following percentage composition:

Acetarsol	26.08%
Carbohydrate	61.22%
Boric acid	2.70%
Sodium bicarbonate	6.76%
Excipient	3.24%

Uses SVC is indicated in the local treatment of vaginitis, especially that due to *Trichomonas vaginalis* when Flagyl is not available.

Dosage and administration SVC Vaginal Tablets are for insertion into the vagina only. When there is marked inflammation of the vaginal walls, a preliminary douche of normal saline or sodium bicarbonate solution is given. Two to four vaginal tablets are then inserted into the fornices, twice a day for the first few days. With relief of symptoms this is done less frequently until finally the vaginal tablets are used only on the days immediately following the menstrual period.

This product is not recommended for children.

Contra-indications, warnings, etc SVC is contra-indicated in cases of known arsenic sensitivity.

Patients should be instructed to stop using the vaginal tablets and obtain medical advice should local irritation or systemic symptoms occur.

A small number of cases of local irritation have been reported. Symptoms of systemic effects are rare, but cases of dermatitis have been reported.

No embryopathic effects have been recorded but as with all drugs SVC should not be given during pregnancy or lactation unless the physician considers it essential.

In the very rare instances of severe systemic side-effects or if the vaginal tablets are accidentally taken orally in an overdose, deep intramuscular injections of dimercaprol (BAL) should be given.

Pharmaceutical precautions SVC should be stored in a dry place.

Legal category POM.

Package quantities Containers of 250.

Further information Nil.

Product licence number 0012/5299.

TIXYLIX*

Presentation Tixylix is presented as a cherry-flavoured cough linctus containing in each 5 ml:

Promethazine Hydrochloride BP	1.5 mg
Pholcodine BP (as citrate)	1.5 mg

Uses Combines the central sedative anti-emetic, anti-histamine, local analgesic and anticholinergic actions of promethazine with the antitussive action of pholcodine. Indicated for the symptomatic relief of cough, and as an adjuvant in the treatment of upper respiratory tract infections in children. Useful for irritating night cough in children.

Dosage and administration Tixylix is usually given undiluted, but for irritating night cough additional benefit may be obtained by giving the last dose of the day at bedtime in some warm water or fruit juice.

The following doses given two or three times daily are recommended:

Children – 1–2 years: 2.5–5 ml.

2–5 years: 5 ml.

5–10 years: 5–10 ml.

For use in older age groups the doses recommended are: 10–20 ml three times daily. Administration to infants below the age of 1 year at the discretion of the physician.

Contra-indications, warnings, etc No side-effects have been observed at the recommended dosage, but drowsiness could possibly occur if a child were hypersensitive to the central sedative effects of promethazine. Should an adult be given Tixylix the remote possibility of hypersensitivity to the central nervous effects of the promethazine content giving rise to disorientation or mental confusion exists. Though this is very unlikely to result from the amount of promethazine in the recommended dosage of Tixylix it is usual to advise that adults taking promethazine-containing products for the first time should not be in charge of vehicles or machinery for the first few days until it is evident that their response has not been adversely affected. Avoid alcoholic drink.

No embryopathic effects have been recorded but as with all drugs Tixylix should not be given during pregnancy or lactation unless the physician considers it essential.

In the event of gross overdosage with Tixylix, gastric lavage should be carried out or vomiting induced at the earliest opportunity.

Treatment is symptomatic according to the reaction to the individual constituents of Tixylix.

Pharmaceutical precautions Protect from light. Incompatible with alkaline substances.

Legal category P. MDA. Inv.

Package quantities Bottles of 125 ml and 2 litres.

Further information Nil.

Product licence number 0012/5027.

VALLERGAN*

Presentation *Tablets:* Dark blue, sugar-coated, imprinted M & B in ivory, each containing 10 mg trimiprazine tartrate.

Syrup: Clear yellow, apricot flavoured, containing 7.5 mg trimiprazine tartrate in each 5 ml.

Forté Syrup: Clear pink, apricot flavoured, containing 30 mg trimiprazine tartrate in each 5 ml.

Uses Vallergran has a central sedative effect comparable to that of chlorpromazine, but largely devoid of the latter's anti-adrenaline action. It has powerful anti-histamine and anti-emetic actions.

Vallergran is indicated in the following conditions:

Urticaria – chronic and acute.

Management of pruritus in conditions such as: infantile eczema, pruritus ani et vulvae, contact dermatitis, neuro-dermatitis, herpes zoster, atopic dermatitis.

Also in more general disorders such as obstructive jaundice.

Pruritus of self-limiting conditions such as sunburn, photosensitivity, measles and chickenpox. Senile pruritus.

Short-term sedation in children.

Pre-anaesthetic medication – children and adults.

Dosage and administration *Urticaria and pruritus:* *Adults:* 10 mg three or four times daily; up to 100 mg per day have been used in intractable cases.

Children: 2.5–5 mg three or four times daily.

Short-term sedation in children: Vallergran Forté Syrup may be given in divided dosage according to the following scheme:

3–6 years: 15–60 mg per day ($\frac{1}{2}$ –2 × 5 ml spoonfuls).

7–12 years: 60–90 mg per day (2–3 × 5 ml spoonfuls).

Pre-anaesthetic medication

Oral administration (children): The appropriate dosage of Vallergran Forté Syrup for this indication will depend to some extent on the preferences and objectives of the individual anaesthetist. In the age group 2–7 years, a dosage of 2 mg per kg body weight will give sedation, whilst 4 mg per kg body weight will usually provide a sleeping patient.

Contra-indications, warnings, etc Skin rashes have occasionally been reported. During the initiation of Vallergran therapy it is advisable that certain activities should be suspended for some days, e.g. the driving of vehicles or handling of power-operated tools, until it is evident that any undue drowsiness has either subsided or not appeared. Avoid alcoholic drink.

The most frequent side-effect observed is drowsiness occurring in the early stages of treatment. Side-effects of rare occurrence are disturbing dreams, oral dryness, nasal stuffiness, headache, elation, depression, abdominal discomfort, galactorrhoea and skin rashes. Agranulocytosis is extremely rare. High dosage may give rise to parkinsonian-like effects and epileptiform convulsions. Vallergran is contra-indicated in cases of coma due to direct central nervous depressants such as alcohol, barbiturates and opiates.

No embryopathic effects have been recorded, but as with all drugs Vallergran should not be given during pregnancy or lactation unless the physician considers it essential.

Treatment of overdosage, in the absence of a specific

antidote, should include gastric lavage; countering of acute hypotension by the adoption of either a supine or head-down position, plasma expanders and possibly the use of phenylephrine or of noradrenaline by intravenous drip infusion; the active symptomatic treatment of central nervous depression as advocated for barbiturate poisoning, including parenteral penicillin and physiotherapy for the prevention of pneumonia. Haemodialysis is ineffective. Body temperature should be allowed to recover naturally unless it falls below about 30°C, at which level cardiac arrhythmias may become apparent. A special watch should be kept for intestinal and urinary bladder distension.

Pharmaceutical precautions Protect from light.

Vallergan Syrup and Vallergan Forte Syrup may be diluted if required, using simple syrup (without preservatives).

Legal category POM.

Package quantities *Tablets*: Containers of 50 and 500.

Syrup: Bottles of 125 ml and 1 litre.

Forte Syrup: Bottles of 125 ml and 1 litre.

Further information Nil.

Product licence numbers

Tablets 0012/5303

Syrup 0012/5019

Forte Syrup 0012/5018

VALLEX*

Presentation Vallex is a brown-coloured linctus containing in each 5 ml:

Trimeprazine Tartrate BP	2.5 mg
Menthol BP	1.2 mg
Phenylpropanolamine hydrochloride	10 mg
Guaiphenesin	25 mg
Citric Acid BP	65 mg
Sodium Citrate BP	200 mg
Liquid Extract Ipecacuanha BP	0.015 ml

Uses Expectorant cough linctus combining the sedative, anti-emetic, antihistamine and local analgesic actions of trimeprazine with the decongestant properties of phenylpropanolamine and the expectorant effect of guaiphenesin, ipecacuanha, sodium citrate and citric acid. Indicated for the symptomatic relief of cough and as an aid to expectoration in inflammatory conditions of

the respiratory tract such as acute and chronic bronchitis. It is also of value in tracheitis and in the cough associated with vasomotor rhinitis.

Dosage and administration Vallex may be administered two or three times a day in the following doses:

Adults and children over 10 years: 5–10 ml.

Children: 5–10 years: 2.5–5 ml.

2–5 years: 2.5 ml.

If required Vallex may be given diluted with hot water or fruit juice.

Contra-indications, warnings, etc Vallex should not be given concurrently with monoamine oxidase inhibitors, or for two weeks after treatment with these compounds has been discontinued, because of the possibility of hypertensive effects when phenylpropanolamine and monoamine oxidase inhibitors are taken together.

Slight drowsiness may occur in a few individuals and where this is undesirable the dose should be reduced. Hypersensitivity to the central nervous effects of trimeprazine may occasionally occur, causing confusion and possibly disorientation. It is therefore recommended that patients should not be in charge of vehicles or machinery for the first few days of taking Vallex, until it is evident that their response is not adversely affected. Avoid alcoholic drink.

The trimeprazine content may enhance the effect of any sedative, hypnotic or other central nervous depressant drug given concurrently.

No embryopathic effects have been recorded, but as with all drugs Vallex should not be given during pregnancy or lactation unless the physician considers it essential.

In the event of gross overdosage, gastric lavage should be carried out or vomiting induced at the earliest opportunity.

Further treatment is symptomatic according to the various constituents of the linctus.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Bottles of 125 ml and 2 litres.

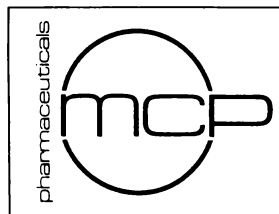
Further information Nil.

Product licence number 0012/5026.

*Trade Mark

MCP Pharmaceuticals Limited

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Livingston, West Lothian
EH54 7BH



BEZALIP* ▼

Presentation Bezalip is available as white, film coated tablets each containing 200 mg bezafibrate. The tablets are marked BM on one face and G6 on the reverse.

Uses Bezalip is indicated for use in hyperlipidaemias of Type IIa, IIb, III, IV and V (Fredrickson Classification) which are illustrated below:

Type	Major Lipid Elevation
IIa	Cholesterol
IIb	Cholesterol and Triglycerides
III	Cholesterol and Triglycerides
IV	Triglycerides
V	Triglycerides (possibly cholesterol)

Bezalip is therefore indicated for use only in patients with a fully defined and diagnosed abnormality where diet alone is insufficient to correct the condition and in whom the long-term risks associated with the condition warrant treatment

The rationale for the use of Bezalip to control abnormal elevations of serum lipids and lipoproteins is to reduce or prevent the long term adverse effects which have been shown by many major epidemiological studies to be positively and strongly correlated with such dyslipidaemias. The possible beneficial and adverse long-term consequences of some drugs used in the hyperlipidaemias are still the subject of scientific discussion, however, and there is currently no clinical evidence to demonstrate that Bezalip is effective in the prevention of heart disease.

Dosage and administration The recommended dosage of Bezalip is three tablets daily, equivalent to 600 mg bezafibrate. The tablets may be taken with or after food. Maintenance dosage may occasionally be reduced to two tablets daily, particularly in the treatment of hypertriglyceridaemia.

The initial response to therapy is normally rapidly apparent although a progressive response over a number of weeks may occur. The patient's response to Bezalip should be monitored at intervals. Treatment should be terminated if an adequate response has not been achieved within 4 to 6 months.

Contra-indications, warnings, etc Bezalip is contra-indicated in patients with severe liver dysfunction or primary biliary cirrhosis, and in those with severe renal disorders (serum creatinine values above 6 mg/100 ml). As bezafibrate is normally highly protein bound it should not be given to patients with the nephrotic syndrome. Although the drug substance has not been shown, in animal studies, to have any adverse effects on the foetus, it is recommended that Bezalip should not be administered either to pregnant women or to those who are breast-feeding. Bezalip is contra-indicated in patients hyper-sensitive to bezafibrate.

The chronic administration of the highest dose of

bezafibrate to rats was associated with hepatic tumour formation in females. This dose was in the order of 30-40 times the human dose. No such adverse effect was apparent at reduced intake levels approximating more closely to the lipid-lowering dosage in humans.

Care is required in administering Bezalip to patients receiving anti-coagulant therapy. The dose of anti-coagulant should be reduced by 50 per cent initially and then titrated to the patient's needs. The dosage of Bezalip may need to be reduced in patients with mild to moderate renal dysfunction (contra-indicated in severe cases). At serum creatinine levels of 1.5 to 2.5 mg per 100 ml the dose of Bezalip should be reduced to two tablets daily, while one tablet daily is recommended when serum creatinine is in the range 2.6 to 6 mg per 100 ml.

Adverse effects in clinical use are rarely seen. Most commonly these effects are gastro-intestinal in nature, such as feelings of fullness of the stomach. This side effect is frequently transitory and does not normally require cessation of treatment. Other adverse effects may include a myositis-like syndrome and rarely disorders of potency and general hypersensitivity. The incidence of all these potential effects is low, and there is no evidence that administration is associated with an increased frequency of gallstones.

No serious clinical or biochemical effects are likely to occur in cases of acute overdosage and treatment in such cases, where necessary, should be symptomatic.

Pharmaceutical precautions Bezalip tablets require no special storage conditions. It is recommended, however, that they be stored in a cool, dry place in accordance with normal pharmaceutical practice.

Legal category POM.

Package quantities Packs of 100 and 500 tablets.

Further information The risks associated with hyperlipidaemia may be increased in a super-additive manner by the presence of other factors such as hypertension, obesity, smoking, genetic predisposition and diabetes. This increased risk of long term adverse effects should be taken into consideration when evaluating whether hyperlipidaemia in any particular patient warrants treatment with Bezalip.

Product licence number 0075/0036.

CANTIL*

Presentation Cantil is available as yellow, scored tablets each containing mepenzolate bromide 25 mg and as Cantil elixir, a clear, red, cherry-flavoured syrup containing in each 5 ml 12.5 mg of mepenzolate bromide.

Uses Cantil tablets and elixir contain mepenzolate

bromide, a synthetic anticholinergic agent with a high degree of specificity for the smooth muscle of the lower gastro-intestinal tract.

Cantil is indicated for the relief of spasm or hypermotility of the lower gastro-intestinal tract such as that associated with the irritable colon syndrome, mucous colitis, spastic colitis, spastic constipation, acute or chronic non-specific diarrhoeas, diverticulitis and ulcerative colitis.

Dosage and administration *Children, 6-12 years:* 5 ml of elixir three or four times daily by mouth.

Adults and older children: 1 or 2 tablets, or 10-20 mls of elixir, three or four times daily by mouth.

Contra-indications, warnings, etc Cantil is contra-indicated in glaucoma and should be used with caution in prostatic hypertrophy. Due to the specificity of action of mepenzolate bromide, typical anticholinergic effects occur only rarely with Cantil. Mild and transient blurring of vision occurs occasionally in patients with ulcerative colitis.

Treatment of overdosage is as for atropine and other anticholinergic drugs: empty the stomach by aspiration and lavage. Give a saline purgative to promote peristalsis (e.g. 30 g sodium sulphate in 250 ml warmed water). A short acting sedative or hypnotic (such as intravenous diazepam) may be given with caution if excitation occurs. Peripheral symptoms may be treated with i.m. or s.c. injection of neostigmine methylsulphate 5 mg at suitable intervals. Assisted respiration may be necessary. Fluids should be given freely and catheterisation may be required if urine is retained.

Pharmaceutical precautions The elixir is incompatible with alkaline solutions. Water is a suitable diluent if required.

Legal category POM.

Package quantities *Cantil Tablets:* Containers of 50 and 500.

Cantil Elixir: Bottles of 100 ml.

Further information Relief from the pain and discomfort of intestinal spasm usually occurs rapidly, typically within 10 to 20 minutes, and the action generally lasts for approximately four hours. Due to the relatively specific nature of the action of Cantil on the lower gastro-intestinal tract, particularly on the colon, Cantil has a low incidence of systemic anticholinergic effects.

Product licence numbers

Cantil Tablets 0075/5002
Cantil Elixir 0075/5003

GASTROCOTE*

Presentation Gastrocote is presented as white, uncoated tablets which are engraved on one side with the name Gastrocote. Each tablet contains:

Alginic Acid BPC	200 mg
Dried Aluminium Hydroxide Gel BP	80 mg
Magnesium Trisilicate BP	40 mg
Sodium Bicarbonate BP	70 mg

Uses Gastrocote acts to reduce the incidence of gastric reflux and thus of associated discomfort and pain. Gastrocote is indicated in heartburn, including heartburn of pregnancy, reflux oesophagitis, particularly where associated with hiatus hernia, and in all cases of

epigastric distress associated with gastric reflux or regurgitation.

Dosage and administration *Adults and older children only:* 1 to 3 tablets to be chewed four times a day, that is, after main meals and at bedtime. Not to be given to children under 6 years.

Important: The tablets must be well chewed before swallowing.

Contra-indications, warnings, etc Care should be exercised in treating diabetic patients as the tablets each contain 1.03 g sucrose. Each tablet also contains 21 mg (0.91 mEq) of sodium which may be important for patients on a low sodium diet. There are no specific contra-indications to the use of Gastrocote and overdosage is virtually free of hazard although gastric bloating may occur.

Pharmaceutical precautions Gastrocote should be stored in a cool dry place.

Legal category P.

Package quantities Gastrocote tablets are supplied in containers of 100 tablets.

Further information When Gastrocote tablets are chewed sodium alginate is formed as a foam with the antacid constituents entrained. The foam coats the oesophagus with a demulcent, antacid layer when swallowed and then forms a viscous, colloidal foam gel floating on the stomach contents. This mild barrier physically impedes reflux. In the event of reflux being forced the demulcent alginate-antacid foam moves into the lower oesophagus before the stomach contents thus protecting the mucosa from further proteolytic attack and allowing healing to occur.

Product licence number 0075/0024.

ISMO* 20

Presentation Ismo 20 tablets are white, circular, uncoated and are embossed on each side with a break line and the code BM/B3. Each tablet contains 20 mg isosorbide mononitrate.

Uses *Pharmacology:* Isosorbide mononitrate is an active metabolite of isosorbide dinitrate and exerts qualitatively similar effects. Unlike the dinitrate, however, isosorbide mononitrate demonstrates virtually complete systemic absorption after oral administration and is only slowly eliminated from the body. The therapeutic action of isosorbide mononitrate is thus predictable, reproducible and of long duration. In long term clinical usage 40 mg of isosorbide mononitrate is equivalent to approximately 80 mg isosorbide dinitrate (in sustained release form), which is a potency ratio in the order of 1:2.

Indications: Ismo 20 tablets are indicated for use in prophylaxis and treatment of angina pectoris.

Dosage and administration A dosage of 40 to 60 mg isosorbide mononitrate daily (2 to 3 Ismo 20 tablets daily) provides control of angina pectoris in the majority of patients although the daily dosage may vary from 20 to 120 mg in appropriate cases. Ismo 20 tablets should be administered in divided doses using either a twice daily or three times daily dosage regime as appropriate. The tablets should be swallowed whole without chewing.

For patients who have not previously received prophylactic nitrate therapy it is recommended that the

dosage should be 20 mg daily (half an Ismo 20 tablet twice daily) for the first two days and that it should be increased gradually until the desired therapeutic effect is achieved. Patients already accustomed to chronic nitrate therapy with, for example, isosorbide dinitrate, may normally be transferred directly to a therapeutic dose of Ismo 20.

Contra-indications, warnings, etc Ismo 20 tablets are contra-indicated in patients with a known hypersensitivity to isosorbide mononitrate or isosorbide dinitrate. A number of nitrate-related adverse effects may occur during treatment, including headache and feelings of dizziness. The incidence of such effects is highest at the commencement of treatment and tends to decline with time. In sensitive patients postural hypotension may occur, especially after a high dose. Other reactions, similar to those associated with isosorbide dinitrate, may occur occasionally. In the event of overdosage the main symptom is liable to be hypotension which should be treated by laying the patient in a supine position with the legs elevated to promote venous return.

Pharmaceutical precautions No special handling or storage precautions apply although it is recommended that Ismo 20 be stored in a cool, dry place in accordance with good pharmaceutical practice.

Legal category POM.

Package quantities Ismo 20 is available in packs of 100 tablets.

Further information Ismo 20 provides long term nitrate prophylaxis for the treatment and control of angina pectoris in a form with complete biological availability due to the lack of any significant hepatic first-pass metabolism. This provides consistently uniform blood levels of drug substance and a more predictable clinical response. The onset of activity occurs within 20 minutes and is maintained for more than 8 hours.

Product licence number 0075/0044.

PALFIUM®

Presentation Palfium products contain Dextromoramide Tartrate BP, and the dose and strength are expressed as dextromoramide base. The presentations available cover the oral, parenteral and rectal routes of administration:

Palfium tablets, 5 mg: white, scored tablets for oral use (Dextromoramide Tablets BP, 5 mg).

Palfium tablets, 10 mg: peach, scored tablets for oral use (Dextromoramide Tablets BP, 10 mg).

Palfium injection, 5 mg and 10 mg per 1.0 ml of solution: a clear, colourless, aqueous solution for parenteral administration (Dextromoramide Injection BPC, 5 mg or 10 mg per 1 ml).

Palfium suppositories, 10 mg: light cream coloured suppositories for rectal administration.

Uses Palfium is a potent analgesic for relief of the severe pain of inoperable carcinoma and for the relief of other forms of severe and intractable pain.

Dosage and administration *Adult dosage:* First dose: Not more than 5 mg by mouth or by subcutaneous or intramuscular injection, or 10 mg rectally.

Subsequent doses: The size of subsequent doses depends upon the needs of the patient, that is, upon the

severity of the pain. In cases of severe pain 10 mg Palfium may be required, repeated as necessary in order to maintain analgesia. The dose required may also be influenced by the patient's body weight. Regardless of body weight, however, not more than 20 mg should be given as a single dose and usually not more than 15 mg by injection. The dose frequency and the total daily dosage may vary significantly and should be titrated according to the needs of the individual patient.

In postoperative pain the initial dose of Palfium in the immediate postoperative period should be restricted, for example, to 2.5 mg, as the patient may still be under the influence of circulating anaesthetic agents and pre-medications. For subsequent postoperative care, 5 mg three or four times daily as required is usually sufficient.

Administration: Palfium is as effective orally as by injection. The oral route of administration thus is to be preferred. Palfium tablets should be given before meals, if possible. Palfium is also fully effective rectally and a 10 mg dose may be administered by suppository, particularly at night. When oral administration is impracticable Palfium injection may be administered by the intramuscular or subcutaneous route. Administration by the intravenous route is not recommended in normal practice.

Child dosage: A paediatric dosage regime has not yet been established. Should the need arise to administer Palfium to a child, the initial dosage should be not more than 0.08 mg per Kg of body weight.

Contra-indications, warnings, etc Palfium is contra-indicated in patients with respiratory depression or obstructive airways disease, and in female patients during child-birth. It is also contra-indicated in patients receiving monamine oxidase inhibitors and two to three weeks should be allowed to elapse before Palfium is administered to patients who have been treated with these agents.

The use of Palfium in pregnant patients is not recommended, although there is no evidence from animal studies to suggest that it is potentially harmful. In cases where the rate of metabolism of dextromoramide may be reduced, such as in the elderly and in patients with hypothyroidism or chronic hepatic insufficiency, it may be advisable to employ a reduced dosage regime.

Palfium may give rise to dizziness and sweating, especially in the ambulant patient. These effects may be minimised by advising the patient to rest, preferably supine, for a short period after administration of the first few doses. Nausea and vomiting may be troublesome but tend to occur only rarely. As with other potent analgesics tolerance and addiction may occur with continued use of Palfium.

Respiratory depression is unlikely to occur when Palfium is employed on its own in a normal therapeutic dosage. In the event of oral overdosage empty the stomach by aspiration and lavage using, for example, a 0.02% aqueous solution of potassium permanganate. If consciousness is impaired and respiration depressed suitable antagonists should be administered. Levallorphan tartrate 1.0 mg intravenously initially, followed by 1 or 2 doses of 0.5 mg may be used. Alternatively, nalorphine or naloxone may be administered using the appropriate dosage.

The circulation should be maintained with intravenous infusion of plasma or suitable electrolyte solutions and assisted respiration may be necessary until spontaneous breathing is restored.

Pharmaceutical precautions Palfium ampoules and tablets require no special precautions. As with all medicines, however, it is preferable that they be stored in a cool, dry place. Palfium suppositories must be stored in a cool location well away from radiators and other sources of heat.

Legal category POM, MDA.

Package quantities Palfium tablets 5 mg and 10 mg, containers of 100.

Palfium injection, 5 mg and 10 mg per ml, packs of 10 1.1 ml ampoules.

Palfium suppositories, packs of 10.

Further information Palfium is as effective when given by mouth as when injected. The analgesic effect is rapid by all routes of administration (typically 20–30 minutes).

Palfium provides pain relief normally without clouding consciousness or mental activity, and does not cause constipation. It may be advantageous in some cases to provide simultaneous administration of a sedative, hypnotic or tranquilliser, such as chlorpromazine, with Palfium. A cautious approach should be made to establish the most satisfactory dosage regime. In most cases only half the normal dose of the ancillary drug will be required.

Product licence numbers

Palfium Tablets 5 mg	0075/5015R
Palfium Tablets 10 mg	0075/0035R
Palfium Injection 5 mg	0075/5012R
Palfium Injection 10 mg	0075/5013R
Palfium Suppositories	0075/5014R

PIPTALIN®

Presentation Piptalin elixir is an orange-flavoured and orange coloured suspension. Each 5 ml of elixir contains pipenzolate bromide 4 mg and simethicone (activated dimethicone) 40 mg.

Uses Piptalin is indicated for the alleviation of the discomfort and pain associated with spasm, hypermotility and gaseous distension in functional and organic digestive disorders, such as in infant colic, regurgitation and vomiting. Piptalin is also indicated for functional abdominal pain in the school child, and for flatulent dyspepsia, aerophagia, cardiospasm and pylorospasm.

Dosage and administration *Infants, up to 10 kg body weight:* 2.5 ml orally 15 minutes before each feed.

Young children, 10–20 kg body weight: 2.5 to 5.0 ml three or four times daily.

Older children, 20–40 kg body weight: 5 ml three or four times daily.

Adults: 10 ml three or four times daily.

Piptalin elixir should be taken approximately 15 minutes before meals. If necessary it may be diluted with water.

Contra-indications, warnings, etc Piptalin elixir is contra-indicated in bowel obstruction and in hypertrophic pyloric stenosis.

Typical anticholinergic side-effects due to pipenzolate bromide occur only rarely. In high doses Piptalin may cause constipation with tenesmus and, rarely, dermal flushing without fever. These effects usually disappear or diminish at lower dose levels.

Treatment of overdosage is as for other anticholinergic

drugs. Empty the stomach by aspiration and lavage. Promote peristalsis with a saline purgative (30 g sodium sulphate in 250 ml warmed water is a suitable solution) and control excitation with a short acting sedative or hypnotic such as intravenous diazepam. Neostigmine methylsulphate may be injected i.m. or s.c. for control of peripheral symptoms. Assisted respiration may be necessary as may catheterisation if urine is retained. Fluids should be given freely.

Pharmaceutical precautions Piptalin elixir should be shaken thoroughly before use. It may be diluted with water or syrup and is incompatible with alkaline solutions.

Legal category POM.

Package quantities Piptalin elixir is available in bottles of 100 ml and 500 ml.

Further information Relief from discomfort and pain due to spasm and flatulence usually occurs within 10 to 20 minutes and the duration of antispasmodic action is normally approximately four hours.

Piptalin combines the antispasmodic activity of pipenzolate bromide with the defatulant effects of simethicone. The former relieves spasm and reduces hypermotility and gastric secretion while simethicone assists in elimination of entrapped gas and in prevention of the formation of mucous-occluded gas pockets in the gastro-intestinal tract.

Product licence number 0075/5017.

SPIROCTAN®

Presentation Spiroctan products contain Spironolactone BP and are available as three dosage forms:

Spiroctan 25	light blue coated tablets marked BM B2 and containing 25 mg spironolactone BP.
Spiroctan 50	green coated tablets marked BM A8 and containing 50 mg spironolactone BP.
Spiroctan 100	light green hard gelatin capsules marked BM A7 and containing 100 mg spironolactone BP.

Uses *Pharmacology:* Spiroctan promotes diuresis by competitive inhibition of aldosterone, a sodium-retaining, potassium-excreting hormone. It acts on the distal portion of the renal tubule and may be used in conjunction with more proximally acting diuretics.

Indications for Use: Spiroctan is recommended for use in the treatment of congestive heart failure, essential hypertension, idiopathic oedema, liver cirrhosis, ascites and nephrotic syndrome. For the prevention and treatment of peri-operative primary aldosteronism and also for the diagnosis and treatment of primary aldosteronism of different aetiology. Spiroctan is recommended for use in hypertension associated with diabetes particularly if the metabolic state deteriorates with other anti-hypertensive medication.

Dosage and administration *Adults:* Adequate maintenance dosage is usually between 50 and 200 mg daily, depending on the patients' response. This may be increased to 300 to 400 mg daily when necessary. An initial dosage of up to 600 mg daily may be employed in appropriate cases.

Children: The daily dosage for children is based on an

intake of 1.5 to 3.0 mg per kg body weight, as shown in the following guidelines:

Age 1 to 3 years (up to approximately 15 kg): One tablet Spiroctan 25 every other day.

Age 4 to 7 years (up to approximately 23 kg): One tablet Spiroctan 25 each day.

Age 8 to 12 years (up to approximately 37 kg): One tablet Spiroctan 25 twice daily.

Spiroctan tablets and capsules should be taken with fluid. When the daily dosage does not exceed 200 mg it may normally be taken as a single dose. For children who cannot swallow solid dose forms the tablets may be crushed and taken with food or drink.

Contra-indications, warnings, etc Spiroctan is contra-indicated in cases of renal failure, acute renal insufficiency, where hyperkalaemia is present, and in patients hypersensitive to spironolactone.

Potassium supplements should not be administered with Spiroctan except initially in cases of hypokalaemia, and the use of Spiroctan with other potassium-sparing diuretics should be avoided.

The use of Spiroctan in women who are pregnant, who may become pregnant or who are breast-feeding is not recommended.

The action of other diuretics may be potentiated. The initial dose should be half that normally administered and the dosage should be adjusted to the patient's needs.

Although the dose of Spiroctan does not generally need to be reduced in hepatic dysfunction, such patients should be carefully monitored as hepatic coma may be precipitated in susceptible subjects.

Periodic estimation of serum electrolytes is recommended.

Adverse effects are infrequent and usually mild. They include drowsiness, mental confusion (especially in conjunction with alcohol) and gastro-intestinal effects. Drivers of vehicles or operators of dangerous machinery should be warned of the effects on alertness.

Gynaecomastia may occur rarely but is normally reversible on cessation of dosage. Very occasionally alterations in voice pitch occur and these may not be reversible. This risk should be carefully considered in patients for whom voice control is important, for example, in actors. Occasional reports of skin rashes, breast enlargement and nipple sensitivity have been made.

Carcinogenicity: Spironolactone has been shown to produce tumours in rats when administered at high doses over a long period of time. The significance of these findings with respect to clinical use is not certain. However, the long-term use of spironolactone in young patients requires careful consideration of the benefits and the potential hazard involved.

Toxic effects in overdosage are due mainly to hyperkalaemia. Clinical symptoms include irregular pulse, lassitude, and muscular weakness and it may be difficult clinically to differentiate from hypokalaemia. Treatment is by cessation of therapy, administration of potassium-excreting diuretics, use of ion-exchange resins, etc.

Pharmaceutical precautions No special storage precautions are necessary. As with all medicines, however, it is recommended that Spiroctan be stored in a cool, dry place.

Legal category POM.

Package quantities

Spiroctan 25 Packs of 100 and 500 tablets.

Spiroctan 50 Packs of 100 tablets.

Spiroctan 100 Blister packs of 28 capsules.

Further information Spiroctan may be administered in combination with more proximally acting diuretics to increase diuresis and to prevent excessive potassium loss.

No metabolic changes occur with Spiroctan in incipient or overt diabetes.

In the treatment of essential hypertension and of oedema of varied aetiology the treatment should be continued for at least two weeks as an adequate response may not occur before this time.

Product licence numbers

Spiroctan 25 0075/0037

Spiroctan 50 0075/0038

Spiroctan 100 0075/0039

SPIROCTAN-M* INJECTION ▼

Presentation A clear, yellow, aqueous solution containing 200 mg potassium canrenoate in each 20 ml ampoule.

Pharmacology: Potassium canrenoate is converted in the body to canrenone, the major active metabolite of spironolactone. It is an aldosterone antagonist with clinical effects similar to those of spironolactone. As potassium canrenoate is administered intravenously, however, its clinical effects are more rapidly apparent. As with spironolactone, potassium canrenoate is capable of producing direct cardiac effects independent of its aldosterone antagonist actions. Potassium canrenoate thus demonstrates a clinically beneficial positive inotropic and anti-arrhythmic cardiac activity at the recommended dosage.

Indications: Spiroctan-M Injection is indicated for use in the treatment of oedema associated with cardiac dysfunction, particularly where cardiac arrhythmias and/or digitalis intolerance due to hypokalaemia occur. It is also indicated for use in the treatment of oedema associated with secondary aldosteronism in clinical cases such as ascites, oedema associated with liver dysfunction, oedema associated with the nephrotic syndrome and responsive oedema of different aetiology.

Spiroctan-M Injection is also indicated for the treatment of hypertension associated with an aldosterone excess.

Dosage and administration For use in adults only. The normal dose is up to 800 mg (up to 4 ampoules) daily by slow intravenous injection. This may be given in a single administration or in divided doses during the day.

In order to avoid irritation and pain at the site of infusion, Spiroctan-M Injection should be administered slowly, 2 to 3 minutes per ampoule, and preferably not into a thin vein.

In severe cases a potent diuretic may be administered together with Spiroctan-M Injection until satisfactory diuresis has been induced.

Contra-indications, warnings, etc *Contra-indications:* Spiroctan-M Injection is contra-indicated in patients with renal failure, hyperkalaemia or hyponatraemia and in those hypersensitive to potassium canrenoate. It should not normally be given together with potassium supplements.

Warnings and precautions: Spiroctan-M Injection is not recommended for administration to children, or to pregnant or breast-feeding women. The administration of Spiroctan-M Injection should occur slowly, 2 to 3 minutes per ampoule, to avoid local venous irritation. It is recommended that for patients on long term therapy the electrolyte balance should be monitored regularly. Normally, however, intravenous treatment is of short duration and therapy may be continued with spironolactone tablets or capsules given orally. As potassium canrenoate yields only one of several active metabolites of spironolactone its aldosterone antagonist potency relative to that of spironolactone in chronic dosage is approximately 0.7. This factor should be considered in transferring from intravenous potassium canrenoate to oral spironolactone tablets or capsules. Potassium canrenoate is metabolised to canrenone which is an active metabolite of spironolactone. Spironolactone has been shown to produce tumours in rats when administered in high doses over a long period of time. The significance of these findings with regard to clinical use is not certain. The long term use of potassium canrenoate in young patients requires careful consideration of the potential benefits and hazards involved.

Adverse effects: Some patients may experience irritation or pain at the site of infusion, particularly if the injection is not administered slowly. A transient confusion syndrome has been observed during therapy with high doses (1,000 mg per day or more). This effect subsided when the dosage was reduced. Nausea and vomiting may also occur soon after a high dose and may be controlled by suitable anti-emetic medication.

It is theoretically possible that in chronic usage there may be androgenic effects in females and gynaecomastia and sexual dysfunction in males. As Spiroctan-M Injection is not generally employed for chronic treatment no evidence of these effects has been reported.

Overdosage: The effects of acute overdosage may include nausea, vomiting, transient confusion and possibly hyperkalaemia. Treatment of overdose involves cessation of therapy, anti-emetic medication and the use of a potassium-eliminating drug if hyperkalaemia is present.

Pharmaceutical precautions Spiroctan-M Injection should be stored away from light.

Legal category POM.

Package quantities The ampoules are supplied in packs of 5.

Further information Potassium canrenoate is converted in the body to canrenone, which is the major active metabolite of spironolactone. The clinical effects of the two drugs are qualitatively similar although potassium canrenoate is more rapidly effective and is able to achieve higher blood levels of canrenone. Diuresis normally commences within the first 24 hours although latent periods of 10 days or more have been reported in very refractory cases. The direct cardiac actions of Spiroctan-M Injection occur soon after administration. After the acute phase of treatment dosage may be reduced and treatment may be continued with spironolactone tablets or capsules. Spiroctan-M Injection does not affect glucose metabolism, does not interfere with the treatment of diabetes, and does not promote hyperuricaemia.

Product licence number 0075/0040.

SUSTAMYCIN*

Presentation Sustamycin is presented as light blue/dark blue hard gelatin capsules. Each capsule contains 250 mg Tetracycline Hydrochloride BP in a sustained release formulation.

Uses Sustamycin is a sustained-action tetracycline formulation with an enhanced biological availability of tetracycline which allows for reduction of dose and of dose frequency. Sustamycin is indicated for the treatment of infections due to organisms susceptible to tetracycline including bronchitis, acute exacerbations of chronic bronchitis, acne and sexually transmitted diseases.

Dosage and administration *For adults and children over 12 years only:* Two capsules initially followed by 1 capsule every 12 hours. In more severe infections dosage may be increased at the discretion of the physician, for example, to 2 capsules twice daily. In acute cases treatment should be maintained for two to three days after the desired clinical response has been achieved. In the treatment of acne, therapy should continue for at least eight weeks although a lower dose, e.g. 1 capsule daily, may be used after the initial period.

Sustamycin should be taken preferably one hour before or two hours after main meals.

Contra-indications, warnings, etc Contra-indicated in patients with known hypersensitivity to tetracyclines.

Sustamycin should be used with caution in patients with renal or hepatic impairment.

If tetracycline is administered to young children (under eight years) or to pregnant women it is selectively taken up in developing bones and teeth and dental staining and enamel hypoplasia may occur. Sustamycin should not be used for such patients unless the potential benefits justify the risks.

The gastro-intestinal adverse effects common to the tetracyclines occur only rarely, due to the sustained release; skin photosensitivity reactions may be seen occasionally. Appropriate measures should be taken in the event of over-growth by a non-susceptible organism.

As with all tetracyclines, the concomitant intake of antacids, mineral supplements (calcium, magnesium and iron) and milk may diminish absorption from Sustamycin capsules.

Pharmaceutical precautions Store in well closed containers at a temperature below 30°C.

Legal category POM.

Package quantities Sustamycin is available in containers of 50 or 500 capsules.

Further information Sustamycin contains tetracycline hydrochloride in a sustained release form facilitating twice daily dosage which leads to increased patient compliance compared with the four times daily dosage regimen of conventional tetracycline. The formulation enables tetracycline to be absorbed throughout the gastro-intestinal tract, not just in the stomach. This enhanced absorption allows a reduction in total tetracycline dosage while maintaining full clinical efficacy.

Product licence number 0075/0017.

*Trade Mark

Medo Pharmaceuticals Limited

130 High Street
Chesham
Buckinghamshire HP5 1EF



CARBELLON*

Presentation Black, uncoated tablet, containing:

Charcoal BP.	100 mg
Belladonna Dry Extract BP	6 mg
Magnesium Hydroxide BP	100 mg
Peppermint Oil BP	0.003 ml

Uses Indigestion, flatulence, dyspepsia, hyperacidity.

Dosage and administration *Children: 1-5 years:* 1½ tablets

6-12 years: 2 tablets.

Adults: 2-4 tablets, three times a day. All dosages are t.d.s.

Contra-indications, warnings, etc

Contra-indications: Prostatic enlargement, glaucoma, paralytic ileus and pyloric stenosis.

Warnings: Activated charcoal adsorbs other drugs, particularly antibiotics such as tetracycline, and they should not be given at the same time as Carbellon.

Pharmaceutical precautions Store in a well closed container in a cool place, protected from light.

Legal category P.

Package quantities 50 and 250.

Further information Nil.

Product licence number 4147/5915.

CELLUCON*

Presentation Chocolate coloured and flavoured uncoated tablet containing Methylcellulose 2500 BP 0.5 g.

Uses To aid reduction of appetite, constipation, colitis, diverticulitis, irritable bowel syndrome and for management of colostomies.

Dosage and administration For appetite reduction, colitis, diverticulitis, and constipation and irritable bowel syndrome.

Adults: 1 to 4 tablets to be chewed half an hour before meals followed by at least one glass of water or other liquid. In constipation, as normal function returns, the dose can be reduced.

Children: 1 to 2 tablets three to four times daily or as advised by the medical practitioner.

For Colostomies: The dose of Cellucon should be varied according to the fluid intake. An initial dose of three tablets two or three times a day should be tried and adjusted according to the patient's requirements. The tablets should be chewed or broken up and swallowed but the quantity of water should be reduced to a minimum, and no fluid should be taken for at least half an hour before and after the tablets. If the stools are too firm the dose of tablets should be decreased; if too loose the

dose should be increased. If the bowels function at inconvenient times additional tablets can be taken to prevent unwanted evacuation.

Contra-indications, warnings, etc Cellucon should not be given if intestinal obstruction is suspected.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities 100 and 250.

Further information Nil.

Product licence number 4147/5911.

CHOCOVITE*

Presentation Chocolate coloured and flavoured, uncoated tablets, containing:

Calcium Gluconate BP	0.5 g
Calciferol BP	15 micrograms

Uses For calcium deficiency combining Calcium in the form of gluconate and Vitamin D₂ to increase absorption of the calcium.

Dosage and administration

Adult: One to three tablets to be sucked three times a day.

Children: According to requirements.

Contra-indications, warnings, etc Chocovite is contra-indicated in patients with severe hypercalcaemia or hypercalciuria.

Pharmaceutical precautions Store in a cool place protected from light.

Legal category P.

Package quantities 100.

Further information Nil.

Product licence number 4147/5906.

DIOCTYL* PREPARATIONS

Presentation *Diocetyl Forte tablets:* Yellow sugar coated tablets containing docusate sodium 100 mg.

Diocetyl Medo Tablets: White scored flat uncoated tablets containing docusate sodium 20 mg.

Diocetyl Medo Syrup: Pale yellow syrup containing docusate sodium 0.25% w/v (12.5 mg in 5 ml).

Diocetyl Concentrate: Pale yellow syrup containing docusate sodium 1% w/v (For hospital use only).

Uses Docusate sodium is an anionic wetting agent which acts as a faecal softener by allowing penetration of the accumulated, hard, dry faeces by water and fats.

Used for the prevention and treatment of chronic constipation.

Dosage and administration *For Constipation:*
Adults: Up to 500 mg in divided doses daily. Treatment should be commenced with large doses which should be decreased as the condition of the patient improves.

Children: 12.5 to 25 mg three times daily.

Infants: 12.5 mg three times daily.

For Barium meals: 400 mg to be taken with the meal.

The tablets should be administered with a glass of liquid and the syrup should be given in an orange flavoured drink or milk to disguise the bitter taste. For dilution of the Concentrate see Pharmaceutical Precautions. Usually effective within one or two days.

Contra-indications, warnings, etc Docusate sodium should be taken in a reduced dose when administered with anthraquinone derivatives as it increases their absorption. Do not use when abdominal pain, nausea or vomiting is present. Do not take concurrently with mineral oil.

Pharmaceutical precautions In cold weather Dioctyl Syrup forms flaky crystals. These are readily re-dissolved by standing the container in water at 40°C or storage in a warm room for two or three days. Shaking also speeds redissolution. Dioctyl Concentrate should be diluted with three parts of Orange Syrup BP and then administered as for Dioctyl Syrup.

Legal category P.

Package quantities

Dioctyl Forte Tablets 100 mg: 100 and 250.

Dioctyl Medo Tablets 20 mg: 100 and 250.

Dioctyl Syrup 0.25% w/v (12.5 mg in 5 ml): 125 ml and 1 litre.

Dioctyl Concentrate 1% w/v: (For hospital use only): 1 litre.

Further information Docusate Sodium is the British Approved name for Dioctyl Sodium Sulphosuccinate.

Product licence numbers

Dioctyl Forte Tablets 4147/5910

Dioctyl Medo Tablets 4147/5907

Dioctyl Syrup 4147/5908

Dioctyl Concentrate 4147/5909

DIOCTYL* EAR DROPS

Presentation A clear liquid containing Docusate Sodium 5% w/w in Polyethylene Glycol in a 7 ml glass amber dropper bottle.

Uses For the softening of ear wax to facilitate its removal.

Dosage and administration Four drops should be instilled into the ear twice daily for 2–3 days. The head should be inclined to one side and the ear plugged with cotton wool soaked in Dioctyl Ear Drops if necessary. After 2–3 days the wax should be easy to remove with a cotton bud or a syringe. Patients prone to persistent problems with ear wax should use Dioctyl Ear Drops every two weeks.

Contra-indications, warnings, etc None.

Pharmaceutical precautions No special pharmaceutical precautions are required with this product.

Legal category GSL.

Package quantities Dioctyl Ear Drops are available in a 7 ml amber glass bottle with a removable glass dropper unit.

Further information Dioctyl Ear Drops are for use only in the ear. Docusate Sodium is the British approved name for Dioctyl Sodium Sulphosuccinate.

Product licence number 4147/0045.

HORMOFEMIN* CREAM

Presentation Smooth off-white cream containing Dienoestrol BP 0.025% w/w in a 40 g tube with a 4 g applicator.

Uses Pruritis vulvae, senile vaginitis, atrophic vaginitis.

Dosage and administration Given for short term use only. The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible.

Attempts to discontinue or taper medication should be made at three to six month intervals, following physical examination. The usual dosage range is a half to one applicator full per day for one or two weeks, then gradually reduced to one half initial dose for a similar period.

Treated patients with an intact uterus should be monitored closely for signs of endometrial cancer and appropriate diagnostic measures should be taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding. As a general rule it is advisable that patients receiving any form of oestrogen replacement therapy should have a complete physical examination at least once a year.

Contra-indications, warnings, etc Prolonged exposure to unopposed oestrogen may increase the risk of development of endometrial carcinoma, induction of other malignant neoplasms, and the risk of cancer of the breast. Long term continuous administration of natural and synthetic oestrogens in certain animal species increases the frequency of carcinomas of the breast, cervix, vagina and liver. There is now evidence that oestrogens increase the risk of carcinoma of the endometrium in humans.

At the present time there is no satisfactory evidence that oestrogens given to post-menopausal women increase the risk of cancer of the breast, although a recent long-term follow up of a single physician has raised the possibility. However, because of animal data there is a need for caution in prescribing oestrogens for women with a strong family history of breast cancer or who have breast nodules, fibrocystic disease or abnormal mammograms.

Pregnancy is an absolute contra-indication to the use of Dienoestrol cream since it may be harmful to the developing foetus.

Oestrogens should not be used in women with any of the other following conditions: known or suspected cancer of the breast, known or suspected oestrogen-dependent neoplasia, undiagnosed abnormal genital bleeding, active thrombophlebitis or thromboembolic disorders, a past history of thrombophlebitis, thrombosis, or thromboembolic disorders.

Thromboembolic disorders: While an increased rate of thromboembolic and thrombotic disease in post-menopausal users of oestrogens has not been found, this does

not rule out the possibility that such an increase may be present or that subgroups of women who have underlying risk factors or who are receiving relatively large doses of oestrogens may have increased risk. Therefore oestrogens should not be used in persons with active thrombophlebitis or thromboembolic disorders, and they should not be used (except in treatment of malignancy) in persons with a history of such disorders. They should be used with caution in patients with cerebral vascular or coronary artery disease and only for those in whom oestrogens are clearly needed.

Gall bladder disease: A recent study has reported a two to three-fold increase in the risk of surgically confirmed gall bladder disease in women receiving post-menopausal oestrogens, similar to the two-fold increase previously noted in users of oral contraceptives.

Hepatic adenoma: Benign hepatic adenomas appear to be associated with the use of oral contraceptives. Although benign, and rare, these may rupture and may cause death through intra-abdominal haemorrhage. Such lesions have not yet been reported in association with other oestrogen or progestogen preparations but should be considered in oestrogen users having abdominal pain and tenderness, abdominal mass, or hypovolemic shock.

Elevated blood pressure: It has been reported that this may occur with the use of oestrogens in the menopause and blood pressure should be monitored with oestrogen use, especially if high doses are used.

Precautions: A complete medical and family history should be taken prior to the initiation of any oestrogen therapy. The pretreatment and periodic physical examinations should include special reference to blood pressure, breasts, abdomen and pelvic organs, and should include a Papanicolaou smear.

A pathologist should be advised of oestrogen therapy when relevant specimens are submitted.

Certain patients may develop undesirable manifestations of excessive oestrogenic stimulations, such as abnormal or excessive uterine bleeding, mastodynia, etc. Pre-existing uterine fibroids may increase in size during oestrogen use.

Patients with a past history of jaundice during pregnancy have an increased risk of recurrence of jaundice while receiving oestrogen therapy. If jaundice develops in any patient receiving oestrogen, the medication should be discontinued while the cause is investigated.

Oestrogens may aggravate cases of porphyria.

Pharmaceutical precautions Store in a cool place.

Legal category POM.

Package quantities 40 g.

Further information Nil.

Product licence number 4147/5916.

MEDOCODENE*

Presentation Yellow scored uncoated tablets each containing Paracetamol PhEur 500 mg and Codeine Phosphate PhEur 8 mg

Uses The treatment of mild to moderate pain and as an antipyretic.

Dosage and administration

The tablets are for oral administration.

Adults: 1–2 tablets four times a day.

Children 6–12 years: $\frac{1}{2}$ –1 tablet 4 times a day.

Not suitable for children under 6 years of age, unless directed by a physician.

At least four hours should be allowed between doses. Not more than four doses in 24 hours.

Contra-indications, warnings, etc Codeine is a narcotic analgesic. Tolerance, psychological and physical dependence may occur. Constipation is common.

As Medocodene contains Paracetamol, an overdose can cause Hepatic Necrosis. Patients who have taken an overdose may appear well for several days, but they may then develop severe Hepatic damage.

Administration of Cysteamine, Methionine or Acetylcysteine within 12 hours of ingestion may prevent liver damage.

There is epidemiological evidence of the safety of Paracetamol in human pregnancy.

There is no, or inadequate evidence of safety of Codeine in human pregnancy, but the drug has been widely used for many years without apparent ill consequence, and animal studies have not shown any hazard.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Medocodene is available in 100 and 250 sizes.

Further information Nil.

Product licence number 4147/0034R.

PHOLCOMED* LINCTUS

PHOLCOMED* DIABETIC LINCTUS

Presentation A red blackcurrant flavoured linctus containing:

Pholcodine BP	5 mg
Papaverine Hydrochloride BP	1.25 mg

The diabetic linctus contains no sugar and has negligible calorific value.

Uses Pholcomed is used for the relief of irritating unproductive coughs. Pholcomed contains a combination of Pholcodine, a cough suppressant, and Papaverine acting on smooth muscle to relax the bronchi.

Pholcodine is less constipating than Codeine.

Dosage and administration **Adults:** Two to three 5 ml spoonfuls.

Children: Over 2 years: One 5 ml spoonful.

Infants: Half a 5 ml spoonful.

Three or four times daily after meals.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Pholcomed: 125 ml and 2 litres. *Pholcomed Diabetic:* 125 ml.

Further information Nil.

Further information Nil.

Product licence numbers

Pholcomed 4147/5901

Pholcomed Diabetic 4147/5902

PHOLCOMED* FORTE LINCTUS
PHOLCOMED* FORTE DIABETIC LINCTUS

Presentation A red blackcurrant flavoured linctus containing:

Pholcodine BP	19 mg
Papaverine Hydrochloride BP	5 mg

The diabetic linctus contains no sugar and has negligible calorific value.

Uses Pholcomed Forte is used for the relief of irritating unproductive coughs. Pholcomed contains a combination of Pholcodine, a cough suppressant, and Papaverine, acting on smooth muscle to relax the bronchi.

Pholcodine is less constipating than Codeine.

Dosage and administration *For adults only:* One 5 ml spoonful three times a day after meals.
Not suitable for children.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities

Pholcomed Forte: 125 ml and 2 litres.

Pholcomed Forte Diabetic: 125 ml.

Further information Nil.

Product licence numbers

Pholcomed Forte	4147/5903
Pholcomed Forte Diabetic	4147/5904

PHOLCOMED* PASTILLES

Presentation Blackcurrant flavoured, sugar coated disc shaped pastilles containing:

Pholcodine BP	4 mg
Papaverine Hydrochloride BP	1 mg

Uses Pholcomed Pastilles are used for the relief of irritating unproductive coughs. Pholcomed pastilles contain a combination of Pholcodine, a cough suppressant, and Papaverine, acting on smooth muscle to relax the bronchi.

Pholcodine is less constipating than Codeine.

Dosage and administration *Dose – Adults:* One to two pastilles hourly.

Children: One pastille hourly.

Maximum adult dose fifteen pastilles daily.

Maximum children's dose seven pastilles daily.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities 30 pastilles.

Further information Nil.

Product licence number 4147/5905.

PHOLCOMED* EXPECTORANT SYRUP

Presentation A red cherry flavoured syrup containing:

Guaiphenesin BP	62.5 mg
Methylephedrine Hydrochloride	0.625 mg

Uses As an expectorant cough syrup with a broncho-dilator action.

Dosage and administration *Adults:* Two to four 5 ml spoonfuls.

Children: Half to one 5 ml spoonful.

Three times a day.

Contra-indications, warnings, etc The dose of Methylephedrine is very small, nevertheless, it should be used with caution in patients with heart disease, hyperthyroidism and closed angle glaucoma. It should not be given to patients treated with monoamine oxidase inhibitors.

Pharmaceutical precautions None.

Legal category P.

Package quantities 125 ml and 2 litres.

Further information Nil.

Product licence number 4147/5914.

POLYVITE* CAPSULES

Presentation Oval red capsule containing:

Vitamin A	4,500 Units
Thiamine Hydrochloride BP	2.5 mg
Riboflavin BP	1.5 mg
Pyridoxine Hydrochloride BP	1.5 mg
Calcium Pantothenate USP	2.0 mg
Nicotinamide BP	15.0 mg
Ascorbic Acid BP	30.0 mg
Calciferol BP	11 mcg

Uses Vitamin deficiency.

Dosage and administration One to two capsules daily depending on requirements.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities 50 and 500.

Further information Nil.

Product licence number 4147/5913.

TONIVITAN* A & D

Presentation A green orange flavoured syrup containing:

Vitamin A	700 Units
Calciferol BP	70 Units
Green Ferric Ammonium Citrate BPC 1954	150 mg
Calcium Glycerophosphate BPC 1963	25 mg
Manganese Glycerophosphate BPC 1949	0.4 mg
Copper Sulphate BPC	0.4 mg
Orange Elixir to	5 ml

Uses Vitamin tonic for all ages.

Dosage and administration *Under 1 year:* Half a 5 ml spoonful.

Up to 10 years: One 5 ml spoonful three times a day.

Over 10 years: Two 5 ml spoonfuls three times a day.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Store in a well closed container protected from light. The preparation tends to darken on standing but this does not affect its efficacy.

Legal category P.

Package quantities 125 ml and 1 litre.

Further information Nil.

Product licence number 4147/5917.

TONIVITAN* B SYRUP

Presentation A cherry flavoured syrup containing:

Thiamine Hydrochloride BP	0.5 mg
Riboflavin BP	0.4 mg
Piridoxine Hydrochloride BP	16.5 mcg
Nicotinamide BP	2.5 mg
Calcium Glycerophosphate BPC 1963	20.0 mg
Manganese Glycerophosphate BPC 1949	5.0 mg

Uses A vitamin tonic containing most of the vitamin B group together with phosphate and minerals.

Dosage and administration Give to 10 ml three times a day according to age and requirements.

Contra-indications, warnings, etc None.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities 125 ml and 1 litre.

Further information Nil.

Product licence number 4147/5900.

TONIVITAN* CAPSULES

Presentation Oval chocolate-brown capsule containing:

Vitamin A	4,500 Units
Thiamine hydrochloride BP	1 mg
Nicotinic Acid BP	15 mg
Ascorbic Acid BP	15 mg
Calciferol BP	600 i.u.
Dried Yeast BPC	50 mg

Uses Vitamin deficiency.

Dosage and administration 1–3 years: 2 capsules daily.

3–7 years: 4 capsules daily.

7–12 years: 2 capsules three times a day.

Over 12 years: 3 capsules three times a day.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities 100.

Further information Nil.

Product licence number 4147/5918.

**Trade Mark*

E. Merck Limited
Four Marks
Alton
Hampshire

MERCK

AMINOFUSIN® L600

Presentation A clear, sterile, pyrogen-free solution for intravenous feeding, containing pure L-amino acids which provide a high level of nitrogen in a low fluid volume.

Active ingredients:

	<i>g/litre</i>
L-Amino acids	
L-Isoleucine	1.55
L-Leucine	2.2
L-Lysine monohydrochloride	2.5
L-Methionine	2.1
L-Phenylalanine	2.2
L-Threonine	1.0
L-Tryptophan	0.45
L-Valine	1.5
L-Arginine (calc. as base)	4.0
L-Histidine (calc. as base)	1.0
L-Alanine	6.0
Glycine	10.0
L-Glutamic acid	9.0
L-Proline	7.0
Total	50.0

Carbohydrates

Sorbitol	100.0
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Vitamins

	<i>mg/litre</i>
Ascorbic acid	400
Inositol	500
Nicotinamide	60
Pyridoxine HCl	40
Riboflavin 5'-phosphate-Na	2.5

Electrolytes

	<i>mmol/litre</i>
Na ⁺	40
K ⁺	30
Mg ⁺⁺	5
Acetate ⁻	10
Malate ⁻	15
(g/litre L-malic acid)	(2.01)
Cl ⁻	14
Total Nitrogen g/litre	7.6
kcal/litre approximately	600
pH	6.8
Osmolality approximately	1,300 mosm/kg

Uses For intravenous parenteral nutrition where the amino acids are in the optimum and balanced proportions together with a correctly balanced calorie supplement necessary to ensure maximum protein synthesis. Aminofusin is indicated whenever oral feeding is impossible or inadequate. Where extra calorie source is required Aminofusin L1000 is available containing 50 g of ethanol.

Dosage and administration The amount of Aminofusin to be administered daily is calculated according to individual patients' requirements of nitrogen, fluid, calories, etc. Adults should receive 0.8–1.6 g amino

acids/kg body weight daily. Children, pregnant women and post-operative patients, 1.6–2.0 g amino acids/kg body weight daily. Newborn and premature infants 2.0–3.0 g amino acids/kg body weight daily.

Infusion rate 40–60 drops per minute (2–4 ml/kg/hr); it should not exceed 4 ml per kg/hour. Optimal utilisation is achieved when the daily dose is given in a continuous infusion over 24 hours. In patients who are unable to tolerate continuous infusions, two infusion periods of four or six hours each per day are recommended.

Contra-indications, warnings, etc Aminofusin L600 is contra-indicated in patients suffering shock, hyperkalaemia, severe disturbances of liver or kidney function and disturbance of amino acid metabolism; its effects should be carefully controlled when given to patients who tend towards elevated serum potassium or urea levels. Too rapid an infusion may result in renal losses, and nausea in sensitive patients.

A pre-existing deficiency of vitamins and, in particular, folic acid and Vitamin B₁₂ may become clinically evident during intravenous nutrition with amino acids. Regular checks of the patients' Vitamin B₁₂ status and folate demand are therefore recommended. Prophylactic administration of adequate vitamins should be given if required.

Pharmaceutical precautions Store between 15° and 25°C. The solution of Aminofusin should be clear at all times before infusion. Store away from light. If a precipitate or severe discoloration occurs, discard. Addition of drugs to the bottle of amino-acid solution or giving set should be avoided.

Legal category POM.

Package quantities 1,000 ml glass bottles. 6 bottles per case.

Further information Nil.

Product licence number 0493/0068.

AMINOFUSIN® L1000

Presentation A clear, sterile, pyrogen-free solution for intravenous feeding, containing pure L-amino acids which provide a high level of nitrogen in a low fluid volume, together with ethanol as a calorie supplement.

Active ingredients

	<i>g/litre</i>
L-Amino acids	
L-Isoleucine	1.55
L-Leucine	2.2
L-Lysine monohydrochloride	2.5
L-Methionine	2.1
L-Phenylalanine	2.2
L-Threonine	1.0
L-Tryptophan	0.45

L-Valine	1.5
L-Arginine (calc. as base)	4.0
L-Histidine (calc. as base)	1.0
L-Alanine	6.0
Glycine	10.0
L-Glutamic acid	9.0
L-Proline	7.0
Total	50.0

Carbohydrates	
Sorbitol	100
Ethanol	52.80

Vitamins	mg/litre
Ascorbic acid	400
Inositol	500
Nicotinamide	60
Pyridoxine HCl	40
Riboflavin 5'-phosphate-Na	2.5

Electrolytes	mmol/litre
Na ⁺	40
K ⁺	30
Mg ⁺⁺	5
Acetate ⁻	10
Malate ⁻	15
(g/litre L-Malic acid)	(2.01)
Cl ⁻	14

Total Nitrogen g/litre	7.6
kcal/litre approximately	1000
pH	6.8

Osmolality approximately 2,700 mosm/kg

Uses For intravenous parenteral nutrition where the amino acids are in the optimum and balanced proportions together with a correctly balanced calorie supplement necessary to ensure maximum protein synthesis. Aminofusin is indicated whenever oral feeding is impossible or inadequate.

Dosage and administration

1. **Adults:** The amount of Aminofusin L1000 to be administered daily is calculated according to individual patients' requirements of nitrogen, fluid, calories, etc. Adults should receive 0.8–1.6 g amino acids/kg body weight daily.

2. **Children:** Not recommended.

Infusion rate 40–60 drops per minute (2–4 ml/kg/hr); it should not exceed 4 ml per kg per hour. Optimal utilisation is achieved when the daily dose is given in a continuous infusion over 24 hours. In patients who are unable to tolerate continuous infusions, two infusion periods of four or six hours each per day are recommended.

Contra-indications, warnings, etc Aminofusin L1000 is contra-indicated in patients suffering shock, hyperkalaemia, severe disturbances of liver or kidney function and disturbance of amino acid metabolism; its effects should be carefully controlled when given to patients who tend towards elevated serum potassium or urea levels. Too rapid an infusion may result in renal losses, and nausea in sensitive patients. This product contains alcohol, therefore its use is at the discretion of the attending Physician.

A pre-existing deficiency of vitamins and, in particular, folic acid and Vitamin B₁₂ may become clinically evident during intravenous nutrition with amino acids. Regular checks of the patients' Vitamin B₁₂ status and folate demand are therefore recommended. Prophylactic ad-

ministration of adequate vitamins should be given if required.

Pharmaceutical precautions Store between 15° and 25°C. The solution of Aminofusin should be clear at all times before infusion. Store away from light. If a precipitate or severe discoloration occurs, discard. Addition of drugs to the bottle of amino-acid solution or giving set should be avoided.

Legal category POM.

Package quantities 1,000 ml glass bottles. 6 bottles per case.

Further information Nil.

Product licence number 0493/0069.

AMINOFUSIN[®] L FORTE

Presentation A clear, sterile, pyrogen-free solution for intravenous feeding, containing pure L-amino acids which provide a high level of nitrogen in a low fluid volume. Aminofusin L Forte contains no calorie source, but is in the same proportion of L-amino acids but in twice the concentration with a total nitrogen content being 15.2 g/l instead of 7.6 g/l as in L 1000.

Active ingredients	
L-Amino acids	g/litre
L-Isoleucine	3.1
L-Leucine	4.4
L-Lysine monohydrochloride	5.0
L-Methionine	4.2
L-Phenylalanine	4.4
L-Threonine	2.0
L-Tryptophan	0.9
L-Valine	3.0
L-Arginine (calc. as base)	8.0
L-Histidine (calc. as base)	2.0
L-Alanine	12.0
Glycine	20.0
L-Glutamic acid	18.0
L-Proline	14.0
Total	100.0

Carbohydrates	
Sorbitol	—
Ethanol	—
Vitamins	mg/litre
Ascorbic acid	—
Inositol	500
Nicotinamide	60
Pyridoxine HCl	40
Riboflavin 5'-phosphate-Na	2.5
Electrolytes	mmol/litre
Na ⁺	40
K ⁺	30
Mg ⁺⁺	5
Acetate ⁻	10
Malate ⁻	5
(g/litre L-malic acid)	(0.67)
Cl ⁻	27.5
Total Nitrogen g/litre	15.2
kcal/litre approximately	400
pH	5.3–5.5
Osmolality approximately	1050 mosm/kg.

Uses Aminofusin L Forte is indicated whenever oral feeding is impossible or inadequate, the Aminofusin L

Forte solution can be used in special circumstances where there is a high N_2 requirement and in combination with other sources of energy such as hypertonic glucose or fat emulsion.

Dosage and administration

1. **Adults:** The amount of Aminofusin L Forte to be administered daily is calculated according to individual patient requirements of nitrogen, fluid, calories, etc. Adults should receive 0.8–1.6 g amino acids/kg body weight daily.

2. **Children:** Not recommended.

Infusion rate 35 drops per minute (1.5 ml/kg/hr); it should not exceed 1.5 ml per kg per hour. Optimal utilisation is achieved when the daily dose is given in a continuous infusion over 24 hours. In patients who are unable to tolerate continuous infusions, two infusion periods of four or six hours each per day are recommended.

Contra-indications, warnings, etc Aminofusin L Forte is contra-indicated in patients suffering shock, hyperkalaemia, severe disturbances of liver or kidney function and disturbance of amino acid metabolism; its effects should be carefully controlled when given to patients who tend towards elevated serum potassium or urea levels. Too rapid an infusion may result in renal losses, and nausea in sensitive patients.

A pre-existing deficiency of vitamins and, in particular, folic acid and Vitamin B_{12} may become clinically evident during intravenous nutrition with amino acids. Regular checks of the patients' Vitamin B_{12} status and folate demand are therefore recommended. Prophylactic administration of adequate vitamins should be given if required.

Pharmaceutical precautions Store between 15° and 25°C. The solution of Aminofusin L Forte should be clear at all times before infusion. Store away from light. If a precipitate or severe discoloration occurs, discard. Addition of drugs to the bottle of amino-acid solution or giving set should be avoided.

Legal category POM.

Package quantities 500 ml glass bottles, 10 bottles per case.

Further information Nil.

Product licence number 0493/0070.

CISTOBIL*

Presentation Cistobil tablets are bi-convex tablets 13 mm in diameter and plain on both sides. Each tablet, white-cream in colour, contains 500 mg Iopanoic acid.

Uses Cistobil tablets are recommended as an oral contrast medium for cholecystography.

Dosage and administration The meal prior to ingestion of the tablets should be a normal meal containing some fat. 15–20 minutes later the standard adult dose of 6 tablets of Cistobil is taken one at a time during 5–10 minutes. The patient should have nothing to eat on the morning prior to the radiological examination which is usually carried out 10–14 hours after ingestion of the contrast medium. A double dose of Cistobil (12 tablets) may be prescribed in special cases, especially where the patient is heavy or obese.

Contra-indications, warnings, etc Like all iodinated media, Cistobil should be used with caution and is contra-indicated in diseases of the liver parenchyma, in renal insufficiency, iodine intolerance, thyrotoxicosis, in myocardial diseases, and in congestive heart failure.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Cartons of 30 tablets packed in unit doses, each unit dose consisting of 6 tablets.

Further information Nil.

Product licence number 0493/0072.

DIUREXAN* ▼

Presentation Tablets each containing 20 mg Xipamide. The tablets are white, round, with bisecting score on one side and debossed A on the other, and have a diameter of 6 mm.

Uses Diurexan is a diuretic and antihypertensive agent having a gentle onset of action and gradual, prolonged effect. Whereas the main diuretic activity lasts for up to 12 hours, the antihypertensive effect is evident for 24 hours or more.

Hypertension: All grades of hypertension respond to treatment with Diurexan. It is an effective treatment on its own in mild to moderate hypertension, and may be used alone or combined with other antihypertensive agents in severe hypertension.

Oedema: Diurexan is indicated whenever diuretic therapy is required including congestive cardiac failure, hepatic oedema, renal oedema, peripheral oedema due to venous insufficiency and oedema of pregnancy in the second and third trimesters.

Dosage and administration For oral administration.

Hypertension: adults: The usual dose is 1 tablet (20 mg) daily, as a single early morning dose. In more severe grades of hypertension, 2 tablets daily, as a single early morning dose, may be required. When using Diurexan in combination with other antihypertensive therapy, the initial dose should not exceed 1 tablet daily.

Children: No dose recommended.

Oedema: Adults: In the initial phase of treatment the usual dose is 2 tablets (40 mg) daily in a single early morning dose. Depending on the patient's response, the dose may be lowered to 1 tablet daily when sufficient control of oedema has been achieved. Higher doses, up to 4 tablets daily (80 mg), may be employed in resistant cases.

Children: No dose recommended.

Contra-indications, warnings, etc

Contra-indications: Diurexan is contra-indicated in severe electrolyte deficiency, precomatose states associated with liver cirrhosis and severe renal insufficiency.

Side-effects and adverse reactions: Diurexan is generally well tolerated. Slight gastro-intestinal disturbances have been reported in a few cases as have episodes of mild dizziness.

Precautions: Like other diuretics, Diurexan may induce hypokalaemia in long-term therapy and potassium supplements may be necessary.

Animal experiments have indicated that Diurexan is devoid of teratogenic properties or effects on fertility and reproduction. Nevertheless, discretion is required before permitting therapy in pregnant patients. As with all drugs, treatment should be avoided in the first trimester of pregnancy.

Warnings: The dosage of other hypotensive drugs and cardiac glycosides may require adjustment when used in conjunction with Diurexan. In common with other diuretics, Diurexan may induce hyperuricaemia or changed glucose metabolism in patients predisposed to these conditions. Diabetic patients will probably require an adjustment of insulin dosage, or other hypoglycaemic agent therapy.

An increased risk of developing acute retention may arise in patients with prostatic hypertrophy.

Overdosage: General measures should be aimed at the maintenance of blood pressure, restoration of blood volume and correction of electrolyte imbalance.

Pharmaceutical precautions Store in a cool, dry place.

Legal category POM.

Package quantities Cartons of 140 tablets in blister packs of 14 tablets.

Further information Nil.

Product licence number 0493/0049.

ENDOBIL* ▼

Presentation Endobil 100 ml bottle contains a 9.91% w/v concentration of the meglumine salt of iodoxamic acid for intravenous infusion, equivalent to an iodine content of 45 mg/ml.

Uses Intravenous cholecystography and cholangiography.

Dosage and administration *Endobil Infusion:* 100 ml.

Adults: The recommended duration of intravenous infusion is between fifteen and thirty minutes.

Patients undergoing cholegraphic procedures with Endobil should be adequately prepared with only a light meal on the night before examination and an enema. Endobil should be warmed to body temperature and administered intravenously with the patient lying down.

Children: The use of Endobil in children is not recommended until further evidence has been accumulated and reviewed.

Contra-indications, warnings, etc

Contra-indications: Proven or suspected hypersensitivity to iodine-containing preparations.

Warnings, side-effects: Endobil should be used with caution in patients with severe functional impairment of the liver, kidneys or myocardium, severe hyperthyroidism and macroglobulinaemia (Waldenströms disease).

Side-effects following the administration of Endobil are generally mild and relatively rare, the most common being facial flushing and nausea.

As with any contrast medium, injection solutions of adrenaline, a vasopressor, a corticosteroid and an antihistamine should be immediately available in case of hypersensitivity. To cover the remote possibility of

delayed hypersensitivity the patient should be attended for 20 minutes following injection.

Pharmaceutical precautions Store away from light.

Legal category POM.

Package quantities *Endobil Infusion:* Box containing 1 × 100 ml bottle for intravenous infusion (4.5g iodine).

Further information Nil.

Product licence number 0493/0074.

GENTIGAN*

Presentation Gentigan ampoules for parenteral use are available as: Gentigan 40 mg/ml. Each 2 ml ampoule contains 133.3 mg of Gentamicin Sulphate BP ≡ 80,000 Units Gentamicin base (80 mg Gentamicin base) in 2 ml aqueous solution with Titriplex III and Sodium Bisulphate as stabilisers.

Uses Gentigan is a broad-spectrum aminoglycoside antibiotic active against a wide variety of gram-negative and gram-positive bacteria, including those which are resistant to other antibiotics. Gentigan is indicated in acute and chronic urinary tract infections, respiratory tract infections, septicaemia, peritonitis, meningitis, acute osteomyelitis, infected wounds and soft tissue infections, burns and severe eye infections, when caused by gentamicin-sensitive organisms.

Dosage and administration Gentigan should be administered by the intramuscular route or by slow intravenous injection.

Patients with normal kidney function: Adults: Urinary tract infections and infections of other organ systems

Sensitive bacteria: 2 mg/kg/day in equally divided doses at 8-hourly intervals;

Moderately sensitive bacteria: 3mg/kg/day in equally divided doses at 8-hourly intervals;

Severe infection and sepsis: Up to 5 mg/kg/day, in equally divided doses at 8-hourly intervals.

Paediatrics: The daily doses quoted in mg/kg are administered.

Neonates and infants up to 3 weeks: The daily dose is administered in two, instead of the normal three individual doses.

Patients with impaired kidney function: Gentigan is largely eliminated via the kidneys. In impaired kidney function, the dosage must be adjusted to allow for the degree of renal insufficiency present.

Duration of Gentigan treatment is governed by bacteriological and clinical findings and is generally between 7 and 10 days. Treatment may be continued beyond this period in which case, kidney status, vestibular and cochlear function should be checked. A daily intake of about 1,500 ml of liquid to produce adequate diuresis must be ensured. If no therapeutic results have been obtained after 14 days of gentamicin administration, the plan of treatment should be checked.

Contra-indications, warnings, etc

Contra-indication: Proven gentamicin hypersensitivity.

Side-effects, warnings, etc: Gentigan serum concentrations of about 12 mcg/ml persisting over a long period

<i>Creatinine clearance (ml/min)</i>	<i>Serum creatinine† (mg/100 ml)</i>	<i>Adults and children initial dose (mg/kg)</i>	<i>All further doses (% of the initial dose)</i>	<i>Dose intervals (hrs)</i>
70	1.2	1-1.5	100%	8
40-69	2.2-1.3	1-1.5	100%	12
30-39	3.0-2.3	1-1.5	50%	8
20-29	4.2-3.1	1-1.5	50%	12
15-19	6.0-4.3	1-1.5	50%	16
10-14	8.5-6.1	1-1.5	50%	24
5-9††	12.0-8.6	1-1.5	50%	36

† The serum creatinine values are standard values which only correlate with the creatinine clearance when kidney impairment remains stable. No correlation is found in elderly and in seriously ill patients.

†† At a creatinine clearance of less than 5 ml/min haemodialysis is indicated. Gentigan is dialysable and must be individually redosed after each dialysis period. In extracorporeal haemodialysis 1 mg/kg should be administered intravenously following each dialysis period.

In impaired kidney function dosages can be checked by determining serum concentrations of gentamicin.

can lead to ototoxic side-effects. These serum concentrations are chiefly the result of failure to adapt the dosage of Gentigan to decreased renal elimination in cases of impaired kidney function. Absolute overdosage, as well as simultaneous or previous administration of other ototoxic antibiotics, may also produce ototoxic side-effects.

The diuretics frusemide and ethacrynic acid may have an ototoxic effect and the simultaneous administration of these substances with gentamicin should be avoided whenever possible.

Where appropriate, checks on vestibular and acoustic function are recommended prior to, during and following treatment with Gentigan.

In animal trials excessively high or toxic doses of gentamicin produce nephrotoxic changes. At doses in the therapeutic range the nephrotoxicity of Gentigan, as found in these animal trials, is of no clinical relevance. A transitory increase in serum levels of urea and creatinine may occur during treatment with Gentigan, whereby the primary disease also plays an important part. For this reason, elderly patients and/or patients with existing kidney damage should be suitably monitored.

The combination of gentamicin with cephalosporins can prove useful in some clinical indications as a result of the synergistic effect and extension of the spectrum of activity. The potential nephrotoxicity of cephalosporins may be increased in the presence of gentamicin and consequently if this combination is used, strict monitoring of kidney function is advised. Concurrent administration of gentamicin and other potentially nephrotoxic drugs should be avoided.

Aminoglycoside antibiotics administered with muscle relaxants may have a potentiating effect during anaesthesia.

Animal trials have not given any cause to suspect a teratogenic effect of gentamicin; nevertheless, Gentigan should only be administered during pregnancy where there is a vital indication and where exclusively gentamicin-sensitive bacteria are the cause of infection.

Pharmaceutical precautions In general, Gentigan injection should not be mixed with any other drug prior to administration. In particular, in the case of penicillins

and cephalosporins administration should only be given at a separate site.

Legal category POM.

Package quantities Packs of 5 ampoules × 2 ml.

Further information Nil.

Product licence numbers

Gentigan 40 mg/ml: 3894/0021

ILIADIN* MINI

ILIADIN* MINI PAEDIATRIC

Presentation A colourless, aqueous, buffered solution of Oxymetazoline hydrochloride 0.05% w/v in polythene unit-dose packs each containing 0.3 ml. Iliadin Mini Paediatric contains 0.025% w/v Oxymetazoline hydrochloride in 0.3 ml unit-dose packs.

Uses Iliadin has a vasoconstrictive and decongestive effect on the naso-pharyngeal mucosa which lasts for up to 12 hours.

Iliadin is indicated for the relief of nasal congestion associated with disorders of the upper respiratory tract including, infective and allergic rhinitis, sinusitis, naso-pharyngitis and coryza.

Dosage and administration *Adults:* Instil half the contents of one mini unit into each nostril. Repeat every 8-12 hours as necessary.

N.B. The 0.05% solution is not recommended for children under the age of 6 years.

Infants and children: Instil half the contents of one mini unit of Iliadin Mini Paediatric into each nostril. Repeat every 8-12 hours as necessary, Iliadin Mini Paediatric can be used for infants whose nasal congestion interferes with feeding.

Contra-indications, warnings, etc Iliadin is contra-indicated in patients with a known sensitivity to sympathomimetics; in patients who are receiving monoamine oxidase inhibitors, or within 14 days of stopping such treatment; and in acute coronary disease, cardiac asthma, hyperthyroidism or closed angle glaucoma. The excessive use of Iliadin may cause reactive hyperaemia.

Cases of rebound congestion and drug induced rhinitis following prolonged use of Iliadin are rare.

Iliadin should not be used during pregnancy unless considered essential by the physician.

Iliadin Paediatric: It is recommended that continuous therapy should not exceed 14 days and that it should be used with caution in infants under 12 weeks of age.

Pharmaceutical precautions Store at a temperature not exceeding 25°C.

Legal category P.

Package quantities Packs of 10 and 20 disposable mini units.

Further information Iliadin has been shown to provide more prolonged relief from nasal congestion than any other nasal decongestant. The unit-dose presentation is hygienic and eliminates the risk of cross infection.

Product licence numbers

Iliadin Mini 0493/0005

Iliadin Mini Paediatric 0493/0010

MERCK SKIN TESTING SOLUTIONS

Presentation Merck Skin Testing Solutions are aqueous allergen extracts containing 50% glycerin and preserved in 0.4% phenol with their strength expressed in PNU. There is a Merck Skin Testing Solution available for each extract in the Norisen range, and the following skin testing solutions are available:

POLLENS

Grasses: Grass Mix (Cocksfoot, Meadow Grass, Rye Grass, Tall Fescue, Timothy, Yorkshire Fog).

Barley, Maize, Oat (Cult.), Rye, Wheat.

Weeds: Weed Mix (Dandelion, Mugwort, Nettle, Pellitory, Plantain).

Dandelion, Mugwort, Nettle, Plantain, Pellitory.

Trees: Tree Mix (Early Blossoming) [Alder, Elm, Hazel, Poplar, Willow].

Tree Mix (Mid-Blossoming) [Beech, Birch, Oak, Plane].

Alder, Ash, Beech, Birch, Elder, Elm, False Acacia, Hazel, Oak, Plane, Poplar, Sycamore, Willow.

Flowers: Flower Mix (Aster, Chrysanthemum, Dahlia, Golden Rod, Marguerite [Daisy]).

Aster, Chrysanthemum, Dahlia, Golden Rod, Marguerite [Daisy].

OTHER ALLERGENS

Moulds: Fungi Mix I (Alternaria, Botrytis, Cladosporium, Curvularia, Fusarium, Helminthosporium).

Fungi Mix II (Aspergillus, Mucor, Pencillium, Pullularia, Rhizopus, Serpula).

Alternaria, Aspergillus, Botrytis, Candida, Chaetomium, Cladosporium, Curvularia, Fusarium, Helminthosporium, Mucor, Neurospora, Penicillium, Phoma, Pullularia, Rhizopus, Serpula (Dry Rot), Sporobolomyces, Trichophyton, Usitlago.

Epithelia: Feather Mix (Duck, Goose, Chicken).

Budgerigar, Cat, Cow, Dog, Goat, Golden Hamster, Guinea Pig, Horse, Pig, Rabbit, Sheep's Wool. (Extracts not available in Norisen range for Goat and Pig.)

Other inhalants: D. pteronyssinus (House Dust Mite).

Hay Dust, House Dust, Rye Flour, Wheat Flour.

Stinging insects: Bee, Hornet, Wasp.

The following control solutions are available: Glycerosaline, histamine acid phosphate.

Form and appearance: The colour of an individual skin testing solution will depend on the source materials used, e.g. grass and weed extracts will be a pale green shade, house dust and house dust mite extracts will be a pale brown colour.

Uses Merck Skin Testing Solutions are used to confirm the provisional diagnosis of an allergic condition obtained from the detailed case history of the patient.

Dosage and administration Merck Skin Testing Solutions may be used for skin testing or nasal provocation testing. However, it is recommended that only an experienced allergist should attempt nasal provocation testing and that for the majority of cases, the modified prick test as described below will be satisfactory.

Modified prick test: The most suitable site for skin testing is on the flexor side of the fore-arm. The skin is first marked, using a ball point or felt tip pen, with those extracts to which the patient is suspected of being sensitive. The negative control is placed near the top of the arm, followed by the allergen extracts, usually with the house dust mite extract at the lower end, before the

final positive control solution. The test sites should be approximately 4 cm apart. One small drop of the test solution is applied to the skin next to the mark for that allergen. A sterile lancet is then placed at an acute angle to the skin and a shallow lift is made. The lancet is raised for a second before the skin is released. This is repeated for each drop of solution, the lancet being wiped carefully on cotton wool before using each solution. Any excess solution remaining on the skin after the prick has been made is removed by placing a paper tissue over the arm for a moment or two.

The results are read after 15 to 20 minutes, when positive reactions will appear as weals and flares. Any weal or flare produced by the negative control must be subtracted from any reactions produced by the other allergens before they are assessed. Where both the weal and flare are only very small, i.e. the reaction is only mild, this is recorded as + against the particular allergen. Where there is a larger reaction, but not as large as the positive control, the reaction is recorded as ++ against the particular allergen. Where the reaction is similar to or greater than the positive control +++ should be recorded against the particular allergen.

Where a permanent record of the skin test reactions is required, the weals may be closely encircled by a ball point pen, and a piece of clear adhesive tape then applied to the arm, when an image of the reactions will be taken onto the tape. The tape may then be placed on the patient's record card.

Information on nasal provocation testing may be obtained from E. Merck Ltd.

Contra-indications, warnings, etc

Contra-indications: None known.

Precautions: Patients should be asked to discontinue any medication that they are receiving for their allergic condition prior to testing, as antihistamines and corticosteroids in high dosage may affect the results of the test. *Blood should not be drawn during testing.* Must not be used for intradermal testing. Adrenaline Injection BP should be available during testing. Particular care should be taken when testing with extracts of stinging insects, as patients may be exquisitely sensitive.

Overdosage: Not applicable.

Main side-effects/adverse reactions: Adverse reactions are extremely rare with the modified prick test, and would normally appear as large local reactions which will normally subside in three hours. In the event of persistent reactions, reference should be made to an experienced allergist. The patient may be assisted by the use of antihistamines.

In the unlikely event of a severe general reaction, a tourniquet should be applied to the upper arm proximal to the site of the skin test that has caused the reaction, and Adrenaline Injection BP should be injected around and beneath the site of the test. Adrenaline Injection BP may also be injected subcutaneously into the other arm if necessary.

Pharmaceutical precautions Merck Skin Testing Solutions should be stored between 4°C and 8°C. The solutions must not be allowed to freeze.

Legal category POM.

Package quantities Each solution is supplied in a 3 ml dropper bottle. Skin testing cases to hold up to 20 and 80 solutions are available.

Further information Nil.

Product licence number 0493/0038.

MULTIBIONTA* INFUSION

Presentation A 10 ml ampoule of an aqueous solution containing:

Vitamin A palmitate (corresponding to 10,000 Units of Vitamin A)	5.9 mg
Vitamin B ₁ hydrochloride	50 mg
Vitamin B ₂ -5 phosphate sodium salt	10 mg
Nicotinamide	100 mg
Pantothenyl alcohol	25 mg
Vitamin B ₆ hydrochloride	15 mg
Vitamin C	500 mg
Vitamin E acetate	5 mg

Uses Intravenous infusions of vitamins should only be considered when oral intake is impossible or inadequate.

Neonates and infants: Multibionta infusion is indicated as part of a total parenteral feeding regimen in neonates and young children in the following conditions.

1. Neonatal surgery involving extensive resection or reimplantation.
2. Protracted diarrhoea unresponsive to dietary treatment.
3. Extreme prematurity.
4. Renal failure.

In older children and adults:

1. Obstructing lesions of the gastro-intestinal tract.
2. Massive bowel resection.
3. Extensive burns.
4. Major trauma and severe infections.
5. Acute states of inflammatory bowel disease.
6. Severe uncontrolled malabsorptive states with undernutrition.
7. Disorders of swallowing as might occur in poliomyelitis, tetanus or following severe trauma.
8. Prolonged coma.

Dosage and administration The exact requirements of intravenously administered vitamins (particularly in sick infants) are not known. For adults 10 ml of Multibionta in an average daily dose should be added to a full infusion bottle containing not less than 250 ml of the infusion. For neonates and small children 2 ml per litre of the infusion fluid is adequate; alternatively the dose can be calculated as 0.15 ml/kilogram/24 hours. However, if preferred, the adult dose may be used with complete safety.

There is no preparation which contains all the essential vitamins in recommended amounts. It is, therefore, suggested that the following are given during prolonged intravenous nutrition in the dosage indicated.

Folic acid	0.1–0.5 mg/day
Vitamin B ₁₂	100 mcg/month
Vitamin D	300 Units/day (administered IM as Calciferol. 1 ml contains 300,000 Units)
Vitamin K	3 mg twice weekly
Choline chloride	500 mg/day (normally present in adequate amounts as cholinephosphatides in fat emulsions)

Their compatibility with the carrier intravenous infusion should always be checked with the pharmacy before addition.

Additional information: The miscibility of 10 ml of Multibionta has been tested and is compatible with:

Most commercially available amino-acid solutions, including Aminofusin.

Most commercially available carbohydrate solutions including glucose at various concentrations with and without other substances including antibiotics, sympathomimetic amines, electrolytes, etc.

Most commercially available fat solutions with and without various additives.

In addition the following drugs have been tested and found compatible with formulations containing Multibionta: Atropine sulphate, Rolitetracycline, Viocin, Streptomycin, Theophyllin, Calcium, Chloramphenicol, Strophanthin, Plasmagel, Povidone and Oxedrine tartrate.

Although Multibionta is compatible with most commercially available infusion fluids like other additives it is best introduced into normal saline or dextrose-saline mixtures.

Contra-indications, warnings, etc Rarely, intravenous B₁ may act as an allergen.

In order to minimise possible loss of active substance in a mixture (masked incompatibility), it is recommended that solutions to which Multibionta is added should not be kept for longer than eight hours.

A mixture should be discarded if visible turbidity or crystallisation appear in the infusion solution.

Especially care should be taken to avoid exposure of a plastic bag or giving set to direct sunlight following addition of Multibionta infusion.

Pharmaceutical precautions Should be stored at a temperature not exceeding 20°C.

Legal category POM.

Package quantities 10 ml ampoules in packs of 3.

Further information Nil.

Product licence number 0493/0076.

NIOPAM* ▼

Presentation Ampoules or bottles containing sterile aqueous solutions of varying strengths of iopamidol.

Niopam 200: contains a 40.8% w/v concentration of the active constituent equivalent to 20% iodine or 200 mg iodine/ml.

Niopam 300: contains a 61.2% w/v concentration of the active constituent equivalent to 30% iodine or 300 mg iodine/ml.

Niopam 370: contains a 75.5% w/v concentration of the active constituent equivalent to 37% iodine or 370 mg iodine/ml.

Uses X-ray contrast media for lumbar and thoracic-cervical myelography, cerebral angiography, peripheral arteriography and venography, angiocardiology, left ventriculography and coronary arteriography, aortography, selective visceral angiography, computer tomography enhancement, urography, arthrography.

Contra-indications, warnings, etc

Contra-indications: Proven or suspected hypersensitivity to iodine containing preparations of this type.

Warnings: As with all other contrast media this product may provoke anaphylaxis or other manifestations of allergy with nausea, vomiting, dyspnoea, erythema, urticaria and hypotension. A positive history of allergy, asthma or untoward reaction during previous similar

Dosage and administration*NIOPAM – Recommended Dosage Schedule*

<i>Procedure</i>	<i>Niopam product and dosage</i>	
Lumbar Myelography	Niopam 200 Niopam 300	Adults 5–15 ml
Thoraco-Cervical Myelography	Niopam 200 Niopam 300	Adults 5–15 ml
Cerebral Angiography	Niopam 300	Adults 5–10 ml* Children 5–7 ml**
Peripheral Arteriography & Venography	Niopam 300 Niopam 370 Niopam 300	Adults 10–50 ml* Children ** Adults 20–50 ml Children **
Angiocardiology & Left Ventriculography	Niopam 370	Adults 30–80 ml Children **
Coronary Arteriography	Niopam 370	Adults 4–8 ml per artery
Aortography —retrograde	Niopam 370	Adults 30–80 ml
Selective Renal Arteriography	Niopam 370	Adults 5–10 ml Children **
Selective Visceral Angiography: Hepatic Coeliac Superior Mesenteric Inferior mesenteric	Niopam 370	Adults 30–70 ml 40–70 ml 25–70 ml 5–30 ml
Computer Tomography Enhancement	Niopam 200 Niopam 300	Adults <i>Brain Scanning</i> 50–100 ml <i>Whole Body Scanning</i> 40–100 ml
Intravenous Urography	Niopam 300 Niopam 370	Adults 40–80 ml In severe renal failure the usual high dose methods should be employed (up to 1.5 ml/kg) Children 1–2.5 ml/kg or **
Arthrography	Niopam 300	Adults 1–10 ml According to joint being examined.

* Repeat as necessary.

** According to body size and age.

investigations indicates a need for extra caution; the benefit should clearly outweigh the risk in such patients. Appropriate resuscitative measures should be immediately available.

Care should be exercised in carrying out radiographic procedures with contrast media in patients with severe functional impairment of the liver or myocardium, severe systemic disease and in myelomatosis. In the latter condition patients should not be exposed to dehydration; similarly abnormalities of fluid or electrolyte balance should be corrected prior to use.

Care should also be exercised in patients with moderate to severe impairment of renal function (as reflected by a raised blood urea) or in diabetes. Substantial deterioration in renal function is minimised if the patient is well hydrated. Renal function parameters should be monitored after the procedure in these patients.

Patients with severe hepato-renal insufficiency should

not be examined unless absolutely indicated. Re-examination should be delayed for 5–7 days.

Special care should be exercised when this product is injected into the right heart or pulmonary artery in patients with pulmonary hypertension. Right heart angiography should be carried out only when absolutely indicated.

During intracardiac and/or coronary arteriography, ventricular arrhythmias may infrequently occur.

Use of this product may interfere with tests for thyroid function.

Niopam should be used with caution in patients with hyperthyroidism. It is possible that hyperthyroidism may recur in patients previously treated for Graves' disease.

X-ray examination of women should if possible be conducted during the pre-ovulation phase of the menstrual cycle and should be avoided during pregnancy; also since it has not been demonstrated that Niopam is safe for use in pregnant women, it should be administered

only if the procedure is considered essential by the physician.

Side Effects: Side effects are infrequent and normally mild and may consist of headache, nausea, vomiting, heat sensation, dyspnoea and hypotension. Skin rashes may occur in some patients.

Following use in myelography, headaches, dizziness, nausea and vomiting may occasionally occur.

More severe reactions involving the cardiovascular system may call for emergency treatment; appropriate resuscitative measures should be immediately available.

No other drugs should be mixed with the contrast medium.

Pharmaceutical precautions Protect the solution from intense light.

Legal category POM.

Package quantities

Niopam 200: Box containing 5 × 10 ml ampoules

Niopam 300: Box containing 5 × 10 ml ampoules
Box containing 1 × 50 ml bottle

Niopam 370: Box containing 5 × 10 ml ampoules
Box containing 1 × 50 ml bottle

Further information Niopam is one of the new generation of water soluble non-ionic contrast media. The development of this compound has led to considerable reduction in general toxicity particularly with regard to vascular endothelium and nervous tissues.

Product licence numbers

Niopam 200 0493/0065

Niopam 300 0493/0066

Niopam 370 0493/0067

NORISEN* ▼

Presentation Norisen is an aluminium adsorbed allergen extract for the specific hyposensitisation of patients sensitive to inhaled allergens or stinging insects. The extracts are suspended in normal saline containing 0.4% phenol as preservative, and their strength is expressed in protein nitrogen units (PNU).

Each treatment set is individually formulated and consists of 3 vials in graded strength as follows:

Vial 1 (Green Label)	100 PNU per ml
Vial 2 (Blue Label)	1,000 PNU per ml
Vial 3 (Red Label)	10,000 PNU per ml

Each maintenance set consists of one Vial 3 (Red Label).

The following allergen extracts are available:

POLLENS

Grasses: Grass Mix (Cocksfoot, Meadow Grass, Rye Grass, Tall Fescue, Timothy, Yorkshire Fog).
Barley, Maize, Oat (Cult.), Rye, Wheat.

Weeds: Weed Mix (Dandelion, Mugwort, Nettle, Pellitory, Plantain).

Dandelion, Mugwort, Nettle, Plantain, Pellitory.

Trees: Tree Mix (Early Blossoming) [Alder, Elm, Hazel, Poplar, Willow].

Tree Mix (Mid-Blossoming) [Beech, Birch, Oak, Plane].

Alder, Ash, Beech, Birch, Elder, Elm, False Acacia, Hazel, Oak, Plane, Poplar, Sycamore, Willow.

Flowers: Flower Mix (Aster, Chrysanthemum, Dahlia, Golden Rod, Marguerite [Daisy]).

Aster, Chrysanthemum, Dahlia, Golden Rod, Marguerite [Daisy].

OTHER ALLERGENS

Moulds: Fungi Mix I (Alternaria, Botrytis, Cladosporium, Curvularia, Fusarium, Helminthosporium).

Fungi Mix II (Aspergillus, Mucor, Pencillium, Pullularia, Rhizopus, Serpula).

Alternaria, Aspergillus, Botrytis, Candida, Chaetomium, Cladosporium, Curvularia, Fusarium, Helminthosporium, Mucor, Neurospora, Penicillium, Pullularia, Phoma, Rhizopus, Serpula (Dry Rot), Sporobolomyces, Trichophyton, Ustilago.

Epithelia: Feather Mix (Duck, Goose, Chicken).

Budgerigar, Cat, Cow, Dog, Golden Hamster, Guinea Pig, Horse, Rabbit, Sheep's Wool.

Other inhalants: D. pteronyssinus (House Dust Mite), House Dust, Hay Dust, Rye Flour, Wheat Flour.

Stinging insects: Bee, Hornet, Wasp.

The extracts of stinging insects are available either individually or mixed with other stinging insect extracts, but may not be mixed with other allergen extracts.

The constituents of a course of treatment are determined by the allergist from the case history and the skin test reactions and indicated on the chart submitted with the order, and will be dependent upon the number of + signs against each allergen extract.

Where a patient is diagnosed as being extremely sensitive, a vial containing a special diluted extract of 10 PNU per ml can be supplied and should be administered before starting the treatment set.

Uses To hyposensitise those patients who have been shown to be sensitive to certain allergens as a result of case history and confirmation by skin testing.

Dosage and administration The dosage schedule, appropriate to the course of injections to be given, is enclosed with each treatment set. Detailed instructions on administration and the precautions that should be adopted are also supplied.

The injections must be given by the subcutaneous route only. As the allergens are slowly released from the aluminium depot, the interval between injections should be at least seven days and not more than two weeks. Before administration the vial must be shaken thoroughly so as to disperse the allergen suspension homogeneously. The course of hyposensitisation must commence with the lowest strength vial and the smallest injection from that vial.

For patients who are sensitive to seasonal allergens, the injections should be administered pre-seasonally and the course completed just before the particular allergens become airborne. For patients who are sensitive to perennial allergens the course of injections may be commenced at any time of the year.

Each course of treatment must be commenced using the initial three vial set, and one of the following dosage schedules should be followed, depending on the sensitivity of the patient. Where a patient suffers with severe symptoms, and has a large reaction to skin testing, it is advisable to start on the very sensitive dosage schedule while, in certain cases, e.g. for children under six years of age and for extremely sensitive patients, the initial course should be preceded by a special dilution vial. Where the sensitivity of the patient is only considered to be average or mild, the mildly sensitive schedule set out below may be used.

Where a patient on the very sensitive course has

reached the third injection (0.25 ml) from the No. 3 vial without any adverse reaction, however small, then the two further injections from the No. 3 vial may be administered, providing, in the case of seasonal allergens, that there is sufficient time before the pollination season.

Maintenance therapy for perennial allergens consists of repeating the top dose achieved on the above schedule at four to six week intervals for up to one year, commencing maintenance injections within six weeks of completing the course. Where seasonal allergens are involved it is recommended that hyposensitisation is carried out pre-seasonally for three successive years, using a three vial treatment set for each year. Where a patient has commenced on the very sensitive schedule, the mildly sensitive schedule should be administered on the second year and the mildly sensitive schedule repeated for the third year.

Where a slightly greater period than that recommended between injection occurs, the previous injection of the course should be repeated or in the case of maintenance injections, a reduced dose should first be given before continuing with the course. Where a considerable period has elapsed between injections, the initial treatment should be reduced further, or, in the case of a maintenance course, the initial treatment set should be repeated before attempting any further maintenance therapy.

A separate dosage schedule is provided with treatment sets containing extracts of stinging insects.

Vial	Very sensitive schedule (ml)	PNU	Mildly sensitive schedule (ml)	PNU
1	0.10	(10)	0.25	(25)
(Green Label)	0.20	(20)	0.50	(50)
100 PNU/ml	0.40	(40)		
	0.80	(80)		
2	0.15	(150)	0.10	(100)
(Blue Label)	0.30	(300)	0.30	(300)
1,000 PNU/ml	0.60	(600)	0.70	(700)
3	0.10	(1,000)	0.15	(1,500)
(Red Label)	0.15	(1,500)	0.25	(2,500)
10,000 PNU/ml	0.25	(2,500)	0.50	(5,000)
	(0.50)	(5,000)	1.00	(10,000)
	(1.00)	(10,000)		

Contra-indications, warnings, etc

Contra-indications: Patients suffering from an acute infectious condition, or who are pregnant, particularly in the first trimester, should not be given a course of hyposensitisation. This also applies to patients during an acute attack of asthma, when 24 hours should be allowed to elapse before commencing the course of injections.

Precautions: Side-effects are relatively rare following the administration of hyposensitisation with Norisen extracts. It is recommended that patients should not eat a heavy meal immediately before the injections are given, and they should remain in the surgery for 20 minutes following the administration of each injection. It is recommended that they should not perform any physically strenuous work for several hours after an injection. Adrenaline Injection BP must be available whenever allergen extracts are administered.

Injections of Norisen must be administered only by the subcutaneous route and must not be injected into a blood vessel. The vial of extract must be shaken well before use, and care should be taken that the treatment

is always commenced with the lowest strength vial and the smallest injection from that vial (see under Dosage and Administration). The interval between injections must be at least one but not more than two weeks in the case of treatment sets, and maintenance set injections should be given at intervals of not less than four weeks and not more than six weeks.

With seasonal allergens, the course of injections should be completed approximately three weeks before the pollens become airborne. In any event, pre-seasonal injections must be terminated before the pollination season commences.

Side-effects and adverse reactions: The occurrence of side-effects is rare, and any which occur normally take a mild course. Local swelling and pain which may appear several hours after the injection has been given can be blocked by oral or parenteral administration of antihistamines.

If there are severe local reactions shortly after the injection, a tourniquet should be applied to the arm above the location of the injection and Adrenaline Injection BP should be injected subcutaneously in the vicinity of the injection site and, if necessary, adrenaline injection should be injected into the other arm as well. The tourniquet can then be released slowly and the patient kept under observation until the reaction has passed. For the next injection of the course, the same injection as caused the reaction may be repeated, or, if the reaction was very severe, the next lower dosage of the course should be repeated before proceeding with the increases in dosage.

A severe general reaction may require the subcutaneous injection of Adrenaline Injection BP which can be repeated if necessary. It may also be necessary to administer antihistamines and/or corticosteroids parenterally if so required.

Pharmaceutical precautions Norisen extracts should be stored between 4° and 8°C. The extracts must not be allowed to freeze.

Use aseptic precautions throughout. If the product is to be kept for more than 4 hours after withdrawing the first dose, the aseptic precautions taken must be sufficient to exclude the risk of microbial contamination.

Legal category POM.

Package quantities Each treatment set consists of three colour coded vials in graded strength numbered No. 1 (green label), No. 2 (blue label), No. 3 (red label). Each maintenance set consists of one No. 3 (red label) vial. All Norisen sets contain a supply of needle-attached syringes for each injection of the course, together with complete instructions on administration and a dosage schedule appropriate to the course of hyposensitisation to be administered.

Where a special dilution vial has been requested this is included in the treatment set and has an orange label.

Further information A Norisen set may be obtained by first completing a Norisen order form ensuring that those allergens that are to be included in the vaccine are clearly marked on the chart. The order form is then taken to a retail chemist or pharmacy together with the appropriate prescription, and the pharmacist then orders the set direct from E. Merck Ltd. All orders are acknowledged and delivery will normally take place within four weeks. Supplies of order forms and skin testing solutions may be obtained from E. Merck Ltd.

Product licence numbers 0493/0037

NORISEN* GRASS ▼

Presentation Norisen Grass is an aluminium adsorbed allergen extract of grass pollens (Cocksfoot, Meadow Grass, Rye Grass, Tall Fescue, Timothy and Yorkshire Fog) for the specific hyposensitisation of patients sensitive to grass pollens. The extract is suspended in normal saline containing 0.4% phenol as a preservative, and its strength is expressed in protein nitrogen units (PNU).

Each treatment set consists of three vials in graded strength as follows:

Vial 1 (Green Label)	100 PNU/ml
Vial 2 (Blue Label)	1,000 PNU/ml
Vial 3 (Red Label)	10,000 PNU/ml

Uses To hyposensitise those patients who are sensitive to grass pollen allergens and who suffer from hay fever.

Dosage and administration Two alternative dosage schedules are enclosed with each treatment set together with detailed instructions on administration and the precautions that should be adopted.

The injections must be given by the subcutaneous route only. As the allergens are slowly released from the aluminium depot, the interval between injections should be at least seven days and not more than two weeks. Before administration the vial must be shaken thoroughly so as to disperse the allergen suspension homogeneously. The course of hyposensitisation must commence with the lowest strength vial and the smallest injection from that vial.

The injections should be administered pre-seasonally and the course completed just before the grass pollens become airborne. This normally occurs at the end of May in the south of England, although the pollination may occur two weeks later in the north of England and Scotland.

The dosage schedule that should be followed will depend on the sensitivity of the patient. Where a patient suffers with severe symptoms, it is advisable to start on the very sensitive dosage schedule while, in certain cases, e.g. for children under six years of age and for extremely sensitive patients, the initial course may be preceded by a special dilution vial, obtainable direct from E. Merck Ltd. Where the sensitivity of the patient is only considered to be average or mild, the mildly sensitive schedule set out below may be used.

Where a patient on the very sensitive course has reached the third injection (0.25 ml) from the No. 3 vial without any adverse reaction, however small, then the two further injections from the No. 3 vial may be administered, providing that there is sufficient time before the pollination season.

It is recommended that hyposensitisation for grass pollen allergy is carried out pre-seasonally for three successive years, using a new Norisen Grass set for each year of treatment. Where a patient has commenced on the very sensitive schedule, the mildly sensitive schedule should be administered on the second year and the mildly sensitive schedule repeated for the third year.

Where a slightly greater period than that recommended between injections occurs, the previous injection of the course should be repeated. Where a considerable period has elapsed between injections, the next injection of the course should be reduced further.

Contra-indications, warnings, etc

Contra-indications: Patients suffering from an acute infectious condition, or who are pregnant, particularly in

Vial	Very sensitive schedule (ml)	PNU	Mildly sensitive schedule (ml)	PNU
1 (green label) 100 PNU/ml	0.10 0.20 0.40 0.80	(10) (20) (40) (80)	0.25 0.50	(25) (50)
2 (blue label) 1,000 PNU/ml	0.15 0.30 0.60	(150) (300) (600)	0.10 0.30 0.70	(100) (300) (700)
3 (red label) 10,000 PNU/ml	0.10 0.15 0.25 (0.50) (1.00)	(1,000) (1,500) (2,500) (5,000) (10,000)	0.15 0.25 0.50 1.00	(1,500) (2,500) (5,000) (10,000)

the first trimester, should not be given a course of hyposensitisation. This also applies to patients during an acute attack of asthma, when 24 hours should be allowed to elapse before commencing the course of injections.

Precautions: Side-effects are relatively rare following the administration of hyposensitisation with Norisen Grass extracts. It is recommended that patients should not eat a heavy meal immediately before the injections are given, and they should remain in the surgery for 20 minutes following the administration of each injection. It is recommended that they should not perform any physically strenuous work for several hours after an injection. Adrenaline Injection BP must be available whenever allergen extracts are administered.

Injections of Norisen Grass must be administered only by the subcutaneous route and must not be injected into a blood vessel. The vial of extract must be shaken well before use, and care should be taken that the treatment is always commenced with the lowest strength vial and the smallest injection from that vial (see under Dosage and Administration).

The interval between injections must be at least one but not more than two weeks, and the course of injections should be completed approximately three weeks before the grass pollens become airborne. In any event, injections of Norisen Grass must be terminated before the grass pollen season commences.

Side-effects and adverse reactions: The occurrence of side-effects is rare, and any which occur normally take a mild course. Local swelling and pain which may appear several hours after the injection has been given can be blocked by oral or parenteral administration of antihistamines.

If there are severe local reactions shortly after the injection, a tourniquet should be applied to the arm above the location of the injection and Adrenaline Injection BP should be injected subcutaneously in the vicinity of the injection site, and, if necessary, adrenaline solution should be injected into the other arm as well. The tourniquet can then be released slowly and the patient kept under observation until the reaction has passed. For the next injection of the course, the same injection as caused the reaction may be repeated, or, if the reaction was very severe, the next lower dosage of the course should be repeated before proceeding with the increases in dosage.

A severe general reaction may require the subcutaneous injection of Adrenaline Injection BP which can be repeated if necessary. It may also be necessary to

administer antihistamines and/or corticosteroids parenterally if so required.

Pharmaceutical precautions Norisen Grass extracts should be stored between 4° and 8°C. The extracts must not be allowed to freeze.

Use aseptic precautions throughout. If the product is to be kept for more than 4 hours after withdrawing the first dose, the aseptic precautions taken must be sufficient to exclude the risk of microbial contamination.

Legal category POM.

Package quantities Each Norisen Grass set consists of three colour coded vials in graded strength numbered No. 1 (green label), No. 2 (blue label), No. 3 (red label). All Norisen sets contain sufficient needle-attached syringes for each injection of the course, together with complete instructions on administration and a dosage schedule (see under Dosage and Administration).

Further information Norisen Grass extracts are prepared by a process which avoids the use of pyridine, a solvent known to have a denaturing effect on allergen source materials. Thus the nature of the original allergic substance is preserved in the extract, and the risk of toxic effects is reduced. The allergens are slowly released from the site of the injection, and the dosage itself is completely flexible and may be modified for each individual patient.

Norisen Grass is immediately available from stock.

Where the patient is suspected of being allergic to allergens other than grass, the Merck range of skin testing solutions may be used to confirm the diagnosis and a specific Norisen treatment set prescribed.

Product licence number 0493/0048.

NUTRIZYM*

Presentation A white, oblong, double sugar-coated tablet. Each white, double-coated tablet contains:

Pancreatin BP	400 mg
Lipase	9,000 Units
Protease	400 Units
Amylase	9,000 Units
Ox bile	30 mg
Bromelains	50 mg

Uses Fibrocystic disease of the pancreas, chronic pancreatitis, steatorrhoea and other pancreatic deficiency states.

Dosage and administration *Adults:* 1-2 tablets during or after meals. In severe cases dosage may be increased to 2 or more tablets.

Children: 1-2 tablets to be taken with meals and further tablets may be taken according to the degree of pancreatic exocrine insufficiency.

Contra-indications, warnings, etc There are no known contra-indications or precautions.

Pharmaceutical precautions No special requirements.

Legal category P.

Package quantities Container of 100 tablets.

Further information Each Nutrizym Tablet has an enteric-coated pancreatin core and a shell of bromelains. The bromelain-proteolytic enzymes are active within the

pH range of pH 3 and pH 8 (even pH 2 for short periods) and therefore act without loss of enzymatic effectiveness both in the stomach and small intestine.

Product licence number 3894/5900.

OPTIMAX*

Presentation Optimax Tablets: Yellow capsule shaped film coated tablets each containing 500 mg L-Tryptophan 5 mg Pyridoxine Hydrochloride, 10 mg Ascorbic acid, bearing the name OPTIMAX on one side and a break line on the other.

Optimax tablets are available without vitamins; they are of similar appearance and are marked OPTIMAX WV.

Optimax Powder: A chocolate-flavoured powder for mixing into a drink with warm milk or water. Each 6 g of powder contains 1 g L-Tryptophan, 10 mg Pyridoxine hydrochloride, 20 mg Ascorbic acid.

Uses Optimax is indicated for the relief of symptoms of mild to moderate depressive illness. Long term efficacy and safety of L-Tryptophan have not been established; therefore, it is recommended that L-Tryptophan be used for short term therapy with a review at three monthly intervals. For the treatment of more severe depressive illness Optimax may be administered with other antidepressant drugs.

Dosage and administration

Adults: The usual dose is two tablets, three times daily or one sachet three times daily (equivalent to 3 g L-Tryptophan daily); for some patients up to 6 g L-Tryptophan may be required.

Children: Not recommended.

When used in combination with other antidepressants it may be necessary to adjust the dosage of either component.

Contra-indications, warnings, etc

Contra-indications: No absolute contra-indications known.

Precautions and Drug Interactions: Where Optimax is combined with an MAO Inhibitor the side effects of the latter may be enhanced.

In patients taking Optimax in conjunction with phenothiazines or benzodiazepines there have been isolated reports of sexual disinhibition.

Pyridoxine should not be administered to patients undergoing treatment with L-Dopa.

L-Tryptophan is not advised, except for relatively short periods, in patients with active bladder disease or known bladder lesions.

Warnings and Adverse Effects: L-Tryptophan may produce drowsiness. Patients should be warned of the possible hazard when driving or operating machinery.

In some patients Optimax may cause a slight feeling of nausea which usually disappears within 2 or 3 days. Such nausea can be minimised by giving Optimax after food. Other adverse reactions include headache and lightheadedness.

Safety in pregnancy has not been established.

Pharmaceutical precautions Store in a cool dry place.

Legal category POM.

Package quantities *Optimax Tablets:* Securitainers of 100 and 500.

Optimax Powder: Cartons of 100 sachets.

Further information L-Tryptophan, one of the essential amino acids, is the major precursor of the brain amine 5-Hydroxytryptamine (5-HT). There is convincing evidence that levels of 5-HT are depleted in the CNS of depressed patients.

Abnormal tryptophan metabolism may occur in patients who are pyridoxine deficient. Such deficiency may occur in women taking oral contraceptives.

For some patients it may be beneficial to prescribe tablets for the morning and midday dose and powder for the night time dose.

Product licence numbers

Optimax Tablets 0493/5903R

Optimax Powder 0493/5902R

Without vitamins 0493/5900R

PENDRAMINE*

Presentation Tablets each containing 125 mg or 250 mg D-penicillamine base. The 125 mg tablets are white, elongated, film coated with bisecting score on one side, and have a length of 11 mm and a width of 5.5 mm. The 250 mg tablets are white, elongated, film coated with bisecting score on one side, debossed HB on the same side, and have a length of 16 mm and a width of 7 mm.

Uses Pendramine is indicated for the treatment of severe active rheumatoid arthritis, Wilson's disease, cystinuria and heavy metal poisoning, active chronic hepatitis, primary biliary cirrhosis.

Dosage and administration For oral administration: (i) *Severe active rheumatoid arthritis*: **Adults**: A dose of 125–250 mg daily for the initial 4 week period, then increasing by similar amounts at intervals of not less than four weeks. The ultimate maintenance dose will depend on the response obtained in individual patients and is usually 500–750 mg in divided doses. Improvement may not occur for some months.

A few patients may require up to 2000 mg daily to obtain benefit.

The minimum maintenance dose to achieve suppression of symptoms should be used. Treatment should be discontinued if no benefit is obtained within 12 months.

When clinical assessment shows that suppression of disease activity has been achieved, the dose should be kept at this maintenance level for six months, thereafter reducing the daily dose by 250 mg at intervals of two or three months. Relapse may occur following withdrawal or when an inadequate dose level is reached, usually within three months, but most patients respond to further courses of Pendramine.

It is preferable to take the drug with food.

Children: 15–20 mg/kg/day is considered appropriate in the majority of cases. It is suggested that the initial dose is lower and increased at four weekly intervals over a period of three to six months.

(ii) *Wilson's Disease*:

D-penicillamine is a copper-chelating agent, and is most effectively used in conjunction with a low-copper diet (below 1 mg of copper per day).

Adults: 1500 to 2000 mg daily in divided doses, to be taken 30 minutes before food. The dose may be reduced to 750–1000 mg daily when disease control is achieved as evidenced by urinary copper excretion. (Twenty-four

hour urine samples should be examined at 3-monthly intervals). A dose of 2000 mg daily should not be continued for more than one year.

Children: Up to 20 mg per kg body weight daily in divided doses before food. Maximum dose 500 mg/day.

(iii) *Cystinuria*: Prevention and treatment of cystine stones.

Treatment of stones: **Adults**: For the treatment of cystine stone, 750 mg daily in divided doses and especially at bedtime, increasing to 1500–2000 mg daily. The dose is adjusted to maintain urine levels of cystine below 100 mg per day. Maintain adequate fluid intake of 3 litres/day to provide a urine flow of 2 ml/min.

Children: Up to 30 mg per kg body weight daily in divided doses and especially at bedtime. The dose should be adjusted to maintain urine cystine levels below 100 mg/day.

Prophylaxis: **Adults**: (No history of stone formation but a cystine output in excess of 300 mg per day) 250–750 mg at night before retiring. The dose is adjusted to maintain overnight urine cystine levels below 100 mg/day.

Fluid intake should not be less than 3 litres/day.

Safety in pregnancy is not yet established but if treatment is unavoidable dosage should not exceed a maximum of 1000 mg/24 hours.

Children: Paediatric dosage not yet established.

(iv) *Heavy Metal Poisoning (Lead)*: **Adults**: Daily oral dose of 1500–2000 mg in divided doses until urinary lead is stabilised at 0.5 mg/day.

Children: 20–25 mg per kg body weight daily in divided doses before food.

(v) *Active Chronic Hepatitis*: **Adults**: Pendramine is intended for the maintenance treatment of active chronic hepatitis. The diagnosis should be based on a history of at least three months duration with features of chronic aggressive hepatitis, with or without cirrhosis. Treatment with Pendramine should not be commenced until the disease process has been brought under control, initially by treatment with corticosteroids (e.g. 30 mg prednisone daily, some times with 75 mg azathioprine daily added to the regime. Disease control should be evidenced by biochemical analysis of liver function to include evaluation of serum bilirubin and transaminase activity.

Pendramine therapy should be commenced with 500 mg daily, in divided doses, increasing gradually over three months to the maintenance dose of 1250 mg daily. Concurrently, the dosage of corticosteroids should be reduced and phased out over a three-month period. Throughout therapy, liver function tests should be carried out at suitable intervals for assessment of the disease status.

Children: Not recommended.

(vi) *Primary Biliary Cirrhosis*: **Adults**: Diagnosis should be on the basis of mitochondrial antibody in the serum and a histological picture compatible with primary biliary cirrhosis. The presence of portal hypertension, manifested by splenomegaly, oesophageal varices, or both, is not a contraindication although patients with a history of bleeding from varices or of hepatic encephalopathy should be excluded.

Dosage should be started at 250 mg daily, increasing weekly to the maintenance dose of 750–1000 mg daily, in divided doses.

Most patients with primary biliary cirrhosis have raised liver-copper concentrations, frequently above the level

found in untreated Wilson's disease. Pendramine promotes a reduction in liver-copper, and a lowering of the maintenance dose is a reasonable step in patients whose liver-copper levels return to normal.

Children: Not recommended.

Contra-indications, warnings, etc

Contra-indications: Renal insufficiency. Lupus erythematosus. Hypersensitivity to D-penicillamine particularly if nephrotic syndrome or bone marrow depression has previously occurred.

Precautions: Known sensitivity to penicillamine. Throughout pregnancy.

Penicillamine should not be used in patients who are receiving concurrent gold therapy, antimalarial or cytotoxic drugs, oxyphenbutazone or phenylbutazone since these drugs have a propensity to cause similar serious haematologic and/or renal adverse reactions.

Establish the lowest effective dose of D-penicillamine by quantitative amino acid chromatography on urine. Urine protein estimations should be carried out initially weekly for the first three months of therapy and thereafter monthly. Renal function should be assessed monthly for 6 months and 3 monthly thereafter.

The observation of proteinuria necessitates repeated quantitative estimations. Heavy or steadily increasing proteinuria or significant haematuria necessitates withdrawal of Pendramine.

With the exception of Wilson's disease patients (see later) platelet and white cell counts must be normal before commencing treatment. Because of the risk of blood dyscrasias and renal disturbances, full blood counts and urine examinations are essential during treatment. Weekly tests are recommended after each increase in dose as well as during the first eight weeks of therapy to monitor thrombocytopenia and neutropenia then monthly when dosage regimes have been stabilised.

Platelet counts below 120,000/cu.mm or leucocyte counts below 2,500/cu.mm necessitate withdrawal of D-penicillamine with resumption at a reduced dosage when counts return to normal. Recurrence of thrombocytopenia or leucopenia are an indication for cessation of treatment.

A low platelet or white cell count is not a contra-indication to commence treatment of Wilson's disease. Treatment should be discontinued however, if a low initial count falls further and/or excessive bruising or petechial haemorrhages occur.

Iron deficiency may occur in menstruating women. Should oral iron therapy be required it should not be given within 2 hours of taking penicillamine.

Allergic phenomena occurring early, unless severe, respond to cyproheptadine and temporary reductions of dose of D-penicillamine. Copper supplements may be necessary for alleviating taste impairment when treating conditions other than Wilson's disease.

Side Effects and Adverse Reactions: Both the frequency and severity of many side-effects and adverse reactions to D-penicillamine are found to be dose-related, hence the importance of initiating therapy at low doses and gradually increasing the quantity of drug given to the optimum level.

Nausea and vomiting may occur.

D-penicillamine may cause allergic reactions such as urticaria and erythema accompanied by hyperpyrexia. Transient rashes and fever may occur early in therapy; if persistent, temporary withdrawal of treatment with or without a short course of steroids may be necessary.

Penicillamine may be reintroduced at a lower dosage. If steroids are given, penicillamine should be reintroduced before steroid withdrawal.

A later rash, which has been called both 'acquired epidermolysis bullosa' and 'penicillamine dermatopathy' may occur, and also elastosis perforans serpiginosa – perhaps up to 2 years after treatment and may necessitate discontinuation of treatment.

Goodpastures Syndrome, haemolytic anaemia and anorexia have been reported.

Other disorders of later onset and attributed to D-penicillamine are rheumatoid-like reactions, stomatitis and taste impairment. Reversible loss of taste occurs frequently. Reactions involving the appearance of thrombocytopenia, neutropenia or proteinuria may occur, particularly with higher dose levels. Less common are nephrotic syndrome and haematuria, purpura and increased skin friability due to increased collagen. Haematuria is rare, but if it occurs, treatment should be stopped immediately.

Serious complications include myasthenia gravis, pemphigus, nephrotic syndrome, Stevens-Johnson-like syndrome and lupus erythematosus. Deaths from agranulocytosis and aplastic anaemia have been recorded.

Pendramine should not be given concurrently with iron or other heavy metals with which it may form complexes.

Warnings: The safety of use of penicillamine in pregnancy has not been established and it should be given in these circumstances only if considered essential by the physician. It has not been shown to be teratogenic in the rat and rabbit.

In the treatment of rheumatoid arthritis, response to Pendramine is often slow and the use of existing analgesics, anti-inflammatories or steroids should be continued and later gradually withdrawn, subject to patient improvement.

Treatment of Overdosage: Treatment of overdosage is symptomatic and withdrawal of the drug is necessary if serious side effects as mentioned above occur.

Pharmaceutical precautions Store in a dry place below 25°C. Keep containers tightly closed.

Legal category POM.

Package quantities

Tablets: 125 mg, plastic bottles of 100

Tablets: 250 mg, plastic bottles of 100

Further information Pendramine may be considered as an alternative to prednisone in the treatment of active chronic hepatitis when the latter drug causes complications such as diabetes, osteoporosis, etc. Occasionally, patients with rheumatoid arthritis who have responded to a particular dose begin to relapse. Most of these will respond to a dose increase which should be gradual.

Product licence numbers

Pendramine 125 mg 0493/0080

Pendramine 250 mg 0493/0081

PERIFUSIN®

Presentation A clear, slightly yellow sterile pyrogen-free solution for intravenous use through a peripheral vein, containing pure L-amino acids with added electrolytes.

Active Ingredients:	g/litre
L-Glutamic acid	5.94
L-Alanine	3.96
L-Proline	4.62
Glycine	6.60
L-Arginine	2.64
L-Histidine	0.66
L-Valine	0.99
L-Tryptophan	0.33
L-Threonine	0.66
L-Phenylalanine	1.45
L-Methionine	1.39
L-Lysine HCl	1.65
L-Leucine	1.45
L-Isoleucine	1.06
Sodium hydroxide (100%)	1.60
Potassium hydroxide (100%)	1.68
Magnesium acetate 4H ₂ O	1.07
L-malic acid	3.00

Electrolytes	Mmol/l	mg/l
Na ⁺	40	920
K ⁺	30	1,171
Mg ⁺⁺	5	121
Cl ⁻	9	320
Acetate ⁻	10.00	589
Malate ⁻	22.5	2,977
Total N g/litre	5.00	
Kcal/litre approximately	132	
pH	7.1	
Osmolality	376.5 mosm/kg	

Uses Perifusin which contains aminoacids in the optimum and balanced proportions with added electrolytes, is indicated for patients undergoing surgery and other cases of trauma in order to improve nitrogen balance and preserve muscle and visceral protein.

It improves patient tolerance to the catabolic phase of the post operative and post traumatic period and decreases susceptibility to complications.

Perifusion, being only slightly hypertonic, can be administered by intravenous infusion using a peripheral vein catheter.

Dosage and administration The amount of Perifusin to be administered daily is calculated according to individual patients' requirements of nitrogen, fluid, calories, etc. Adults should receive 0.8–1.6 g aminoacids/kg body weight daily. The average adult requirement is met by the infusion of 2–2½ litres of Perifusin per day. Children, pregnant women and post-operative patients, 1.6–2.0 g aminoacids/kg body weight daily. Newborn and premature infants, 2.0–3.0 g aminoacids/kg body weight daily.

Infusion rate 40–60 drops per minute (2–4 ml/kg/hr); it should not exceed 4 ml/kg/hr. Optimal utilisation is achieved when the daily dose is given in a continuous infusion over 24 hours. In patients who are unable to tolerate continuous infusions, two infusion periods of four or six hours each per day are recommended.

Contra-indications, warnings, etc Perifusin is contra-indicated in patients suffering shock, hyperkalaemia, severe infections (e.g. septicaemia), severe disturbances of liver or kidney function and disturbance of aminoacid metabolism: its effects should be carefully controlled when given to patients who tend towards elevated serum potassium or urea levels. Too rapid an infusion may result in renal losses, and nausea in sensitive patients.

Perifusin is not suitable for severely malnourished

patients where total parenteral nutrition will be required. Shock should be treated before administration of Perifusin.

A pre-existing deficiency of vitamins and, in particular, folic acid and Vitamin B₁₂ may become clinically evident during intravenous nutrition with aminoacids. Regular checks of the patients' Vitamin B₁₂ status and folate demand are therefore recommended. Prophylactic administration of adequate vitamins should be given if required.

As with similar solutions which do not contain fat, the possible occurrence of hypophosphataemia should be monitored.

Pharmaceutical precautions Store between 15° and 25°C. The solution of Perifusin should be clear at all times before infusion. Store away from light. If a precipitate or severe discolouration occurs, discard. Addition of drugs to the bottle of amino acid solution or giving set should be avoided.

Legal category POM.

Package quantities 1 litre glass bottles, 6 bottles per case.

Further information Nil.

Product licence number 0493/0082.

REACTIVAN®

Presentation A round, yellow, sugar-coated tablet. Each tablet of Reactivan contains:

Fencamfamin hydrochloride	10 mg
Vitamin B ₁ (thiamine-o-phosphoric acid ester phosphate)	10 mg
Vitamin B ₆ (pyridoxine phosphate)	20 mg
Vitamin B ₁₂ (cyanocobalamin)	10 mcg
Vitamin C	100 mg

Uses Debility and fatigue. Convalescence after infections or surgery.

Depressed mood in the elderly.

Dosage and administration *Adults:* 2 tablets at breakfast and, if required, 1 tablet at midday.

Children: At the physician's discretion.

Contra-indications, warnings, etc Reactivan should be used with caution in patients with coronary and cardiovascular disease, hyperthyroidism and glaucoma.

It is inadvisable to give Reactivan to patients with angina or to those who exhibit symptoms of hyperexcitability or marked agitation.

Reactivan should not be given with or within 14 days of having MAOI drugs.

Overdosage: Treatment consists of the induction of vomiting and/or gastric lavage together with appropriate symptomatic and supportive measures. Excessive stimulation may be treated with a non-barbiturate tranquilliser such as diazepam.

Pharmaceutical precautions Store in a well closed container.

Legal category POM.

Package quantities Reactivan is available in bottles of 100 sugar-coated tablets.

Further information Nil.

Product licence number 0493/5001.

SEPTOPAL® CHAINS

Presentation Methylmethacrylate-methylacrylate copolymer (PMMA) Beads (7 mm in diameter) each containing Gentamicin sulphate 7.5 mg (corresponding to 4.5 mg of Gentamicin base) and 20 mg of Zirconium dioxide as X-ray medium.

Each Chain consists of 30 beads threaded on multiple-thread surgical wire.

Uses Gentamicin is a proven broad spectrum antibiotic active against both gram-positive and gram-negative organisms. Following insertion of the Chains, Gentamicin is released gradually from the PMMA beads over a prolonged period and the high bactericidal concentrations of the antibiotic reached at the site of infection enable the infection to be controlled, or provide protection against infection when used prophylactically.

Septopal Chains are indicated for short term and longer term administration in bone infection, e.g. chronic forms of osteomyelitis (post traumatic, haematogenous), infected pseudoarthroses, infected osteosyntheses.

Preventive treatment of potentially infected bone injuries.

Dosage and administration Septopal Chains have been sterilised in ethylene oxide. They are contained in a double sachet. The outer sachet (peel-off pack) is opened first and the inner sterile packaging then removed under aseptic conditions.

The cavity resulting after thorough surgical removal of the infected bone tissue sequestra is completely filled up with Septopal Chains; the number of Chains used will depend on the size of the cavity. Usually 1–3 Chains are inserted but up to 5 Chains have been used. Inserted Chains will be completely enclosed by primary wound closure.

Septopal Chains may be used as follows:

1. **Short Term Application:** For the implantation of Chains, it is recommended to take into account the direction in which the Chain will later be pulled out and to let the last bead project above the skin level in order that the Chain may be removed by careful, steady traction.

The Chains are in general removed 10–14 days following insertion and preferably not more than 10 days after the operation.

The less the Chains are fixed to connective tissue, the easier it is to remove them; this procedure is thus also less painful and more comfortable for the patient.

If the beads become fixed to connective tissue to an advanced extent, or if the traction of the beads is not adapted to the tissue conditions, one or several beads may rarely detach themselves from the multistranded wire or, in exceptional circumstances, the wire may break on the removal of the Chain. In such an event one should generally try to remove the single beads (together with the remaining wire). Should, however, extensive surgical procedures be necessary, the single beads may be left in the body, taking into consideration the comparative risk of reoperation.

2. **Longer Term Application:** If circumstances require it, the Chains may be implanted completely below the skin level, and removed by reoperation up to 3 months later.

Control of local infection allows optimum conditions for subsequent surgical procedures, e.g. cancellous bone grafting.

Wherever possible, primary wound closure should be employed; this avoids excessive loss of secretion which would automatically reduce the Gentamicin concentration at the site of infection. An overflow drain can be employed only when considered necessary. Suction drainage is not employed but may be temporarily used in cases of obstructed wound secretion flow.

Contra-indications, warnings, etc There is no absolute contra-indication other than established intolerance of Gentamicin.

Since the beads are strung on surgical wire containing chrome and nickel, there is a potential for local sensitivity reactions to these metals.

Septopal can be used in all orthopaedic procedures where Gentamicin sensitive organisms are found to be present from routine bacteriological screening. Where resistant organisms are encountered to the standard 10 mcg disc test, a MIC determination is recommended. In view of the high bactericidal Gentamicin concentration at the infection site, organisms found resistant to the standard 10 mcg sensitivity disc screen may in fact be sensitive and therefore results of such screening may not give a true reflection of clinical effectiveness.

Toxic effects due to the antibiotic are not anticipated since after use of Septopal Chains, barely detectable Gentamicin concentrations (no more than 0.5 mcg/ml) are found in serum for up to four days postoperatively following insertion of the Chains.

Pharmaceutical precautions Store at room temperature – do not freeze.

Septopal Chains should not be used beyond the expiry date (2 years).

Resterilisation of Septopal Chains should not be attempted under any circumstances.

Legal category POM.

Package quantities One Chain consisting of 30 beads threaded on surgical wire in a sterile inner sachet (peel-off pack).

Packs of 1 Chain.

Packs of 5 Chains.

Further information Gentamicin is released in bactericidal concentrations at the site of infection, the flow of secretion during filling of the bone cavities is not inhibited and the biomechanics of the bone are not changed, granulation tissue grows into the hollow spaces between the beads during the healing process and only traces of the antibiotic are detectable in serum in spite of high local Gentamicin concentration. Local control of infection lessens the risk of secondary infection developing with subsequent bone grafting.

Product licence number 0493/0091.

TRIOSORBON®

Presentation A white soluble tasteless powder of high nutritional value which is readily absorbed and completely utilised. Triosorbon is packed in foil sachets containing 85 g of powder providing 400 kilocalories (1.67 MJ).

Triosorbon makes a palatable drink when mixed with water and it can be sprinkled over already prepared food.

The fat consists mainly of medium chain triglycerides.

The protein component is provided by a combination of whey protein, L-Cystine and Casein.

Carbohydrates are present in a well balanced mixture of mono, oligo and polysaccharides. The formulation is gluten free and virtually free of lactose.

Approximately 5 sachets of Triosorbon meet the adult daily nutritional requirements.

Composition: 100 g contains:

Protein	19 g
Nitrogen	3.05 g
Fat	19 g
Carbohydrates	56 g
Sodium 20 mmol	(0.46 g)
Potassium 20 mmol	(0.78 g)
Calcium 6 mmol	(0.24 g)
Magnesium 3.5 mmol	(0.085 g)
Phosphorus 9 mmol	(0.28 g)

Additions of vitamins and other substances

Vitamin A	1,250 Units
Vitamin B ₁	0.38 mg
Vitamin B ₂	0.45 mg
Nicotinamide	5.0 mg
Vitamin B ₆	0.5 mg
Vitamin B ₁₂	0.75 mcg
Folic acid	47.5 mcg
Biotin	0.1 mg
Pantothenic acid	2.0 mg
Vitamin C	15.5 mg
Vitamin D ₃	94 Units
Vitamin E	3.75 mg
Vitamin K ₁	0.25 mg
L-Cystine	300 mg
Ferrous gluconate (Iron)	32.5 mg 3.75 mg

Uses Triosorbon can be used as a complete diet or to supplement food intake, or as a tube feed (naso-gastric or via a jejunostomy) in diseases where normal ingestion is inadequate or impossible, i.e. malabsorption and mal digestion syndromes.

Dosage and administration *Neonates and infants:* Up to one year 20 g of Triosorbon per kg body weight per day (1–2 sachets).

The calculated quantity is divided into 5–8 individual meals according to the age of the child.

Children and youths: They should receive 10–15 g Triosorbon per kg body weight per day (3–5 sachets).

Adults: Adults are given 7 g of Triosorbon per kg body weight per day (5 sachets).

Five sachets of Triosorbon meet the daily nutritional requirement approximately.

Dilution: One sachet of 85 g is mixed with 400 ml water. This produces a virtually iso-osmolar solution (238 mosm/l) giving 400 kcal.

Hints: It is recommended, particularly in bottle feeding and tube feeding, to follow the indicated dosage because of the hazards of hyperosmolar dehydration.

Triosorbon should not be cooked with meals but should be added to meals already prepared.

If indicated salt can be added.

Initially mix with a small amount of water into a smooth paste, then add the remainder of the water slowly.

Contra-indications, warnings, etc Not for intra-venous use. Once Triosorbon has been mixed it should be used as soon as possible.

Pharmaceutical precautions Store in cool dry place.

Legal category No restrictions on sale or supply.

Package quantities Triosorbon is supplied in boxes containing 10 sachets of 85 g powder each.

Further information Borderline product.

Product licence number Not applicable.

UNGUENTUM MERCK*

Presentation Unguentum Merck is a stable emulsion system with a uniform distribution of fat and water (ambiphilic); thus it combines the properties of a) an oil in water emulsion (cream) and b) a water in oil emulsion (ointment), for use on dry or weeping conditions of the skin.

Composition:

Lipoid component: about 60%
Polyoxyethylene sorbitan fatty acid ester
Cetyl stearyl alcohol
Glycerin mono fatty acid ester
Propylene glycol
Paraffin hydrocarbons
Saturated neutral oil
Dispersed silicic acid
Sorbic acid
Water content: about 40%

Uses Unguentum Merck is to be used as a diluent for various topical corticosteroid formulations in those instances where a lower strength preparation is considered desirable by the physician and as a general base for extemporaneous dispensing.

Unguentum Merck has emollient properties and is recommended for the symptomatic treatment of dermatitis, nappy rash, ichthyosis, eczema, protection of raw and abraded skin areas, pruritus and related conditions where dry scaly skin is a problem, and as a pre-bathing emollient for dry/eczematous skin, to alleviate drying effects.

Dosage and administration *Administration:* A thin application of the cream should be gently massaged into the skin three times daily or at appropriate intervals.

When used as a protective cream Unguentum Merck should be applied sparingly to the affected areas of the skin before, or immediately after, exposure to a potentially harmful factor.

Contra-indications, warnings, etc Unguentum Merck should not be used for the treatment of patients sensitive to any of the ingredients.

Pharmaceutical precautions No special requirements.

Legal category P.

Package quantities Tubes of 50 g, 100 g. Jars of 900 g and 5 kg.

Further information Unguentum Merck contains no common allergens such as lanolin or parabens.

Product licence number 0493/0013.

UROMIRO* 300, 340, 380, 420 SODIUM UROMIRO* 300

Presentation Ampoules or bottles containing sterile aqueous solutions of varying strengths of meglumine and sodium iodamide.

Uromiro 300: Contains a 65% w/v concentration of the meglumine salt of iodamide equivalent to 30% iodine or 300 mg/ml.

Uromiro 340: Contains a concentration of 18.3% w/v meglumine iodamide and 43.4% w/v of sodium, iodamide equivalent to 34% iodine or 340 mg/ml.

Uromiro 380: Contains a concentration of 70% w/v meglumine iodamide and 9.7% w/v sodium iodamide equivalent to 38% iodine or 380 mg/ml.

Uromiro 420: Contains a concentration of 40.8% w/v meglumine and 39.4% w/v sodium iodamide equivalent to 42% iodine or 420 mg/ml.

Sodium Uromiro 300: Contains a concentration of 52.66% w/v sodium iodamide equivalent to 30% iodine or 300 mg/ml.

Uses X-ray contrast media for the opacification of the vascular and renal systems, e.g. urography, cerebral angiography, peripheral arteriography, venography, operative and T-tube cholangiography, angiocardiology, coronary arteriography and aortography.

Contra-indications, warnings, etc

Contra-indications: Proven or suspected hypersensitivity to iodine-containing preparations of this type.

Warnings, side-effects: Care should be exercised in patients with severe systemic disease, in hyperthyroidism, during pregnancy, in allergic subjects and in myelomatosis; patients with this condition should not be exposed to dehydration.

Use of the product may give rise to side-effects including anaphylactoid or shock-like manifestations with nausea, vomiting, widespread reddening of the skin and heat sensation, headache, and sometimes coryza; oedema of the larynx, fever, sweating, asthenia, dizziness, pallor, dyspnoea, and moderate hypotension. Skin rashes of various description may occur in some patients.

More severe reactions involving the cardiovascular system may call for emergency treatment. No other drugs should be mixed with the contrast medium.

Fluid intake should not be limited in neonates and small children.

Before using hypertonic contrast media any abnormalities of water and electrolyte balance should be corrected.

Pharmaceutical precautions Store away from light.

Legal category POM.

Package quantities

Uromiro 300:

Box containing 5 × 20 ml ampoules.

Box containing 1 × 50 ml bottle.

Uromiro 340:

Box containing 5 × 20 ml ampoules.

Box containing 1 × 50 ml bottle.

Dosage and administration

Intravenous Urography	Sodium Uromiro 300 Uromiro 300 Uromiro 340 Uromiro 380 Uromiro 420	Adults 40–80 ml Children 1 ml/kg	In severe renal failure the usual high dose methods of Urography should be applied (up to 1.5 ml/kg)
Cerebral Angiography	Uromiro 300	Adults 8 ml Children 5–7 ml according to body size and age	
Angiocardiology	Uromiro 380 Uromiro 420	Adults 20–50 ml Children 1 ml/kg In both adults and children requiring frequent multiple injections, a total of 3–5 ml per kg should seldom be exceeded. Inject rapidly within 1–2 sec.	
Coronary Arteriography	Uromiro 380	Adults 5–8 ml per artery	
Peripheral Arteriography	Uromiro 300 Uromiro 340 Uromiro 380	Adults 20–30 ml Children according to body size and age	
Venography	Uromiro 300 Uromiro 340	Adults 20–30 ml Children according to body size and age	
Operative and T-tube Cholangiography	Uromiro 300	During the period of operation 10–15 ml of contrast medium are injected into the cystic duct or its stump by means of a fine needle. In the postoperative period this may be done through a T-tube left in situ at operation	
Aortography retrograde	Uromiro 380 Uromiro 420	Adults 20–40 ml Children according to body size and age	
Selective renal arteriography	Uromiro 380 Uromiro 420	Adults 8 ml Children according to body size and age	

Uromiro 380:

Box containing 5 × 20 ml ampoules.

Box containing 1 × 50 ml bottle.

Uromiro 420:

Box containing 5 × 20 ml ampoules.

Box containing 1 × 50 ml bottle.

Sodium Uromiro 300:

Box containing 5 × 20 ml ampoules.

Box containing 1 × 50 ml bottle.

Further information Nil.

Product licence numbers

Uromiro 300 0493/0086

Uromiro 340 0493/0087

Uromiro 380 0493/0088

Uromiro 420 0493/0089

Sodium Uromiro 300 0493/0085

** Trade Mark*

Merck Sharp & Dohme Limited
Hertford Road
Hoddesdon
Hertfordshire EN11 9BU



ALDOMET®

Presentation Yellow, film-coated tablets containing Methylodopa BP equivalent to the following amounts of anhydrous methylodopa: 125 mg (marked 'MSD 135' or 'ALDOMET MSD 135'), 250 mg (marked 'MSD 401' or 'ALDOMET MSD 401'), or 500 mg (marked 'MSD 516' or 'ALDOMET MSD 516').

Fruit-flavoured, oral suspension containing 250 mg of methylodopa per 5 ml.

Injection, ampoules containing, per millilitre, 50 mg Methylodopa Hydrochloride BP, as a colourless solution.

Uses Hypertension (mild, moderate, and severe). Aldomet Injection may be used to initiate treatment in acute hypertensive crises.

Dosage and administration *Oral therapy: Adults:* Initial dosage: Usually 250 mg two or three times a day, for two days.

Adjustment: Usually adjusted at intervals of not less than two days, until an adequate response is obtained. The maximum recommended daily dosage is 3 g.

Many patients experience sedation for two or three days when therapy with Aldomet is started or when the dose is increased. When increasing the dosage, therefore, it may be desirable to increase the evening dose first.

General considerations: Methylodopa is largely excreted by the kidney and patients with impaired renal function may respond to smaller doses. Syncope in older patients may be related to an increased sensitivity and advanced arteriosclerotic vascular disease. This may be avoided by lower doses.

Withdrawal of Aldomet is followed by return of hypertension, usually within 48 hours. This is not complicated generally by an overshoot of blood pressure.

Therapy with Aldomet may be initiated in most patients already on treatment with other antihypertensive agents by terminating these antihypertensive medications gradually if required (see manufacturer's recommendations on stopping these drugs). Following such previous antihypertensive therapy, Aldomet should be limited to an initial dose of not more than 500 mg daily and increased as required at intervals of not less than two days.

Aldomet may also be used concomitantly with Moduretic® (amiloride hydrochloride and hydrochlorothiazide, MSD) or beta-blocking agents, such as Blocadren® (timolol maleate MSD).

When methylodopa is given to patients on other antihypertensives the dose of these agents may need to be adjusted to effect a smooth transition.

Oral therapy: Children: Initial dosage is based on 10 mg/kg of body weight daily in 2-4 oral doses. The daily dosage then is increased or decreased until an adequate response is achieved. The maximum dosage is 65 mg/kg or 3.0 g daily, whichever is less.

Intravenous therapy: Aldomet Injection is for intravenous use only, it must not be given intramuscularly or subcutaneously. An effective dose will produce a fall in blood pressure that may begin in 4 to 6 hours and be maintained for 10 to 16 hours.

Usual adult dosage: 250-500 mg (5-10 ml) six-hourly. In severe cases, up to 1 g (20 ml) six-hourly may be needed, and this is the maximum recommended dosage. If there is renal impairment, lower dosages should suffice.

Children's dosage: The recommended intravenous dosage for children is 20-40 mg/kg of body weight in divided doses every six hours. The maximum dosage is 65 mg/kg or 3.0 g daily, whichever is less. When the blood pressure is under control, continue with oral therapy. If there is renal impairment, lower dosages should suffice.

The required dose should be added to 100 ml of 5% dextrose, and the resulting solution given by intravenous infusion over a period of 30-60 minutes. When control of the hypertensive crisis has been obtained with Aldomet Injection, oral therapy with Aldomet Tablets may be substituted, starting with the same dosage as that being used intravenously.

Contra-indications, warnings, etc

Contra-indications: Active hepatic disease, such as acute hepatitis and active cirrhosis; hypersensitivity (including hepatic disorders associated with previous methylodopa therapy).

Precautions: Acquired haemolytic anaemia has occurred rarely. Should symptoms suggest anaemia, haemoglobin and/or haematocrit determinations should be made. If anaemia is confirmed, tests should be done for haemolysis. If haemolytic anaemia is present, Aldomet should be discontinued. Stopping therapy, with or without giving a corticosteroid, has usually brought prompt remission. Rarely, however, deaths have occurred.

Some patients on continued therapy with methylodopa develop a positive direct Coombs test. From the reports of different investigators, the incidence averages between 10% and 20%. A positive Coombs test rarely develops in the first six months of therapy, and if it has not developed within 12 months, it is unlikely to do so later on continuing therapy. Development is also dose-related, the lowest incidence occurring in patients receiving 1 g or less of methylodopa per day. The test becomes negative usually within weeks or months of stopping methylodopa.

Prior knowledge of a positive Coombs reaction will aid in evaluating a cross-match for transfusion. If a patient with a positive Coombs reaction shows an incompatible minor cross-match, an indirect Coombs test should be performed. If this is negative, transfusion with blood compatible in the major cross-match may be carried out. If positive, the advisability of transfusion should be determined by a haematologist.

Reversible leucopenia, with primary effect on granu-

locytes has been reported rarely. The granulocyte count returned to normal on discontinuing therapy. Reversible thrombocytopenia has occurred rarely.

Occasionally, fever has occurred within the first three weeks of therapy, sometimes associated with eosinophilia or abnormalities in liver function tests. Jaundice, with or without fever, also may occur. Its onset is usually within the first two or three months of therapy. In some patients the findings are consistent with those of cholestasis. Rare cases of fatal hepatic necrosis have been reported. Liver biopsy, performed in several patients with liver dysfunction, showed a microscopic focal necrosis compatible with drug hypersensitivity. Liver function tests and a total and differential white blood cell count are advisable at intervals during the first six weeks to twelve weeks of therapy, or whenever an unexplained fever occurs. Should fever, abnormality in liver function, or jaundice occur, therapy should be withdrawn. If related to methyl dopa, the temperature and abnormalities in liver function will then return to normal. Methyl dopa should not be used again in these patients. Methyl dopa should be used with caution in patients with a history of previous liver disease or dysfunction.

When methyl dopa is used with other antihypertensive drugs, potentiation of antihypertensive action may occur. The progress of patients should be carefully followed to detect side reactions or manifestations of drug idiosyncrasy.

A paradoxical pressor response has been reported with Aldomet Injection.

Patients may require reduced doses of anaesthetics when on methyl dopa. If hypotension does occur during anaesthesia, it can usually be controlled by vasopressors. The adrenergic receptors remain sensitive during treatment with methyl dopa.

Dialysis removes methyl dopa; therefore, hypertension may recur after this procedure.

Rarely, involuntary choreo-athetotic movements have been observed during therapy with methyl dopa in patients with severe bilateral cerebrovascular disease. Should these movements occur, therapy should be discontinued.

Interference with laboratory tests: Methyl dopa may interfere with the measurement of urinary uric acid by the phosphotungstate method, serum creatinine by the alkaline picrate method, and SGOT by colorimetric method. Interference with spectrophotometric methods for SGOT analysis has not been reported.

As methyl dopa fluoresces at the same wavelengths as catecholamines, spuriously high amounts of urinary catecholamines may be reported interfering with a diagnosis of phaeochromocytoma.

It is important to recognise this phenomenon before a patient with a possible phaeochromocytoma is subjected to surgery. Methyl dopa does not interfere with measurement of VMA (vanillylmandelic acid) by those methods which convert VMA to vanillin. Methyl dopa is not recommended for the treatment of patients with phaeochromocytoma.

Rarely, when urine is exposed to air after voiding, it may darken because of breakdown of methyl dopa or its metabolites.

Pregnancy and nursing mothers: Aldomet has been used under close medical supervision for the treatment of hypertension during pregnancy. There was no clinical evidence that Aldomet caused foetal abnormalities or affected the neonate.

Methyl dopa crosses the placental barrier and appears in cord blood and breast milk.

Although no obvious teratogenic effects have been reported, the possibility of foetal injury cannot be excluded and the use of the drug in women who are, or may become, pregnant or who are nursing their newborn infant requires that anticipated benefits be weighed against possible risks.

Side-effects: Sedation, usually transient, may occur during the initial period of therapy or whenever the dose is increased. Headache, asthenia or weakness may be noted as early and transient symptoms.

Significant side-effects due to Aldomet have been infrequent and this agent usually is well tolerated.

The following reactions have been reported:

Central nervous system: Sedation (usually transient, headache, asthenia or weakness), paraesthesiae, parkinsonism, Bell's palsy, involuntary choreoathetotic movements. Psychic disturbances including nightmares, impaired mental acuity and reversible mild psychoses or depression. Dizziness, light-headedness, and symptoms of cerebrovascular insufficiency (may be due to lowering of blood pressure).

Cardiovascular: Bradycardia, aggravation of angina pectoris. Orthostatic hypotension (decrease daily dosage). Oedema (and weight gain) usually relieved by use of a diuretic. (Discontinue methyl dopa if oedema progresses or signs of heart failure appear.)

Gastro-intestinal: Nausea, vomiting, distension, constipation, flatus, diarrhoea, mild dryness of mouth, sore or 'black' tongue, pancreatitis, sialadenitis.

Haematological: Positive Coombs test, haemolytic anaemia, bone marrow depression, leucopenia, granulocytopenia, thrombocytopenia. Positive tests for anti-nuclear antibody, LE cells, and rheumatoid factor.

Allergic: Drug-related fever and abnormal liver function tests with jaundice and hepatocellular damage, lupus-like syndrome, myocarditis.

Dermatological: Rash as in eczema or lichenoid eruption, toxic epidermal necrolysis.

Other: Nasal stuffiness, rise in blood urea, breast enlargement, gynaecomastia, lactation, impotence, decreased libido, mild arthralgia, myalgia.

Treatment of overdosage: If ingestion is recent, emesis may be induced or gastric lavage performed. There is no specific antidote. Methyl dopa is dialysable. Treatment is symptomatic. Infusions may be helpful to promote urinary excretion. Special attention should be directed towards cardiac rate and output, blood volume, electrolyte balance, paralytic ileus, urinary function and cerebral activity. Administration of sympathomimetic agents may be indicated. When chronic overdosage is suspected, Aldomet should be discontinued. Aldomet Suspension should not be diluted.

Pharmaceutical precautions Keep tablet container well closed. Store tablets and injection in a cool place, protected from light. The injection should also be protected from freezing. Only 5% dextrose should be used as diluent for the injection.

Legal category POM.

Package quantities *Tablets 125 mg:* Bottles of 100. *Tablets 250 mg:* Bottles of 100 and 500. *Tablets 500 mg:* Bottles of 100 and 500.

Oral Suspension, 250 mg/5 ml: Bottles of 200 ml.

Injection: Ampoules of 5 ml.

Further information Aldomet reduces both supine and standing blood pressure. Symptomatic postural hypotension, exercise hypotension and diurnal blood pressure variations rarely occur. By adjustment of dosage, morning hypotension can be prevented without sacrificing control of afternoon blood pressure.

Methyldopa has no direct effect on cardiac function and usually does not reduce glomerular filtration rate, renal blood flow or filtration fraction. Cardiac output usually is maintained without cardiac acceleration. In some patients, the heart rate is slowed.

Because of its relative freedom from adverse effects on kidney function, methyldopa can be of benefit in the control of high blood pressure, even in the presence of renal impairment. It may help arrest or retard the progression of renal function impairment and damage due to sustained elevation of blood pressure.

Normal or elevated plasma renin activity may decrease in course of methyldopa therapy.

Product licence numbers

Tablets 125 mg	0025/0098
Tablets 250 mg	0025/0099
Tablets 500 mg	0025/0100
Oral Suspension 250 mg/5 ml	0025/0154
Injection	0025/5003

ARAMINE*

Presentation A clear, colourless solution containing, in each millilitre, Metaraminol tartrate BP equivalent to 10 mg metaraminol. Aramine also contains methylparaben, propylparaben and sodium bisulphite as preservatives.

Uses Sympathomimetic amine (vasopressor agent). For the prevention and treatment of acute hypotension occurring with spinal anaesthesia. Also recommended as an adjunct in the treatment of hypotension due to haemorrhage, reaction to medication, surgical complications, and shock associated with brain damage due to tumour or trauma, may be useful as an adjunct in cardiogenic shock, or septicaemia.

The pressor effect of a single dose of Aramine lasts from about twenty minutes up to one hour. Its onset is around one or two minutes after direct intravenous injection, five to twenty minutes after subcutaneous injection, approximately ten minutes after intramuscular injection.

Dosage and administration Aramine Injection may be administered subcutaneously, Intramuscularly, or intravenously (injection or infusion). Because the maximum effect is not immediately apparent, allow at least ten minutes before increasing the dose. Since the vasopressor effect tapers off when therapy is stopped, be prepared to restart promptly if the blood pressure falls too rapidly. Patients with coexistent shock and acidosis may show poor response.

Established methods for the management of shock, such as blood or fluid replacement where necessary, and other measures directed to the specific cause of the shock, should be instituted or continued during therapy with Aramine.

Direct intravenous injection is recommended only in grave emergencies. *Particular care should be taken to use the correct dose.*

Intramuscular or subcutaneous injection (for prevention of hypotension): 2–10 mg (0.2–1 ml). Only the preferred sites of injection, as set out in standard texts, should be used.

Intravenous infusion (for adjunctive treatment of hypotension): 15–100 mg (1.5–10 ml) in 500 ml of Sodium Chloride Injection BP or 5% Dextrose Injection BP, adjusting the rate of infusion to maintain the blood pressure at the desired level. Higher concentrations of Aramine 150–500 mg per 500 ml of infusion fluid, have been used. If the patient needs additional saline or dextrose at a rate of flow that would provide an excessive dose of Aramine when used as recommended, the volume of infusion fluid should be increased accordingly. Aramine may also be added to less than 500 ml of infusion fluid if a smaller volume is desired.

Aramine is physically and chemically compatible with Injection Sodium Chloride BP, 5% Injection Dextrose BP, Ringer's Injection USP, Lactated Ringer's Injection USP, Dextran 70 Injection.

When Aramine is mixed with an infusion solution, sterile precautions should be observed. Mixtures should be used within 24 hours since infusion solutions do not contain preservatives.

Direct intravenous injection (to be employed only in grave emergencies, when immediate action is necessary to save life): 0.5–5 mg (0.05–0.5 ml), followed by an infusion of 15–100 mg (1.5–10 ml) in 500 ml of infusion liquid. *Particular care should be taken to use the correct dose when injecting undiluted Aramine.*

Contra-indications, warnings, etc

Contra-indications: Concurrent use with cyclopropane or halothane anaesthesia, unless clinical circumstances demand it. Hypersensitivity to any component of Aramine.

Precautions and side-effects: Abscess formation, tissue necrosis, and sloughing rarely may follow the use of Aramine. In choosing the site for injection, it is important to avoid those areas generally recognised as being unsuitable for the use of any pressor agent and to discontinue the infusion immediately if infiltration or thrombosis occurs. Although the urgent nature of the patient's condition may force the choice of an unsuitable injection site, the preferred areas of injection should be used when possible. The larger veins of the antecubital fossa or thigh are preferred to the veins in the ankle or dorsum of the hand, particularly in patients with peripheral vascular disease, diabetes mellitus, Buerger's disease or conditions with coexistent hypercoagulability. Caution should be exercised to avoid excessive blood pressure response.

Rapidly induced hypertensive responses have been reported to cause acute pulmonary oedema, cardiac arrhythmias and arrest. Aramine should be used with caution in patients with cirrhosis; electrolyte levels should be adequately restored if a diuresis ensues. A fatal ventricular arrhythmia was reported in a patient with Laënnec's cirrhosis while receiving metaraminol tartrate. In several instances, ventricular extrasystoles that appeared during infusion of Aramine promptly subsided when the rate of flow was reduced. Aramine should be used with caution in digitalised patients since the combination of digitalis and sympathomimetic amines is capable of causing ectopic arrhythmic activity.

With the prolonged action of Aramine, a cumulative effect is possible. An excessive vasopressor response may cause a prolonged elevation of blood pressure, even after discontinuation of therapy.

Monoamine oxidase inhibitors have been reported to potentiate the action of sympathomimetic amines. The pressor effect of Aramine is decreased but not reversed by alpha-adrenergic blocking agents.

Because of its vasoconstrictor action, Aramine should be used with caution in cases of heart disease, hypertension, thyroid disease, or diabetes mellitus.

Sympathomimetic amines may provoke a relapse in patients with a history of malaria. Sympathomimetic amines, including Aramine, may cause sinus or ventricular tachycardia, or other arrhythmias, especially in patients with myocardial infarction.

When vasopressor amines are used for long periods, the resulting vasoconstriction may prevent adequate expansion of circulating volume and may cause perpetuation of the shock state. There is evidence that plasma volume may be reduced in all types of shock, and that the measurement of central venous pressure is useful in assessing the adequacy of the circulating blood volume. Blood, or plasma-volume expanders, should therefore be employed when the principal reason for hypotension or shock is decreased circulating volume.

Treatment of overdose: If the drug has been ingested, induce emesis or perform gastric lavage. If Aramine has been administered by subcutaneous or intramuscular injection, local ice packs may be applied to delay absorption. Intravenous infusion should be stopped immediately, but reinstated if hypotension occurs. If needed, a sympatholytic agent may be given to reduce hypertension. Intravenous procainamide hydrochloride may also be useful for reducing hypertension, and may have a beneficial effect on cardiac arrhythmia, if present. Oral procainamide hydrochloride is useful in arrhythmia, but does not have a hypotensive effect. A parenteral barbiturate may be given for convulsions, but with care, since metaraminol has been found to prolong barbiturate narcosis in animals. Chlorpromazine may be tried if vomiting is a problem.

Pharmaceutical precautions Store in a cool place, protected from light and from freezing. Aramine is physically and chemically compatible with Injection Sodium Chloride BP, 5% Injection Dextrose BP, Ringer's Injection USP, Lactated Ringer's Injection USP, Dextran 70 Injection.

Legal category POM.

Package quantities Ampoules of 1 ml and vials of 10 ml.

Further information Aramine is a potent sympathomimetic amine which increases the force of myocardial contractions as well as having a peripheral vasoconstrictor action. It increases both systolic and diastolic blood pressures.

Renal, coronary, and cerebral blood flow are a function of perfusion pressure and regional resistance. In most instances of cardiogenic shock, the beneficial effect of sympathomimetic amines is attributable to their positive inotropic effect. In patients with insufficient or failing vasoconstriction, there is additional advantage to the peripheral action of Aramine, but in most patients with shock, vasoconstriction is adequate and any further increase is unnecessary. Therefore, blood flow to vital

organs may decrease with Aramine if the regional resistance increases excessively.

The pressor effect of Aramine is decreased but not reversed by alpha-adrenergic blocking agents. Primary or secondary fall in blood pressure and tachyphylactic response to repeated use are uncommon.

Aramine may be autoclaved or immersed in a sterilising solution.

Product licence number 10 mg/ml injection 0025/5020.

BENEMID*

Presentation White, half-scored tablets, marked 'MSD 501', containing 500 mg Probenecid BP.

Uses Inhibits the reabsorption of urate ions in the renal tubules, thus increasing urinary excretion of uric acid and decreasing serum uric acid levels. This reduces the miscible urate pool, retards the deposition of urates, and promotes reabsorption of urate deposits. Also selectively inhibits the urinary excretion of β -lactam antibiotics (other than cephaloridine).

Gout and other forms of hyperuricaemia: Benemid is an effective uricosuric agent for the treatment of hyperuricaemia in gout and gouty arthritis. Time is required to achieve clinical results with Benemid despite its marked uricosuric activity. Although acute attacks may occur in the early stages of therapy, as therapy is continued, these attacks should become less frequent and less intense. With prolonged use, formation of new gouty tophi can be prevented; existing tophi decrease in size and may eventually disappear.

Benemid may also be given prophylactically to treat the asymptomatic hyperuricaemia that often occurs in 'gouty' families, in an attempt to forestall the development of acute gouty attacks and urate deposition in tissues.

Benemid may be used to control the hyperuricaemia induced or aggravated by diuretics employed in oedema and hypertension.

β -lactam antibiotic therapy: Benemid is indicated as an adjunctive therapy with β -lactam antibiotics (other than cephaloridine). It elevates and prolongs the plasma levels by whatever route the antibiotics are given. A twofold to fourfold increase in plasma concentration has been demonstrated for penicillin G, or V, the synthetic penicillins, ampicillin, methicillin, oxacillin, cloxacillin, and carbenicillin, and for the cephamycins, Mefoxin* (cefoxitin sodium, MSD), and the cephalosporins, cephalothin, cephalexin and cephaloglycin (but not cephaloridine).

Adjunctive therapy of this type is particularly useful when treating severe or resistant infections, such as gonorrhoea, subacute bacterial endocarditis, staphylococcal osteomyelitis, staphylococcal septicaemia, and meningitis due to Gram-positive organisms.

Dosage and administration *Uricosuric therapy:* Usual adult dosage: $\frac{1}{2}$ tablet (250 mg) twice a day for one week, followed thereafter by 1 tablet (500 mg) twice a day.

Some degree of renal impairment is common in patients with gout, therefore, a daily dosage of 2 tablets (1 g) may be adequate in many patients. If, however, symptoms of gouty arthritis remain uncontrolled or the 24-hour urate excretion is not above 700 mg, the daily

dosage may be increased by 1 tablet (500 mg) every four weeks within tolerance [usually not more than 4 tablets (2 g) a day]. Benemid may not be effective in chronic renal insufficiency, particularly when the glomerular filtration rate is 30 ml/min or less.

Gastric intolerance may be indicative of overdosage, and may be corrected by reducing the dosage without losing the therapeutic response.

When acute attacks have been absent for at least six months and serum uric acid remains within normal limits, dosage may be reduced by 1 tablet (500 mg) a time over a period of months to the minimum effective dosage. The dosage should not be reduced to the point where serum uric acid levels tend to rise. Once a patient has been stabilised on Benemid, the usual restrictions on purine-producing foods may be somewhat relaxed.

β-lactam antibiotic therapy (general): *Adults:* 4 tablets (2 g) a day in divided doses. Elderly patients with suspected renal impairment should be given a smaller dosage, and Benemid should not be given concurrently with a β-lactam antibiotic in known cases of renal impairment.

Children over 2 years: 25 mg per kg body weight (or 0.7 g/m² body surface) initially, followed by 40 mg per kg (or 1.2 g/m²) a day in divided doses every six hours. For children weighing more than 50 kg, the adult dosage is recommended.

Gonorrhoea: For uncomplicated gonorrhoea in men or women: a single dose of 2 tablets (1 g) with adequate doses of either oral ampicillin or intramuscular aqueous procaine penicillin or cefoxitin. If oral ampicillin is used, Benemid should be given simultaneously; if a parenteral antibiotic is administered, Benemid should be given at least 30 minutes beforehand.

Contra-indications, warnings, etc

Contra-indications: Known hypersensitivity to probenecid. History of blood dyscrasias. Uric acid kidney stones. Children under two years old. Therapy with Benemid should not be started until an acute gouty attack has subsided. Salicylates are contra-indicated in patients taking Benemid.

Precautions: Benemid should be used with caution in patients with a history of peptic ulcer. If hypersensitivity reactions appear during therapy, the drug should be withdrawn. If patients on Benemid need a mild analgesic, paracetamol is preferred.

Haematuria, renal colic, costovertebral pain and the formation of urate stones may be prevented by a liberal fluid intake and enough sodium bicarbonate (3–7.5 g daily) or potassium citrate (7.5 g daily) to keep the urine alkaline. When alkali is given, the acid-base balance of the patient should be carefully monitored.

Exacerbation of gout during therapy with Benemid may occur; if so, a full therapeutic dosage of colchicine, Indocid* (indomethacin) or other appropriate therapy should be given. A reducing substance may appear in the urine of patients receiving Benemid. This may give a false-positive Benedict's test, but the substance disappears when therapy is discontinued.

Drug interactions: The use of acetylsalicylic acid and pyrazinamide antagonises the uricosuric action of probenecid.

Probenecid produces an insignificant increase in free sulphonamide plasma concentrations but a significant increase in total sulphonamide plasma levels. Since probenecid decreases the renal excretion of conjugated

sulphonamides, plasma concentrations of the latter should be determined from time to time when a sulphonamide and probenecid are given together for prolonged periods.

Probenecid may prolong or enhance the action of oral sulphonylureas and thereby increase the risk of hypoglycaemia.

When probenecid is given to patients receiving indomethacin, the plasma levels of indomethacin are likely to be increased. Therefore, a lower dosage of indomethacin may be required to produce a therapeutic effect, and increases in the dosage of indomethacin should be made cautiously and in small increments. Probenecid may increase plasma levels of rifampicin. The clinical significance of this is not known.

Benemid increases the plasma concentration of methotrexate. If Benemid is given with methotrexate, the dosage of methotrexate should be reduced and serum levels may need to be monitored.

In addition to its effects on the excretion of uric acid and the β-lactam antibiotics (other than cephaloridine). Benemid decreases the urinary excretion of p-aminosalicylic acid (PAS), p-aminohippuric acid (PAH), phenolsulphonylphthalein (PSP), pantothenic acid, 17-ketosteroids, and sodium iodomethamate. Benemid decreases both hepatic and renal excretion of sulphabromophthalein (BSP). The renal tubular reabsorption of phosphorus is inhibited in hypoparathyroid but not in euparathyroid individuals.

Benemid does not affect the excretion of streptomycin, chloramphenicol, chlortetracycline, or neomycin. The effects on the excretion of cephaloridine are not clinically significant.

Use in pregnancy: Probenecid crosses the placental barrier and appears in cord blood. Its use in women of childbearing age requires that the anticipated benefit be weighed against possible hazards.

Side-effects: Headache, gastro-intestinal symptoms (e.g. anorexia, nausea, vomiting), frequency of micturition, hypersensitivity reactions (including anaphylaxis, dermatitis, pruritus, fever), sore gums, flushing, dizziness, anaemia and haemolytic anaemia (in some cases associated with genetic deficiency of glucose-6-phosphate dehydrogenase in red blood cells) have occurred. Rarely, the nephrotic syndrome, hepatic necrosis, and aplastic anaemia. In gouty patients, exacerbation of gout, and uric acid stones with or without haematuria, renal colic, or costovertebral pain, has been seen.

Treatment of overdosage: Emesis should be induced or gastric lavage performed. If signs of CNS excitation are present, a short-acting barbiturate should be given parenterally. Adrenaline should be given for anaphylactoid reactions. For less severe hypersensitivity reactions, antihistamines or corticosteroids may be given.

Pharmaceutical precautions Keep container tightly closed. Store in a cool place, protected from light.

Legal category POM.

Package quantities Bottles of 100 and 500.

Further information Benemid has been in use since 1952. It can generally be given indefinitely because of its low toxicity.

Product licence number 0025/5021.

BLOCADREN®

Presentation Blue, half-scored tablets, marked 'MSD 136' on one side with or without 'BLOCADREN' on the other, containing 10 mg timolol maleate, MSD.

Uses Beta-adrenergic-receptor blocking agent. For the treatment of essential hypertension and in angina pectoris due to ischaemic heart disease.

Blocadren is also indicated for the long-term prevention of myocardial infarction and cardiac death (including sudden death) in those who have survived the acute phase of a myocardial infarction.

Prophylactic management of common and classic migraine.

Dosage and administration

Hypertension: The initial dosage is 10 mg a day in a single or divided dosage. Depending on the response of the patient, increases in dosage can be made to a maximum of 60 mg daily. Daily dosages above 20 mg should be given on a divided dose schedule.

Use with Moduretic® (amiloride hydrochloride and hydrochlorothiazide, MSD): Studies have shown that Blocadren can be administered once daily when used concomitantly with Moduretic. The majority of patients will respond to a regimen of 10 or 20 mg of Blocadren once a day and 1 tablet of Moduretic.

Use with other antihypertensives: Blocadren may be used with thiazides, hydralazine, or methyldopa. Dosage adjustments are usually required.

For concomitant use with catecholamine-depleting drugs such as reserpine or guanethidine, see 'Precautions'.

Angina: Therapy should be initiated with 5 mg two or three times a day. Dosage increases may be necessary, depending on the symptomatic response, pulse rate, and blood pressure. The first increase should not exceed 10 mg a day in divided doses, and subsequent increases should not exceed 15 mg a day in divided doses. There should be an interval of at least three days between increases in dosage.

The recommended dosage range is 15 to 45 mg a day. The majority of patients respond to a dosage in the range of 35 to 45 mg a day.

Preventive use in ischaemic heart disease: For long-term preventive use in patients who have survived the acute phase of myocardial infarction, the maintenance dose is 10 mg twice daily. Therapy should be initiated with 5 mg twice daily and the patient observed carefully. If no adverse reaction occurs, the dosage should then be increased after 2 days to 10 mg twice daily. In the studies evaluating Blocadren following myocardial infarction, treatment was begun 7 to 28 days after the acute phase.

Migraine: The recommended dosage in the prophylactic treatment of common and classic migraine is 10 to 20 mg administered once-a-day.

Contra-indications, warnings, etc

Contra-indications: Bronchospasm (including bronchial asthma), or chronic obstructive pulmonary disease; sinus bradycardia; second- and third-degree atrioventricular block; anaesthesia with agents that produce myocardial depression; congestive heart failure (see 'Precautions'); right ventricular failure secondary to pulmonary hypertension; significant cardiomegaly; cardiogenic shock; hypersensitivity.

See also 'Use in pregnancy', under 'Precautions'.

Precautions: *Congestive heart failure:* Patients with a

history of cardiac failure should be carefully evaluated for evidence of cardiac failure resulting from continued depression of myocardial function through beta-adrenergic receptor blockade. Even in patients without a history of cardiac failure, continued myocardial depression from the use of beta-adrenergic blockers over a period of time may lead to cardiac failure. While therapy with beta-adrenergic blocking agents may be continued, full digitalisation should be employed at the first sign of impending heart failure and the patient should be closely observed until the danger of failure is past. Diuretic therapy may also be considered for control of oedema and congestive phenomena. Glucagon may be useful in the treatment of acute heart failure associated with beta-adrenergic-receptor blockade.

The patient should be observed especially for signs of congestive heart failure, bradycardia, atrioventricular block, or respiratory distress. If severe bradycardia occurs, the use of intravenous atropine should be considered, followed, if not improvement is seen, by intravenous isoprenaline.

Beta-adrenergic receptor blocking agents may mask the clinical signs of developing or continuing hyperthyroidism. Blocadren does not alter thyroid function tests.

Ischaemic heart disease (angina pectoris and post-myocardial infarction): Patients with ischaemic heart disease should be warned against stopping Blocadren abruptly. Myocardial infarction, ventricular arrhythmias, or sudden death has been reported in such patients following abrupt discontinuation of therapy with beta-adrenergic receptor blocking agents, with or without preceding exacerbation of angina pectoris. Therefore, in angina and post-myocardial infarction, the dosage of Blocadren should be gradually reduced over about two weeks (maintaining the same frequency of administration) and the patient should be carefully observed. In patients with angina pectoris, if the angina still markedly worsens, or in any patient if acute coronary insufficiency develops, it is recommended that Blocadren is reinstated, at least temporarily.

Elective or emergency surgery: Because beta-adrenergic-receptor blockade impairs the heart's response to beta-adrenergic reflex stimuli, some patients on beta-adrenergic receptor blocking agents have shown protracted severe hypotension during anaesthesia. Difficulty in restarting and maintaining the heartbeat has also been reported.

Some authorities now recommend gradual withdrawal of beta-adrenergic receptor blocking agents from anginal patients before elective surgery. In emergency surgery, since timolol maleate is a competitive inhibitor of beta-adrenergic-receptor agonists, its effects may be reversed, if necessary, by sufficient doses of such agonists as isoprenaline or noradrenaline.

Blocadren should be administered with caution to patients liable to spontaneous hypoglycaemia, or to diabetic patients (especially those with labile diabetes) who are receiving insulin or oral hypoglycaemic agents. Beta-adrenergic receptor blocking agents may mask the premonitory signs and symptoms of acute hypoglycaemia.

Close observation of the patient is recommended when Blocadren is administered to patients on catecholamine-depleting drugs such as reserpine or guanethidine.

As with any relatively new drug, suitable laboratory tests should be carried out at appropriate intervals.

Caution should be observed in patients with impaired renal or hepatic function.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic receptor blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuation of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy involving beta-blockade should be gradual.

Since Blocadren is excreted mainly by the kidneys, dosage reduction may be necessary when renal insufficiency is present.

Use in pregnancy: Since Blocadren has not been studied in human pregnancy, it should not be given to pregnant women. The use of any drug in patients of childbearing potential requires that the anticipated benefit be weighed against possible hazards.

Side-effects: In most patients, Blocadren causes little interference with physical or mental activity.

The most commonly reported side-effects have been gastro-intestinal symptoms (e.g. epigastric distress, nausea, vomiting, diarrhoea), dizziness, weakness, headache, and dyspnoea. Congestive heart failure, severe bradycardia, bronchospasm, atrioventricular block, postural hypotension, cold extremities, Raynaud's phenomenon, fatigue, sedation, insomnia, increased dreaming, nightmares and mental depression have been reported infrequently. Hallucinations have occurred rarely.

A low incidence of various rashes and pruritus have been reported. A single case of exfoliative dermatitis has been reported.

Overdosage: The most common signs and symptoms to be expected following overdosage with a beta-adrenergic receptor blocking agent are symptomatic bradycardia, hypotension, bronchospasm, and acute cardiac failure. If overdosage occurs, the following measures are suggested. In all cases therapy with Blocadren should be stopped, and the patient closely observed.

1. Severe symptomatic bradycardia: atropine sulphate, 0.25 to 2 mg intravenously, should be used to induce vagal blockade. If bradycardia persists, intravenous isoprenaline hydrochloride should be administered cautiously. In refractory cases, the use of a cardiac pacemaker may be considered.

2. Severe hypotension: a sympathomimetic pressor agent such as noradrenaline or adrenaline should be used. In refractory cases, the use of glucagon has been reported to be useful.

3. Bronchospasm: isoprenaline hydrochloride should be used. Additional therapy with aminophylline may be considered.

4. Acute cardiac failure: conventional therapy with digitalis, diuretics, and oxygen should be instituted immediately. In refractory cases, the use of intravenous aminophylline is suggested. This may be followed, if necessary, by glucagon which has been reported useful.

Pharmaceutical precautions Keep container well closed; store in a cool place, protected from light.

Legal category POM.

Package quantities Bottles of 100.

Further information Blocadren reduces blood pressure without acute hypotensive episodes in most patients with essential hypertension. The exact mechanism of action is still unknown. Blocadren does not usually affect

normal blood pressure. Orally, Blocadren may lower intra-ocular pressure.

Blocadren effectively delays or prevents the development of anginal pain in most patients. It acts by modifying the cardiac response to stress or exercise. Blocadren antagonises the stimulation of the beta-adrenergic receptor sites caused by an excess of circulating catecholamines. In this way, Blocadren often increases the capacity for work and exercise in the patient with angina by reducing the incidence and severity of anginal attacks.

Product licence number 0025/0091.

CLINORIL*

Presentation Brilliant yellow, scored, hexagonal tablets, biconvex in shape, containing 200 mg and 100 mg Sulindac, MSD. The 200 mg tablets are marked 'MSD 942' and the 100 mg tablets are marked 'MSD 943'.

Uses Non-steroidal, analgesic/anti-inflammatory agent with antipyretic properties.

Indicated in osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, acute gouty arthritis, peri-articular disorders such as bursitis, tendinitis, and tenosynovitis.

Dosage and administration The dosage should be adjusted to the severity of the disease. The optimal dosage for many patients to achieve maximum relief of pain and inflammation is 400 mg a day, in particular, during the first week of treatment.

In the treatment of acute gouty arthritis, therapy is 200 mg twice a day for 7 to 10 days.

In clinical studies to date, the usual maximum dosage was 400 mg per day. Although a few patients have received higher dosages, until further clinical experience is obtained, dosages above 400 mg per day are not recommended.

Peri-articular conditions such as bursitis, tendinitis and tenosynovitis usually respond rapidly to a dose of 100 to 200 mg twice a day. Alternative treatment should be instituted if effective response has not been achieved within 7 to 10 days.

Clinoril should be administered twice a day with fluids or food.

Contra-indications, warnings, etc

Contra-indications: The use of Clinoril is contra-indicated in patients known to be allergic to the drug.

Clinoril should not be used in patients in whom acute asthmatic attacks have been precipitated by aspirin or other non-steroidal anti-inflammatory agents.

The drug should not be administered to patients with active gastro-intestinal bleeding.

The use of Clinoril should be avoided in patients with active peptic ulcer.

Since paediatric indications and dosage have not yet been established, Clinoril should not be given to children.

Clinoril should not be given to pregnant or lactating women, since safety for its use has not been established.

Precautions: Clinoril should be used with caution in patients having a history of gastro-intestinal haemorrhage or ulcers. In patients with renal functional impairment, since the major route of excretion of the drug is via the kidneys, the dosage may need to be reduced. In a drug interaction study, an antacid (magnesium and aluminium hydroxides, in suspension, 30 ml) was administered with Clinoril with no significant difference in absorption.

While Clinoril has less effect on platelet function and bleeding time than aspirin, it is a moderate to weak inhibitor of platelet function and therefore patients who may be adversely affected by these actions should be carefully observed when Clinoril is administered.

Drug interactions: Although sulindac and its sulphide metabolite are highly bound to protein, studies (in which Clinoril was given at a dose of 400 mg daily) have shown no clinically significant interaction with oral anticoagulants or oral hypoglycaemic agents. However, patients should be monitored carefully until it is certain that no change in their anticoagulant or hypoglycaemic dose is required.

Probenecid given concomitantly with sulindac had only a slight effect on plasma sulphide levels, while plasma levels of sulindac and sulphone were increased. Sulindac was shown to produce a modest reduction in the uricosuric action of probenecid which probably is not usually significant.

Neither dextropropoxyphene hydrochloride nor paracetamol had any effect on the plasma levels of sulindac or its sulphide metabolite.

Side-effects: Clinoril is generally well tolerated. Those side-effects experienced are usually mild and may often respond to a reduction in dosage.

Gastro-intestinal: The most frequent types of side-effects occurring with Clinoril are gastro-intestinal; these include gastro-intestinal pain, dyspepsia, nausea with or without vomiting, diarrhoea, constipation, flatulence, anorexia and gastro-intestinal cramps.

Dermatological: Rash, pruritus.

Central nervous system: Dizziness, headache, nervousness.

Special senses: Tinnitus.

Miscellaneous: Oedema.

The following side-effects were reported less frequently in clinical trials or have been reported since the drug has been available in practice. The probability exists of a causal relationship between Clinoril and these side-effects:

Gastro-intestinal: Gastritis or gastro-enteritis. Peptic ulcer, as well as gastro-intestinal bleeding and perforations have been reported rarely. Liver function abnormalities, jaundice sometimes with fever, cholestasis, hepatitis, pancreatitis.

Dermatological: Stomatitis, sore or dry mucous membranes have occurred infrequently, and in some cases disappeared with continued treatment. Erythema multiforme, toxic epidermal necrolysis, Stevens-Johnson syndrome.

Cardiovascular: Congestive heart failure in patients with marginal cardiac function; palpitation.

Haematological: Thrombocytopenia; leucopenia; increased prothrombin time in patients on oral anticoagulants.

Nervous system: Vertigo, somnolence, insomnia, sweating, asthenia.

Special senses: Blurred vision.

Hypersensitivity reactions: Anaphylaxis and angioneurotic oedema. In a few patients, an apparent hypersensitivity syndrome has been reported. This has consisted of some or all of the following findings: fever, chills, pruritus, skin rash, angioneurotic oedema, changes in liver function, jaundice, leucopenia, and eosinophilia. Rarely, fatalities have been reported.

Causal relationship unknown: Other reactions have been reported in clinical trials or since the drug was marketed, but occurred under circumstances where a causal relationship could not be established. However, in these rarely reported events, that possibility cannot be excluded. Therefore, these observations are listed to serve as alerting information to physicians.

Cardiovascular: Hypertension.

Haematological: Bone marrow depression, including aplastic anaemia.

Nervous system: Paraesthesiae, neuritis.

Special senses: Transient visual disturbances, decreased hearing.

Respiratory: Epistaxis.

Psychiatric: Depression; psychic disturbances including acute psychosis.

Genito-urinary: Vaginal bleeding, haematuria, azotaemia usually in patients with pre-existing renal disease.

Treatment of overdosage: There is no experience with acute overdosage, consequently the signs, symptoms, and treatment have not been identified. Isolated cases of patients receiving up to 900 mg a day have been reported, with no adverse effects.

In the event of acute overdosage, the stomach should be emptied by inducing vomiting or by gastric lavage, and the patient carefully observed and given symptomatic and supportive treatment.

Animal studies show that absorption is decreased by the prompt administration of activated charcoal and excretion is enhanced by alkalinisation of the urine.

Pharmaceutical precautions Keep container well closed; store in a cool place, protected from light.

Legal category POM.

Package quantities 200 mg: Bottles of 100 and 500. 100 mg: Bottles of 100.

Further information Clinoril usually provides symptomatic relief of inflammation, pain and tenderness and promotes early restoration of joint mobility. The drug has a prolonged duration of activity, which permits a twice-a-day dose schedule. Based on extensive studies, Clinoril has been shown to be suitable for the long-term relief of pain and inflammation.

Prostaglandin synthetase inhibition is hypothesised as the basis by which non-steroidal anti-inflammatory agents act. Following absorption, sulindac undergoes two major biotransformations: reversible reduction to the sulphide metabolite; and irreversible oxidation to the inactive sulphone metabolite. The sulphide metabolite is a potent inhibitor of prostaglandin synthesis and accounts for the activity of sulindac (Clinoril). Sulindac is thus a prodrug.

Product licence numbers

100 mg 0025/0121

200 mg 0025/0122

CODELCORTONE®

Presentation White, half-scored, oval tablets, marked 'MSD 56', containing 5 mg Prednisolone BP.

Uses Corticosteroid.

Allergic states: Severe or incapacitating allergies unresponsive to conventional treatment; seasonal or perennial allergic rhinitis, bronchial asthma, contact dermatitis,

atopic dermatitis, serum sickness, drug hypersensitivity reactions.

Rheumatic disorders: As adjunctive therapy for short-term administration during an acute episode or exacerbation of psoriatic arthritis, rheumatoid arthritis including juvenile rheumatoid arthritis (selected cases may require low-dosage maintenance therapy), ankylosing spondylitis, acute and subacute bursitis, acute non-specific tenosynovitis, acute gouty arthritis, post-traumatic osteoarthritis, synovitis of osteoarthritis, epicondylitis.

Dermatological diseases: Pemphigus, bullous dermatitis herpetiformis, severe erythema multiforme (Stevens-Johnson syndrome), exfoliative dermatitis, mycosis fungoides, severe psoriasis, severe seborrhoeic dermatitis.

Ophthalmic diseases: Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa, such as: allergic conjunctivitis, keratitis, allergic corneal marginal ulcers, herpes zoster ophthalmicus, iritis, iridocyclitis, chorioretinitis, diffuse posterior uveitis and choroiditis, optic neuritis, sympathetic ophthalmia.

Endocrine disorders: Primary or secondary adrenocortical insufficiency (the first choice is hydrocortisone or cortisone, but synthetic analogues may be used with mineralocorticoids where applicable; in infancy, mineralocorticoid supplementation is particularly important), congenital adrenal hyperplasia, non-suppurative thyroiditis, hypercalcaemia associated with cancer.

Respiratory diseases: Symptomatic sarcoidosis, Löf-ler's syndrome not manageable by other means, berylliosis, fulminating or disseminated pulmonary tuberculosis (when accompanied by appropriate concurrent antituberculous chemotherapy), aspiration pneumonitis.

Haematological disorders: Idiopathic thrombocytopenic purpura in adults and secondary thrombocytopenia in adults, acquired (auto-immune) haemolytic anaemia, red blood cell anaemia, congenital hypoplastic anaemia.

Neoplastic diseases: Palliative management of leukaemias and lymphomas in adults, and of acute leukaemia in children.

Oedematous states: To induce a diuresis or remission of proteinuria in the nephrotic syndrome, without uraemia, of the idiopathic type or due to lupus erythematosus.

Gastro-intestinal diseases: During a critical period of the disease in: ulcerative colitis, regional enteritis.

Other indications: Tuberculous meningitis with subarachnoid block or impending block used concurrently with appropriate antituberculous chemotherapy; trichinosis with neurological or myocardial involvement; during an exacerbation or as maintenance therapy in some cases of systemic lupus erythematosus and acute rheumatic carditis; for diagnostic testing of adrenocortical hyperfunction.

Dosage and administration *General considerations:* Therapy is governed by the following principles:

1. Dosage should be adjusted to the severity, prognosis and expected duration of the disease, and the response of the individual patient. For infants and children, the recommended dosages will usually have to be reduced, but dosage should be governed by the severity of the condition rather than by age or body weight.

2. Corticosteroid therapy is an adjunct to conventional therapy and does not replace it. Appropriate conventional therapy should be instituted as indicated.

3. If therapy is continued for more than a few days, any decrease in dosage must be *gradual*.

4. Continued supervision of the patient after cessation of corticosteroid therapy is essential, since there may be a sudden reappearance of severe manifestations of the disease for which the patient was being treated.

In acute conditions where prompt relief is urgent, high dosages are permissible and may be mandatory for a short time.

In chronic conditions requiring long-term therapy, the lowest dosage which provides adequate (but not necessarily complete) relief should be used. If a high dosage is considered essential for prolonged periods, patients should be closely observed for any signs that might indicate that a reduction in dosage or discontinuation of corticosteroid therapy is necessary. Chronic conditions are subject to periods of spontaneous remission. When such periods occur, corticosteroids should be gradually discontinued.

Routine investigations, such as urine analysis, two-hour post-prandial blood sugar, determination of blood pressure and body weight, and a chest X-ray should be carried out at regular intervals if therapy is prolonged. Periodic determinations of serum potassium are advisable if high dosages are being used. Upper gastrointestinal tract X-rays should be taken when treatment is prolonged, in patients with a history of ulcer, or when there is gastric distress. Corticosteroid therapy may cause hyperacidity or peptic ulcer. Antacids, and dietary measures should also be considered.

Patients may be transferred to Codelcortone from other glucocorticoids with proper adjustment in dosage.

Specific dosage recommendations:

In chronic, non-fatal diseases (e.g. rheumatoid arthritis, chronic bronchial asthma), it is recommended that therapy be initiated with a low dosage (5–10 mg a day) which is gradually increased to the smallest amount that gives the desired degree of symptomatic relief.

When adequate suppression of symptoms is achieved, dosage should be maintained at the minimum amount capable of providing sufficient relief without excessive hormonal effects. This amount may be as low as 5 mg a day.

In acute, non-fatal diseases (e.g. severe seasonal asthma, self-limited ocular and dermatological disorders), most patients initially require 20–30 mg a day. Some patients require more. Since these conditions are self-limited in their course, prolonged maintenance therapy is not necessary.

In chronic, potentially fatal diseases (e.g. disseminated lupus erythematosus, pemphigus, sarcoidosis, nephrotic syndrome), 30 mg a day will be sufficient for some patients, others may require considerably more.

As soon as adequate relief is obtained, dosage should be reduced gradually to the minimum amount that will produce the desired therapeutic effect. Five to 20 mg a day will be adequate for many patients during maintenance therapy.

In acute and life-threatening diseases (e.g. acute rheumatic fever, crisis of disseminated lupus erythematosus, severe allergic reactions), an initial dosage of 30 mg is usually necessary. This dosage may have to be increased in some patients to establish control. As soon as control is attained, dosage should be reduced gradually to the minimum amount that will maintain relief.

When extremely rapid onset of action is desired, one of the soluble adrenocortical hormone preparations, for

example. Decadron® Injection, may be administered intravenously for the first 2 or 3 doses.

In severe allergic reactions, adrenaline is the drug of first choice: Codelcortone Tablets are useful as concurrent or supplementary therapy.

In adrenocortical insufficiency and the adrenogenital syndrome, daily dosages within the range of 2.5–10 mg are usually sufficient.

In malignant diseases (e.g. lymphocytic leukaemia, Hodgkin's disease), 30 mg a day or more are usually necessary, and temporary symptomatic benefit is all that can be expected.

Contra-indications, warnings, etc

Contra-indications: Systemic fungal infections; hypersensitivity to Codelcortone.

Precautions: the lowest dosage that will control the condition under treatment should be used. Any reduction in dosage should be made gradually.

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, retention of salt and water, and increased excretion of potassium, but these effects are less likely to occur with synthetic derivatives, except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

When large doses are given, some authorities advise that corticosteroids be taken with meals, and antacids taken between meals.

In patients on corticosteroid therapy subjected to unusual stress, dosage should be increased before, during and after the stressful situation.

Drug-induced secondary adrenocortical insufficiency may result from too rapid withdrawal of corticosteroids and may be minimised by gradual dosage reduction, but may persist for months after discontinuation of therapy. In any stressful situation during that period, therefore, corticosteroid therapy should be reinstated. If the patient is receiving steroids already, the dosage may have to be increased. Salt and/or mineralocorticoid should be given concurrently, since mineralocorticoid secretion may be impaired.

Following prolonged therapy, stopping treatment may result in withdrawal symptoms including fever, myalgia, arthralgia, and malaise. This may occur in patients even without evidence of adrenal insufficiency.

Administration of live virus vaccines, including smallpox, is contra-indicated in individuals receiving immunosuppressive doses of corticosteroids. If inactivated viral or bacterial vaccines are administered to individuals receiving immunosuppressive doses of corticosteroids, the expected serum antibody response may not be obtained. However, immunisation procedures may be undertaken in patients who are receiving corticosteroids already, e.g. for Addison's disease.

Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinaemia.

The use of Codelcortone Tablets in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate antituberculous regime. If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive prophylactic chemotherapy.

Corticosteroids should be used with caution in: non-

specific ulcerative colitis, if there is a probability of impending perforation, abscess or other pyogenic infection; diverticulitis; fresh intestinal anastomoses; active or latent peptic ulcer; renal insufficiency; hypertension; osteoporosis; and myasthenia gravis. Signs of peritoneal irritation following gastro-intestinal perforation in patients receiving large doses of corticosteroids may be minimal or absent. Fat embolism has been reported as a possible complication of hypercorticism.

Corticosteroids should be used cautiously in patients with ocular herpes simplex, because of possible corneal ulceration.

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis.

Corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance and inability to localise infection in patients on corticosteroids. Moreover, corticosteroids may affect the nitroblue-tetrazolium test for bacterial infection and produce false negative results.

Corticosteroids may activate latent amoebiasis. Therefore, it is recommended that latent or active amoebiasis be ruled out before initiating corticosteroid therapy in any patient who has spent time in the tropics or any patient with unexplained diarrhoea.

Various psychic derangements may appear in patients on corticosteroids, ranging from euphoria, insomnia, mood swings, personality changes and severe depression, to frank psychotic manifestations. Existing emotional instability of psychotic tendencies may be aggravated by corticosteroids.

Prolonged use of corticosteroids may produce posterior subcapsular cataracts, and glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses.

Growth and development of infants and children who are on prolonged corticosteroid therapy should be carefully scrutinised.

Corticosteroids may increase or decrease motility and number of spermatozoa in some patients.

Because phenytoin, phenobarbitone, ephedrine, and rifampicin may enhance the metabolic clearance of corticosteroids, resulting in decreased blood levels and reduced physiological activity, the dosage may have to be adjusted.

The prothrombin time should be checked frequently in patients who are receiving corticosteroids and coumarin anticoagulants at the same time because of reports that corticosteroids have altered the response to these anticoagulants.

Studies have shown that the usual effect produced by adding corticosteroids is inhibition of response to coumarins, although there have been some conflicting reports of potentiation not substantiated by studies.

When corticosteroids are administered concomitantly with potassium-depleting diuretics, patients should be observed closely for development of hypokalaemia.

Use in pregnancy and the nursing mother: Since adequate human reproduction studies have not been done with corticosteroids use of these drugs in pregnancy or in women of childbearing potential requires that the anticipated benefits be weighed against possible hazards to the mother and foetus or child. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Corticosteroids appear in breast milk and could

suppress growth, interfere with endogenous corticosteroid production, or cause other unwanted effects. Mothers taking pharmacological doses of corticosteroids should be advised not to nurse.

Side-effects: *Fluid and electrolyte disturbances:* Sodium retention, fluid retention, congestive heart failure in susceptible patients, potassium loss, hypokalaemic alkalosis, hypertension.

Musculoskeletal effects: Muscle weakness, steroid myopathy, loss of muscle mass, osteoporosis, vertebral compression fractures, aseptic necrosis of femoral and humeral heads, pathological fracture of long bones, tendon rupture.

Gastro-intestinal: Peptic ulcer with possible perforation and haemorrhage, perforation of the small and large bowel particularly in patients with inflammatory bowel disease, pancreatitis, abdominal distension, ulcerative oesophagitis.

Dermatological: Impaired wound healing, thin fragile skin, petechiae and ecchymoses, erythema, increased sweating, suppressed reaction to skin tests.

Other cutaneous reactions such as allergic dermatitis, urticaria, angioneurotic oedema.

Neurological: Convulsions, vertigo, headache. Following withdrawal of therapy, increased intracranial pressure with papilloedema (pseudotumour cerebri) may occur.

Endocrine: Menstrual irregularities, development of Cushingoid state, suppression of growth in children, secondary adrenocortical and pituitary unresponsiveness (particularly in times of stress, as in trauma, surgery of illness), decreased carbohydrate tolerance, manifestation of latent diabetes mellitus, increased need for insulin or oral hypoglycaemic agents in diabetics.

Ophthalmic: Posterior subcapsular cataracts, increased intra-ocular pressure, glaucoma, exophthalmos.

Metabolic: Negative nitrogen balance due to protein catabolism.

Other: Hypersensitivity; thromboembolism; weight gain; increased appetite; nausea; malaise.

Treatment of overdosage: Anaphylactic and hypersensitivity reactions may be treated with adrenaline, positive-pressure artificial respiration and aminophylline. The patient should be kept warm and quiet.

Treatment is probably not indicated for reactions due to chronic poisoning unless the patient has a condition that would render him unusually susceptible to ill effects from corticosteroids. In this case, symptomatic treatment should be instituted as necessary.

Pharmaceutical precautions Keep container well closed; store in a cool place protected from light.

Legal category POM.

Package quantities Bottles of 500.

Further information Nil.

Product licence number 0025/5039.

CODELSOL* INJECTION

Presentation A clear, colourless solution containing, per millilitre, Prednisolone Sodium Phosphate BP equivalent to 16 mg prednisolone (approximately 20 mg prednisolone phosphate).

Uses Corticosteroid.

Systemic administration: Recommended for systemic administration by intravenous or intramuscular injection when oral therapy is not feasible in the following conditions.

Endocrine disorders: Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisone is the first choice; synthetic analogues may be used with mineralocorticoids where applicable, and in infancy mineralocorticoid supplementation is particularly important).

Acute adrenocortical insufficiency (hydrocortisone or cortisone is the first choice; mineralocorticoid supplementation may be necessary, particularly when synthetic analogues are used).

Pre-operatively, and during serious trauma or illness in patients with known adrenal insufficiency of doubtful adrenocortical reserve.

Congenital adrenal hyperplasia, non-suppurative thyroiditis, hypercalcaemia associated with cancer.

Rheumatic disorders: As adjunctive therapy for short-term administration (to support the patient during an acute episode or exacerbation in: post-traumatic osteoarthritis, synovitis of osteoarthritis, rheumatoid arthritis including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy), acute and subacute bursitis, epicondylitis, acute non-specific tenosynovitis, acute gouty arthritis, psoriatic arthritis, ankylosing spondylitis).

Collagen diseases: During an exacerbation or as maintenance therapy in selected cases of systemic lupus erythematosus, acute rheumatic carditis, and systemic dermatomyositis (polymyositis).

Dermatological diseases: Pemphigus, severe erythema multiforme (Stevens-Johnson syndrome), exfoliative dermatitis, bullous dermatitis herpetiformis, severe seborrhoeic dermatitis, severe psoriasis, mycosis fungoides.

Allergic states: Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment in bronchial asthma, contact dermatitis, atopic dermatitis, serum sickness, seasonal or perennial allergic rhinitis, drug hypersensitivity reactions, urticarial transfusion reactions, and acute non-infectious laryngeal oedema (adrenaline is the drug of first choice).

Ophthalmic diseases: Severe, acute and chronic allergic and inflammatory processes involving the eye, such as herpes zoster ophthalmicus, iritis, iridocyclitis, choroiditis, diffuse posterior uveitis, choroiditis, optic neuritis, sympathetic ophthalmia, anterior segment inflammation, allergic conjunctivitis, keratitis, allergic corneal marginal ulcers.

Gastro-intestinal diseases: To support the patient during a critical period of the disease in ulcerative colitis and regional enteritis (as systemic therapy).

Respiratory diseases: Symptomatic sarcoidosis, berylliosis, fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate anti-tuberculous chemotherapy, Löfller's syndrome not manageable by other means, aspiration pneumonia.

Haematological disorders: Acquired (auto-immune) haemolytic anaemia, idiopathic thrombocytopenic purpura in adults (intravenous only; intramuscular administration is contra-indicated), secondary thrombocytopenia in adults, erythroblastopenia (RBC anaemia), congenital (erythroid) hypoplastic anaemia.

Neoplastic diseases: For palliative management of leu-

kaemias and lymphomas in adults, acute leukaemia of childhood.

Oedematous states: To induce diuresis or remission of proteinuria in the nephrotic syndrome, without uraemia of the idiopathic type or that due to lupus erythematosus.

Miscellaneous: Tuberculous meningitis with subarachnoid block or impending block when used concurrently with appropriate antituberculous chemotherapy, trichinosis with neurological or myocardial involvement.

Local administration: Codelsol is suitable for intra-articular or soft-tissue injection as adjunctive therapy for short-term administration (to support the patient over an acute episode or exacerbation) in: synovitis of osteoarthritis, rheumatoid arthritis, acute and subacute bursitis, acute gouty arthritis, epicondylitis, acute non-specific tenosynovitis, post-traumatic osteoarthritis.

Codelsol may be injected intralesionally for keloids; localised hypertrophic, infiltrated, inflammatory lesions of lichen planus, psoriatic plaques, granuloma annulare, and lichen simplex chronicus (neurodermatitis); discoid lupus erythematosus; necrobiosis lipoidica diabetorum; alopecia areata. Codelsol may also be useful in cystic tumours of an aponeurosis or tendon (ganglia).

Dosage and administration *Dosage requirements are variable and must be determined individually on the basis of the disease and the response of the patient.*

Intravenous and intramuscular injection. Codelsol Injection can be given directly from the vial, or added to sodium chloride injection or dextrose injection and given by intravenous drip.

When Codelsol Injection is added to an infusion solution, the mixture must be used within 24 hours, since infusion solutions do not contain preservatives. The usual aseptic techniques governing injections should be observed.

The usual initial daily dosage of Codelsol is 4–60 mg. The daily parenteral dose of Codelsol is usually the same as the daily oral dose of prednisolone, and the dosage interval is every four to eight hours.

Maintain or adjust the initial dosage until the patient's response is satisfactory. If there is a lack of satisfactory clinical response, Codelsol should be discontinued. Maintenance dosage should be determined by decreasing the initial dosage in small amounts at appropriate intervals until the lowest effective dosage is reached. Constant monitoring is needed. If the drug is to be stopped after more than a few days, it should be withdrawn gradually rather than stopped abruptly.

Intra-articular, intralesional and soft-tissue injection: In general, intra-articular, intralesional, and soft-tissue injections are employed when only one or two joints or areas are affected.

Frequency of injection ranges from once every three to five days to once every two to three weeks, depending on the response. Frequent administration may result in tissue damage. Codelsol is particularly recommended for use with one of the less soluble, longer-acting parenteral steroids.

Contra-indications, warnings, etc

Contra-indications: Systemic fungal infection; hypersensitivity to any component.

Precautions: Corticosteroids may exacerbate systemic fungal infections and should not be used unless they are needed to control drug reactions due to amphotericin B.

Cases have been reported in which concomitant use

Some of the usual single doses for intrasynovial and soft tissue injection:

Site of injection	Volume of Codelsol injection (ml)	Amount of prednisolone (mg)
Large joints (e.g. knee)	0.5–1	8–16
Small joints (e.g. interphalangeal, temporomandibular)	0.2–0.25	3.2–4
Bursae	0.5–0.75	8–12
Tendon sheaths*	0.1–0.25	1.6–4
Soft-tissue infiltration	0.5–1.5	8–24
Ganglia	0.25–0.5	4–8

* Injection should be made into the tendon sheath, and not directly into the tendon.

of amphotericin B and hydrocortisone was followed by cardiac enlargement and congestive heart failure.

The lowest possible dose of corticosteroid should be used, and reduction to this dose should be gradual.

Corticosteroids should be used cautiously in patients with ocular herpes simplex, because of possible corneal perforation.

In patients on corticosteroid therapy subjected to unusual stress, dosage should be increased before, during and after the stressful situation.

Drug-induced secondary adrenocortical insufficiency may be minimised by gradual dosage reduction, but may persist for months after discontinuation of therapy. In any stressful situation during that period, therefore, corticosteroid therapy should be reinstated.

If the patient is receiving steroids already, the dosage may have to be increased. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

Corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance and inability to localise infection when corticosteroids are used.

Corticosteroids may also affect the nitroblue-tetrazolium test for bacterial infection producing false negative results.

Corticosteroids may activate latent amoebiasis. Therefore, it is recommended that latent or active amoebiasis be ruled out before initiating corticosteroid therapy in any patient who has spent time in the tropics, or any patient with unexplained diarrhoea.

Prolonged use of corticosteroids may produce posterior subcapsular cataracts, and glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses.

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, retention of salt and water, and increased excretion of potassium, but these effects are less likely to occur with synthetic derivatives, except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

Administration of live virus vaccines, including smallpox, is contra-indicated in individuals receiving immunosuppressive doses of corticosteroids. If inactivated viral or bacterial vaccines are administered to individuals

receiving immunosuppressive doses of corticosteroids, the expected serum antibody response may not be obtained. However, patients may be immunised if they are receiving corticosteroids as replacement therapy, e.g. for Addison's disease.

The use of Codelsol Injection in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate antituberculosis regime. If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation may occur. During prolonged corticosteroid therapy, these patients should receive prophylactic chemotherapy.

Because anaphylactoid reactions have occurred, rarely, in patients receiving parenteral corticosteroid therapy, appropriate precautions should be taken prior to administration, especially when the patient has a history of allergy to any drug.

Withdrawal of corticosteroids after prolonged therapy may result in symptoms of corticosteroid withdrawal, including fever, myalgia, arthralgia, and malaise. These reactions may occur in patients without evidence of adrenal insufficiency.

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis.

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes and severe depression, to frank psychotic manifestations. Also, existing instability or psychotic tendencies may be aggravated by corticosteroids.

Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinaemia.

Corticosteroids should be used with caution in: non-specific ulcerative colitis, if there is a probability of impending perforation, abscess or other pyogenic infection; diverticulitis; fresh intestinal anastomosis; active or latent peptic ulcer; renal insufficiency; hypertension; osteoporosis; ocular herpes simplex for fear of corneal perforation; and myasthenia gravis. Signs of peritoneal irritation following gastro-intestinal perforation in patients receiving large doses of corticosteroids may be minimal or absent. Fat embolism has been reported as a possible complication of hypercortisone.

When large doses are given, some authorities advise that antacids be administered between meals.

Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.

Corticosteroids may increase or decrease motility and number of spermatozoa in some patients.

Because phenytoin, phenobarbitone, ephedrine, and rifampicin may enhance the metabolic clearance of corticosteroids, resulting in decreased blood levels and reduced physiological activity, the dosage of Codelsol may have to be adjusted.

The prothrombin time should be checked frequently in patients who are receiving corticosteroids and coumarin anticoagulants concurrently, because of reports that corticosteroids have altered the anticoagulant response. Studies have shown that the usual effect produced by adding corticosteroids is inhibition of response to coumarins, although some conflicting reports of potentiation are not substantiated.

When corticosteroids are administered concomitantly with potassium-depleting diuretics, patients should be observed closely for development of hypokalaemia.

Intra-articular injection of a corticosteroid may produce systemic as well as local effects.

Appropriate examination of any joint fluid present is necessary to exclude a septic process.

A marked increase in pain accompanied by local swelling, further restriction of joint motion, fever, and malaise is suggestive of septic arthritis. If this complication occurs and the diagnosis of sepsis is confirmed, appropriate antimicrobial therapy should be instituted.

Injection of a steroid into an infected site is to be avoided.

Corticosteroids should not be injected into unstable joints. Patients should be impressed strongly with the importance of not overusing joints in which symptomatic benefit has been obtained, while the inflammatory process remains active.

Frequent intra-articular injection may result in damage to joint tissues.

The slower rate of absorption by intramuscular administration should be recognised.

Use in pregnancy and the nursing mother: Since adequate human reproduction studies have not been done with corticosteroids, use of these drugs in pregnancy or in women of childbearing potential requires that the anticipated benefits be weighed against the possible hazards to the mother and embryo or foetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Corticosteroids appear in breast milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other unwanted effects. Mothers taking pharmacological doses of corticosteroids should be advised not to nurse.

Side-effects: Fluid and electrolyte disturbances: Sodium retention, fluid retention, congestive heart failure in susceptible patients, potassium loss, hypokalaemic alkalosis, hypertension.

Musculoskeletal: Muscle weakness, steroid myopathy, loss of muscle mass, osteoporosis, vertebral compression fractures, aseptic necrosis of femoral and humeral heads, pathological fracture of long bones, tendon rupture.

Gastro-intestinal: Peptic ulcer and possible subsequent perforation and haemorrhage, perforation of the small and large bowel particularly in patients with inflammatory bowel disease, pancreatitis, abdominal distension, ulcerative oesophagitis.

Dermatological: Impaired wound healing, thin fragile skin, petechiae and ecchymoses, erythema, increased sweating, suppression of skin tests, burning or tingling especially in the perineal area (after intravenous injection), other cutaneous reactions such as allergic dermatitis, urticaria, angioneurotic oedema.

Neurological: Convulsions, increased intracranial pressure with papilloedema (pseudotumour cerebri) usually after treatment, vertigo, headache.

Endocrine: Menstrual irregularities, development of Cushingoid state, suppression of growth in children; secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery or illness; decreased carbohydrate tolerance, manifestations of latent diabetes mellitus, increased requirements for insulin or oral hypoglycaemic agents in diabetics.

Ophthalmic: Posterior subcapsular cataracts, increased intra-ocular pressure, glaucoma, exophthalmos.

Metabolic: Negative nitrogen balance due to protein catabolism.

Other: Anaphylactoid or hypersensitivity reactions;

thrombo-embolism; weight gain; increased appetite; nausea; malaise.

Additional side-effects related to parenteral corticosteroid therapy only: Rare instances of blindness associated with intrascleral therapy around the face and head, hyperpigmentation or hypopigmentation, subcutaneous and cutaneous atrophy, sterile abscess, post-injection flare (following intra-articular use), Charcot-like arthropathy.

Treatment of overdosage: Codeisol Injection must be discontinued immediately. Anaphylactic and hypersensitivity reactions may be treated with adrenaline, positive-pressure artificial respiration, and aminophylline. The patient should be kept warm and quiet.

Pharmaceutical precautions Codeisol Injection is sensitive to heat and should not be autoclaved. Keep in a cool place, protected from light and freezing. Only sodium chloride injection or dextrose injection should be used as diluent. Any infusion mixture must be used within 24 hours.

Legal category POM.

Package quantities Vials of 2 ml.

Further information Nil.

Product licence number 0025/5041.

COGENTIN®

Presentation White, quarter-scored tablets, marked 'MSD 60', containing 2 mg Benztropine Mesylate BP.

An injection containing in each millilitre 1 mg Benztropine Mesylate BP, as a colourless solution.

Uses Anti-parkinsonian agent with powerful anticholinergic effects.

For symptomatic treatment of all types of 'classical' (arteriosclerotic, postencephalitic, idiopathic) parkinsonism, and of extrapyramidal reactions induced by phenothiazines or reserpine.

Cogentin is particularly effective in the relief of rigidity and tremor. Among other symptoms which it can ameliorate are; sialorrhoea, drooling, mask-like facies, oculogyric crises, speech and writing difficulties, gait disturbances, dysphagia, and pain and insomnia due to muscle spasm and cramps.

Acute dystonic reactions such as torticollis, and oculogyric crises usually respond rapidly to Cogentin Injection, prior to oral therapy.

Dosage and administration As Cogentin is cumulative in action, treatment should begin with a low dosage, which can be increased by amounts of 0.5 mg at intervals of five to six days, to the smallest dosage necessary for optimal relief without excessive side-effects. Maximum dosage, 6 mg a day.

Cogentin Injection may be used intramuscularly or intravenously, in emergencies or for patients unable to swallow tablets. (As there is no significant difference in time of onset of effect between intramuscular and intravenous administration, the intravenous route is not usually necessary.)

In emergencies, 1–2 ml (1–2 mg) of Cogentin Injection will normally provide quick relief. If signs of parkinsonism begin to return, the dose can be repeated.

'Classical' parkinsonism: Usual dosage: 1–2 mg a day, with a range of 0.5–6 mg a day, orally or parenterally.

Dosage must be adjusted on an individual basis, taking into consideration the age and weight of the patient, and the type of parkinsonism. Older patients, thin patients and those with arteriosclerotic parkinsonism usually cannot tolerate large dosages. Most patients with post-encephalitic parkinsonism need and indeed tolerate fairly large dosages. Patients with a poor mental outlook may respond poorly. In arteriosclerotic and idiopathic parkinsonism, therapy may be initiated with a single daily dose of 0.5–1 mg at bedtime. This dosage will be adequate in some patients, whereas 4–6 mg a day may be required by others. In post-encephalitic parkinsonism, therapy may be initiated in most patients with 2 mg a day in one or more doses. In highly sensitive individuals, therapy may be initiated with 0.5 mg at bedtime, and increased as necessary.

Some patients obtain greatest relief by taking the entire dose at bedtime; others react more favourably to divided dosage, two to four times a day. One dose a day frequently is sufficient; divided doses may be unnecessary or even undesirable.

See also 'Further information'.

Drug-induced parkinsonism: Usual dosage range: 1–4 mg once or twice a day.

Acute dystonic reactions: 1–2 ml (1–2 mg) by intravenous injection followed usually by 1–2 mg orally twice a day.

Extrapyramidal reactions appearing soon after starting phenothiazine or reserpine therapy are likely to be temporary, and are usually controlled in one or two days by 1–2 mg of Cogentin orally two or three times a day. Cogentin should be withdrawn after one or two weeks to determine if it is still needed. It can be reinstated if necessary.

Certain extrapyramidal reactions which develop slowly (e.g. tardive dyskinesia) do not usually respond to Cogentin.

Contra-indications, warnings, etc

Contra-indications: Because of its atropine-like side-effects, Cogentin is contra-indicated in children under 3 years old and should be used with caution in older children.

Precautions: The safety of Cogentin for use during pregnancy has not been established.

Cogentin may impair the mental alertness and physical ability required for the performance of such hazardous tasks as driving a car or operating machinery.

Continued supervision of patients is recommended as Cogentin has a cumulative action. Patients with a tendency towards tachycardia and those with prostatic hypertrophy, should be closely observed.

Patients with mental disorders should be carefully supervised when Cogentin is used to control drug-induced extrapyramidal reactions, especially when therapy is started or the dosage of Cogentin is increased. Intensification of mental symptoms may occasionally occur. Cogentin should be temporarily withdrawn if the reactions are severe. (In such cases, increased dosage of the anti-parkinsonian agent could precipitate a toxic psychosis.)

When Cogentin is given concomitantly with phenothiazines or other drugs with anticholinergic activity, patients should be advised to report gastro-intestinal complaints promptly. Paralytic ileus, sometimes fatal, has occurred in patients taking anticholinergic-type anti-parkinsonian drugs, including Cogentin, in combination with phenothiazines and/or tricyclic antidepressants.

Tardive dyskinesia may appear in some patients on long-term therapy with phenothiazines or related agents, or after discontinuation of such therapy. Anti-parkinsonian agents do not usually alleviate symptoms of tardive dyskinesia, and in some cases may aggravate or unmask them. Cogentin is not recommended in tardive dyskinesia.

Cogentin has anticholinergic effects, and glaucoma is a possibility. Although Cogentin does not appear to have any adverse effect on simple glaucoma, its use is probably not advisable in narrow-angle glaucoma. It may cause anhidrosis; this should be borne in mind, particularly in hot weather, especially when given concomitantly with other atropine-like drugs to the chronically ill, alcoholics, or patients with a central nervous system disease. Cogentin should be used cautiously in patients with or prone to abnormalities of sweating. If there is evidence of anhidrosis, the possibility of hyperthermia should be considered. Dosage should be decreased as necessary to maintain body heat equilibrium by the action of perspiration. Severe anhidrosis and fatal hyperthermia have occurred.

Side-effects: Dry mouth, blurred vision, nervousness, nausea and (infrequently) vomiting; these may be controlled by dosage adjustment or temporary withdrawal. Constipation, numbness of the fingers, listlessness, depression, dysuria (rarely a problem). Mental confusion, excitement and visual hallucinations have been reported with high dosage or in particularly susceptible patients. Allergic reactions such as skin rash may require dosage reduction or withdrawal.

Treatment of overdose: Physostigmine salicylate (1–2 mg, subcutaneously or intravenously) is reported to reverse symptoms of anticholinergic intoxication. A second injection may be given after two hours if needed. Otherwise, treatment is symptomatic and supportive.

Emesis should be induced or gastric lavage performed. A short-acting barbiturate may be used for CNS excitement, but with caution to avoid subsequent depression. Supportive care for CNS depression may be required (such convulsant stimulants as picrotoxin, leptazol or bemegride should be avoided). In severe respiratory depression, artificial respiration may be required. Also needed may be a local miotic for mydriasis and cycloplegia, ice bags or other cold applications and alcohol sponges for hyperpyrexia, a vasopressor and fluids for circulatory collapse, and a darkened room for photophobia.

Pharmaceutical precautions *Tablets:* Keep container tightly closed; store in a cool place, protected from light.

Injection: Store in a cool place, protected from light and freezing.

Legal category POM.

Package quantities *Tablets:* Bottles of 100 and 500. *Injection:* Ampoules of 2 ml.

Further information Cogentin may be used in combination with other agents employed in the treatment of parkinsonism; the dosage of such agents may be reduced or they may be gradually discontinued. Many patients obtain greatest relief with a combination of Cogentin and other agents.

Cogentin may be used concomitantly with levodopa, in which case the usual dosage of each may need to be reduced. However, if Cogentin is continued when

Sinemet* (carbidopa and levodopa, MSD) is introduced the dosage of Cogentin may need to be adjusted.

Product licence numbers

Tablets 0025/5023
Injection 0025/5024

CONCORDIN*

Presentation Concordin-5, salmon-red, film-coated tablets, marked 'MSD 26', containing 5 mg Protriptyline Hydrochloride BP.

Concordin-10, white, film-coated tablets, marked 'MSD 47', containing 10 mg Protriptyline Hydrochloride BP.

Uses Antidepressant (member of the 'tricyclic' group).

It may be used successfully in depression that is a manifestation of psychosis or neurosis, whether endogenous or reactive. Endogenous depression is more likely to respond. Concordin is especially recommended in apathetic, withdrawn patients, because it promptly relieves anergia, and it lacks sedative activity.

Concordin has been reported to be able to improve markedly hypoactivity and accessibility in anergic schizophrenic patients. As with all potent antidepressants, however, the schizophrenic symptoms may be activated, requiring concurrent administration of a phenothiazine tranquilliser (see also 'Precautions').

The following 'target' symptoms of depression may be expected to respond well to Concordin: depressed mood; excessive crying; apathy; withdrawal; psychomotor retardation; loss of interest; fatigue; lassitude; feelings of guilt; anorexia; headache; functional somatic complaints (e.g. gastro-intestinal symptoms).

Dosage and administration Dosage should be adjusted for each patient, bearing in mind the cyclic nature and variable severity of depression, the danger of relapse, and the possibility of spontaneous remission.

Dosage range, 15–60 mg. Usual starting dosage, 30–40 mg a day, divided into 3 or 4 doses. Any increase in dosage should be made gradually, and added to the morning dose first. If insomnia is present, the last dose should be given no later than mid-afternoon. When a satisfactory response is noted, the dosage should be reduced to the smallest amount necessary to maintain relief. Maintenance therapy should be continued for at least three months after satisfactory improvement. If relapse occurs, Concordin may be reinstated.

If the dosage required for adequate antidepressant effect produces overstimulation, concurrent use of a tranquilliser will provide effective control. Overstimulation is unlikely if the dosage of Concordin is kept below 20 mg a day.

Elderly and adolescent patients: Initially 5 mg three times a day. These patients may not tolerate higher doses as well as other patients. If the elderly receive more than 20 mg a day, they should be observed for effects on the cardiovascular system.

Children: As a paediatric dosage has not been established, Concordin is not recommended for children under 12 years old.

Contra-indications, warnings, etc

Contra-indications: Concurrent use with a monoamine oxidase inhibitor. Hyperpyretic crises, severe convulsions, and deaths have occurred when tricyclic antidepressants and MAOIs have been given simultaneously (see also 'Precautions'); the acute recovery phase after

myocardial infarction; known sensitivity to protriptyline. Heart block or other cardiac arrhythmias, mania, marked agitation, severe liver disease, during breast feeding. For 'Use in pregnancy', see 'Precautions'.

Precautions: A minimum of 14 days should elapse between discontinuing a monoamine oxidase inhibitor and introducing Concordin, which should then be started cautiously, with gradual increases in dosage until optimum response is achieved.

Protriptyline may block the antihypertensive effect of guanethidine or similar compounds. Review all antihypertensive therapy during treatment. It should be used with caution in patients with a history of epilepsy, impaired liver function, a tendency to urinary retention, prostatic hypertrophy, or increased intra-ocular pressure.

Concordin should be used cautiously in elderly patients and patients with cardiovascular disorders. Such patients should be closely observed because of the tendency of protriptyline to produce tachycardia, hypotension, arrhythmias, and prolongation of the conduction time. The elderly are particularly liable to experience agitation and confusion. Myocardial infarction and stroke have occurred with drugs of this class. On rare occasions, hyperthyroid patients or those receiving thyroid medication may develop arrhythmias when protriptyline is given.

Concordin may impair abilities needed for performing hazardous tasks, such as driving a vehicle or operating machinery.

Psychotic symptoms may be aggravated when Concordin is used in schizophrenic patients. Manic depressive patients may shift towards the manic phase. Paranoid delusions, with or without hostility, may be exaggerated. In any of these circumstances, it may be advisable to reduce the dosage, or to use a major tranquilliser concurrently. An antidepressant with a sedative component, such as amitriptyline hydrochloride may be given before bedtime to help relieve insomnia, and control lesser degrees of anxiety and agitation. There has been no evidence of potentiation when Concordin has been replaced immediately by Tryptizol (see separate entry under Thomas Morson Pharmaceuticals), or vice versa.

Concordin may aggravate anxiety or agitation in over-active or agitated patients.

Protriptyline should not be given with sympathomimetic agents such as ephedrine, isoprenaline, nor-adrenaline, phenylephrine, and phenylpropanolamine. Protriptyline may enhance response to alcohol, barbiturates and other CNS depressants.

The possibility of suicide in depressed patients remains during treatment until significant remission has occurred: suicidal patients should not have access to large quantities of Concordin Tablets.

Concurrent administration of Concordin may increase the hazards of electroconvulsive therapy. Such combined treatment should be limited to those for whom it is essential.

Anaesthetics given during tricyclic antidepressant therapy may increase the risk of arrhythmias and hypotension. If surgery is necessary, the anaesthetist should be informed that the patient is receiving protriptyline.

The natural course of depression often is of many months' duration. It is appropriate therefore to continue maintenance therapy for three months or longer to lessen the possibility of relapse.

Use during pregnancy: Avoid during pregnancy, espe-

cially during the first and last trimesters, unless there are compelling reasons.

There is no evidence as to drug safety in human pregnancy, nor is there evidence from animal work that it is free from hazard.

Warnings and adverse effects: Some of the adverse reactions below have not been specifically reported for Concordin, but are included because of the similar pharmacological properties of the tricyclic group of antidepressants. Concordin is more likely to aggravate anxiety and agitation and to produce such cardiovascular reactions as tachycardia and hypotension.

As improvement may not occur during the first two to four weeks of treatment, patients should be closely monitored during this period.

Cardiovascular: Hypotension, hypertension, tachycardia, palpitation, myocardial infarction, arrhythmias, heart block, stroke.

Psychiatric: Confusional states (especially in the elderly) with hallucinations, disorientation, delusions, anxiety, restlessness, agitation; insomnia, panic and nightmares; hypomania; exacerbation of psychosis.

Neurological: Numbness, tingling, and paraesthesiae of extremities; incoordination, ataxia, tremors, peripheral neuropathy; extrapyramidal symptoms; seizures; alteration in EEG patterns, tinnitus.

Anticholinergic: Dry mouth and rarely associated sublingual adenitis; blurred vision, disturbance of accommodation, mydriasis; constipation, paralytic ileus; urinary retention, delayed micturition, dilatation of the urinary tract.

Allergic: Skin rash, petechiae, urticaria, itching, oedema (general, or of face and tongue), drug fever. Some rashes have been associated with photosensitisation. In view of this, patients should avoid excessive exposure to sunlight, including sunbathing.

Haematological: Bone-marrow depression; agranulocytosis; leucopenia; eosinophilia; purpura; thrombocytopenia.

Gastro-intestinal: Nausea and vomiting, anorexia, epigastric distress, diarrhoea, peculiar taste, stomatitis, abdominal cramps, black tongue.

Endocrine: Gynaecomastia in the male; breast enlargement and galactorrhoea in the female; increased or decreased libido, impotence; testicular swelling; elevation or depression of blood sugar levels.

Other: Jaundice (simulating obstructive); altered liver function; weight gain or loss; perspiration; flushing; urinary frequency, nocturia; drowsiness, dizziness, weakness and fatigue; headache; parotid swelling; alopecia.

Withdrawal symptoms: Though not indicative of addiction, abrupt cessation of treatment after prolonged therapy may produce nausea, insomnia, irritability, excessive perspiration, headache and malaise.

Withdrawal symptoms in neonates whose mothers received tricyclic antidepressants during the third trimester have also been reported.

Treatment of overdose: Symptomatic and supportive; there is no specific antidote.

The stomach should be emptied as quickly as possible by emesis or gastric lavage. If the patient is stuporous but responds to some stimuli, only close observation and nursing care for a day or two may be needed. If the patient is comatose, supportive measures will be re-

quired. An open airway and an adequate fluid intake should be maintained, and body temperature regulated. Cardiac arrhythmias may be treated with neostigmine, pyridostigmine or propranolol. Close monitoring of cardiac function is advisable for not less than five days. Intravenous, physostigmine salicylate, 1 to 3 mg, has been reported to reverse the symptoms of amitriptyline poisoning in man. Animal studies have shown that physostigmine also reverses certain toxic effects of protriptyline. Because physostigmine is rapidly metabolised, the dosage should be repeated as required, particularly if life threatening signs such as arrhythmias, convulsions and deep coma recur or persist after the initial dose of physostigmine. If convulsions occur, they should be treated with anticonvulsants. Barbiturates should not be used. CNS depression may be treated with non-convulsant doses of CNS stimulants. Cardiac monitoring may be desirable, and use of digitalis should be considered if serious cardiovascular abnormalities occur. Standard measures may be used to manage shock and metabolic acidosis. Dialysis is not of value.

Treatment should be continued for at least 48 hours in patients who do not respond earlier. There have been instances where patients have been in coma for several days and have eventually recovered. Deaths by deliberate or accidental overdose have occurred with this class of medicament. Since overdose is often deliberate, patients may attempt suicide by other means during the recovery phase.

Pharmaceutical precautions Keep container well closed; store in a cool place, protected from light.

Legal category POM.

Package quantities 5 mg: Bottles of 100 and 500.

10 mg: Bottles of 100 and 500.

Further information Concoridin is a member of the tricyclic group of antidepressants. It is not a monoamine oxidase inhibitor, and dietary restrictions are not necessary. It has not produced addiction or habituation.

Concoridin has a rapid onset of effect, which can be of particular importance where there is a risk of suicide. It is advisable, however, to administer a tranquilliser and to ensure preventative supervision when starting Concoridin in suicidal patients since they usually have a high level of anxiety, and especially because Concoridin may relieve the anergia before there is complete recovery from the depressed state.

When Concoridin has to be used in conjunction with ECT, the total number of shock treatments required may be reduced.

Product licence numbers

5 mg 0025/5004

10 mg 0025/5005

CORTISONE ACETATE (MSD)

Presentation White tablets, marked 'MSD 126', containing 5 mg Cortisone Acetate BP.

White, half-scored tablets, marked 'MSD 219', containing 25 mg Cortisone Acetate BP.

Uses Corticosteroid.

Allergic states: Control of severe or incapacitating allergic conditions not responsive to adequate trials of conventional treatment: seasonal or perennial allergic rhinitis, bronchial asthma, contact dermatitis, atopic

dermatitis, serum sickness, drug hypersensitivity reactions.

Rheumatic disorders: As adjunctive therapy for short-term administration during an acute episode or exacerbation of: psoriatic arthritis, rheumatoid arthritis including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy), ankylosing spondylitis, acute and subacute bursitis, acute non-specific tenosynovitis, acute gouty arthritis, post-traumatic osteoarthritis, synovitis of osteoarthritis, epicondylitis.

Dermatological diseases: Pemphigus, bullous dermatitis herpetiformis, severe erythema multiforme (Stevens-Johnson syndrome), exfoliative dermatitis, mycosis fungoides, severe psoriasis, severe seborrhoeic dermatitis.

Ophthalmic diseases: Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as: allergic conjunctivitis, keratitis, allergic corneal marginal ulcers, herpes zoster ophthalmicus, iritis and iridocyclitis, chorioretinitis, anterior segment inflammation, diffuse posterior uveitis and choroiditis, optic neuritis, sympathetic ophthalmia.

Endocrine disorders: Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisone is the first choice; synthetic analogues may be used in conjunction with mineralocorticoids where applicable; in infancy mineralocorticoid supplementation is of particular importance), congenital adrenal hyperplasia, non-suppurative thyroiditis, hypercalcaemia associated with cancer.

Respiratory diseases: Symptomatic sarcoidosis, Löf- fler's syndrome not manageable by other means, berylliosis, fulminating or disseminated pulmonary tuberculosis when concurrently accompanied by appropriate antituberculous chemotherapy, aspiration pneumonitis.

Haematological disorders: Idiopathic thrombocytopenic purpura in adults, secondary thrombocytopenia in adults, acquired (auto-immune) haemolytic anaemia, erythroblastopenia (RBC anaemia), congenital (erythroid) hypoplastic anaemia.

Neoplastic diseases: For palliative management of: leukaemias and lymphomas in adults, acute leukaemia of childhood.

Oedematous states: To induce a diuresis or remission of proteinuria in the nephrotic syndrome without uraemia, of the idiopathic type or that due to lupus erythematosus.

Gastro-intestinal diseases: During a critical period of the disease in: ulcerative colitis, regional enteritis.

Miscellaneous: Tuberculous meningitis with subarachnoid block or impending block when concurrently accompanied by appropriate antituberculous chemotherapy, trichinosis with neurological or myocardial involvement. During an exacerbation or as maintenance therapy in selected cases of: systemic lupus erythematosus; acute rheumatic carditis; systemic dermatomyositis herpetiformis (polymyositis).

Dosage and administration *General considerations:* Therapy is governed by the following principles:

1. Dosage should be adjusted according to the severity, prognosis and expected duration of the disease, and the response of the individual patient. For infants and children, the recommended dosages will usually have to be reduced, but dosage should be governed by the severity of the condition rather than by age or body weight.

2. Corticosteroid therapy is an adjunct to conventional therapy and does not replace it. Appropriate conventional therapy should be instituted as indicated.

3. If therapy is continued for more than a few days, any decrease in dosage must be *gradual*.

4. Continued supervision of the patient after cessation of corticosteroid therapy is essential, since there may be a sudden reappearance of severe manifestations of the disease for which the patient was being treated.

In acute conditions where prompt relief is urgent, high dosages are permissible and may be mandatory for a short time.

In chronic conditions requiring long-term therapy, the lowest dosage which provides adequate (but not necessarily complete) relief should be used. If a high dosage is considered essential for prolonged periods, patients must be closely observed for any signs that might indicate that a reduction in dosage or discontinuation of corticosteroid therapy is necessary. Chronic conditions are subject to periods of spontaneous remission. When such periods occur, corticosteroids should be gradually discontinued.

Routine investigations, such as urine analysis, two-hour post-prandial blood sugar, determination of blood pressure and body weight, and a chest X-ray should be carried out at regular intervals if therapy is prolonged. Periodic determinations of serum potassium are advisable if high dosages are being used. Upper gastrointestinal tract X-rays should be taken when treatment is prolonged, in patients with a history of ulcer, or when there is gastric distress.

The daily dosage should be divided into four doses.

Specific dosage recommendations: In chronic, usually non-fatal diseases, including endocrine and chronic rheumatic disorders, oedematous states, respiratory and gastro-intestinal diseases, some dermatological diseases and haematological disorders, therapy should be initiated with a low dosage (25 to 50 mg a day) which is gradually increased to the smallest amount that gives the desired degree of symptomatic relief.

When symptoms have been suppressed adequately, dosage should be maintained at the minimum amount capable of providing sufficient relief without excessive hormonal effects.

In chronic adrenocortical insufficiency, the usual daily dosage is 10–25 mg, though more is occasionally required, with 4–6 g of sodium chloride or 1–3 mg of desoxycorticosterone acetate. When immediate support is mandatory, one of the soluble adrenocortical steroid preparations (i.e. Decadron[®] Injection), which may be effective within minutes after parenteral administration, can be life-saving.

In congenital adrenal hyperplasia, the usual daily dosage is 15–50 mg.

In acute, non-fatal diseases, including allergic states, ophthalmic diseases, acute and subacute rheumatic disorders, dosage ranges between 75 and 150 mg a day; however, higher doses are necessary in some patients. Since the course of these conditions is self-limited, prolonged maintenance therapy is not usually necessary.

In chronic, potentially fatal diseases such as systemic lupus erythematosus, pemphigus, symptomatic sarcoidosis, the recommended initial dosage is 75–150 mg a day; higher doses are necessary in some patients.

As soon as adequate relief is obtained, the dosage should be reduced gradually to the minimum amount that will produce the desired therapeutic effect.

When the disease is acute and life-threatening (e.g. acute rheumatic carditis, crisis of systemic lupus erythematosus, severe allergic reactions, pemphigus, neoplastic diseases), the initial dosage is between 125 and 300 mg a day, administered in at least 4 divided doses; this dosage may have to be increased in some patients to establish control. As soon as control is attained, the dosage should be reduced gradually to the minimum amount that will maintain relief.

When an extremely rapid onset of action is desired, one of the soluble adrenocortical steroid preparations (Decadron Injection) may be administered intravenously for the first 2 or 3 doses.

In severe allergic reactions adrenaline is the drug of first choice. Cortisone Acetate, MSD Tablets are useful either concurrently or as supplementary therapy.

Contra-indications, warnings, etc

Contra-indications: Systemic fungal infections. Hypersensitivity to the drug.

Precautions: The lowest possible dosage of corticosteroid should be used to control the condition under treatment, and when reduction in dosage is possible, the reduction should be gradual.

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. These effects are less likely to occur with the synthetic derivatives except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

When large doses are given, some authorities advise that corticosteroids be taken with meals and antacids taken between meals to help to prevent peptic ulcer.

In patients on corticosteroid therapy subjected to unusual stress, increased dosage of rapidly acting corticosteroids before, during and after the stressful situation is indicated.

Drug-induced secondary adrenocortical insufficiency may result from too rapid withdrawal of corticosteroids and may be minimised by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, corticosteroid therapy should be reinstituted. If the patient is receiving steroids already, the dosage may have to be increased. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

Stopping corticosteroids after prolonged therapy may cause withdrawal symptoms including fever, myalgia, arthralgia, and malaise. This may occur in patients even without evidence of adrenal insufficiency.

Patients should not be vaccinated against smallpox while on corticosteroid therapy. Other immunisation procedures should not be undertaken in patients who are receiving corticosteroids, especially on high dosage, because of possible hazards of neurological complications and a lack of antibody response. However, immunisation procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e.g. for Addison's disease.

Acetylsalicylic acid should be used cautiously in conjunction with corticosteroids in hypoprothrombinaemia.

The use of Cortisone Acetate, MSD Tablets in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the

corticosteroid is used for the management of the disease in conjunction with an appropriate antituberculous regimen. If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive prophylactic chemotherapy.

Steroids should be used with caution in: non-specific ulcerative colitis if there is a probability of impending perforation, abscess or other pyogenic infection; diverticulitis; fresh intestinal anastomoses; active or latent peptic ulcer; renal insufficiency; hypertension; osteoporosis; and myasthenia gravis. Fat embolism has been reported as a possible complication of hypercortisolemia.

Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.

There is an enhanced effect of corticosteroids on patients with hypothyroidism and in those with cirrhosis.

Corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance and inability to localise infection when corticosteroids are used. Moreover, corticosteroids may affect the nitroblue-tetrazolium test for bacterial infection and produce false negative results.

Corticosteroids may activate latent amoebiasis. Therefore it is recommended that latent or active amoebiasis be ruled out before initiating corticosteroid therapy in any patient who has spent time in the tropics or any patient with unexplained diarrhoea.

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes and severe depression, to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Prolonged use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses.

Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.

Steroids may increase or decrease motility and number of spermatozoa in some patients.

Phenytoin, ephedrine, phenobarbitone and rifampicin may enhance the metabolic clearance of corticosteroids, resulting in decreased blood levels and lessened physiological activity, thus requiring adjustment in corticosteroid dosage.

The prothrombin time should be checked frequently in patients who are receiving corticosteroids and coumarin anticoagulants at the same time because of reports that corticosteroids have altered the response to these anticoagulants. Studies have shown that the usual effect produced by adding corticosteroids is inhibition of response to coumarins, although there have been some conflicting reports of potentiation not substantiated by studies.

When corticosteroids are administered concomitantly with potassium-depleting diuretics, patients should be observed closely for development of hypokalaemia.

Use in pregnancy and nursing mothers: Since adequate human reproduction studies have not been done with corticosteroids, the use of these drugs in pregnancy, or women of child-bearing potential requires that the possible benefits of the drug be weighed against the

potential hazards to the mother and embryo or foetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Corticosteroids appear in breast milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other unwanted effects. Mothers taking pharmacological doses of corticosteroids should be advised not to nurse.

Side-effects: Fluid and electrolyte disturbances: Sodium retention, fluid retention, congestive heart failure in susceptible patients, potassium loss, hypokalaemic alkalosis, hypertension.

Musculoskeletal: Muscle weakness, steroid myopathy, loss of muscle mass, osteoporosis, vertebral compression fractures, aseptic necrosis of femoral and humeral heads, pathological fracture of long bones, tendon rupture.

Gastro-intestinal: Peptic ulcer with possible perforation and haemorrhage, pancreatitis, abdominal distension, ulcerative oesophagitis.

Dermatological: Impaired wound healing, thin fragile skin, petechiae and ecchymoses, erythema, increased sweating, may suppress reactions to skin tests, other cutaneous reactions such as allergic dermatitis, urticaria, angioneurotic oedema.

Neurological: Convulsions, increased intracranial pressure with papilloedema (pseudotumour cerebri) usually after treatment, vertigo, headache.

Endocrine: Menstrual irregularities, development of Cushingoid state, suppression of growth in children, secondary adrenocortical and pituitary unresponsiveness (particularly in times of stress, as in trauma, surgery or illness), decreased carbohydrate tolerance, manifestations of latent diabetes mellitus, increased requirements for insulin or oral hypoglycaemic agents in diabetics.

Ophthalmic: Posterior subcapsular cataracts, increased intra-ocular pressure, glaucoma, exophthalmos.

Metabolic: Negative nitrogen balance due to protein catabolism.

Other: Hypersensitivity, thrombo-embolism, weight gain, increased appetite, nausea, malaise.

Treatment of overdose: None indicated, unless patient has ingested a very large amount, and has one of the conditions which might predispose to adverse effects of adrenocortical steroids, in which case it is probably best to empty the stomach by inducing emesis or performing gastric lavage.

Pharmaceutical precautions Keep container well closed; store in a cool place, protected from light.

Legal category POM.

Package quantities 5 mg: Bottles of 50.
25 mg: Bottles of 100.

Further information Nil.

Product licence numbers

5 mg 0025/5043

25 mg 0025/5044

COSMEGEN,* LYOVAC*

Presentation Yellow, lyophilised powder, in a vial containing 0.5 mg dactinomycin with 20 mg of mannitol.

Uses Cytotoxic, antineoplastic agent.

Recommended only in the treatment, under appropriate supervision, of hospitalised patients with Wilms' tumour, rhabdomyosarcoma, and carcinoma of the testis or uterus. All other indications for dactinomycin are as yet experimental (e.g. Ewing's sarcoma, osteogenic sarcoma).

Wilms' tumour: The neoplasm responding most frequently to Cosmegen is Wilms' tumour. With low doses of both dactinomycin and radiotherapy, temporary objective improvement may be as good as, and may last longer than, that obtained with higher doses of each given alone.

Rhabdomyosarcoma: Temporary regression of the tumour and beneficial subjective results have occurred with dactinomycin in rhabdomyosarcoma, which, like most soft-tissue sarcomas, is comparatively radio-resistant.

Carcinoma of testis and uterus: The sequential use of dactinomycin and methotrexate, along with meticulous monitoring of human chorionic gonadotrophin levels until normal, has resulted in survival in the majority of women with metastatic choriocarcinoma.

Sequential therapy is used if there is:

1. Stability in gonadotrophin titres following two successive courses of an agent.
2. Rising gonadotrophin titres during treatment.
3. Severe toxicity preventing adequate therapy.

In patients with non-metastatic choriocarcinoma, dactinomycin or methotrexate or both, have been used successfully, with or without surgery.

Cosmegen has been beneficial as a single agent in the treatment of metastatic non-seminomatous testicular carcinoma.

Other neoplasms: Dactinomycin has been given intravenously or by regional perfusion, alone or with other antineoplastic compounds or with X-ray therapy, in the palliative treatment of Ewing's sarcoma and sarcoma botryoides. For non-metastatic Ewing's sarcoma, promising results were obtained when dactinomycin (45 mcg/m^2) and cyclophosphamide ($1,200 \text{ mg/m}^2$) were given sequentially and with radiotherapy, over an eighteen-month period. Those with metastatic disease remain the subject of continued investigation with a more aggressive chemotherapeutic regimen employed initially.

Temporary objective improvement and relief of pain and discomfort have followed the use of dactinomycin, usually in conjunction with radiotherapy for sarcoma botryoides. This palliative effect ranges from transitory inhibition of tumour growth to a considerable but temporary regression in tumour size.

Cosmegen and radiation therapy: Much evidence suggests that Cosmegen potentiates the effects of X-ray therapy. The converse also appears likely; that Cosmegen may be more effective when radiation therapy is given concurrently.

With combined Cosmegen and radiation therapy, the normal skin, as well as the buccal and pharyngeal mucosa, shows early erythema. When given with dactinomycin, a smaller than usual X-ray dose causes erythema and vesiculation, which progresses more rapidly through the stages of tanning and desquamation. Healing may occur in four to six weeks rather than in two to three months. Erythema from previous X-ray therapy may be reactivated by the administration of Cosmegen alone, especially when the interval between the two forms of therapy is brief. This potentiation of radiation

effects represents a special problem when the irradiation treatment area includes the mucous membrane. When irradiation is directed towards the nasopharynx, the combination may produce severe oropharyngeal mucositis. *Severe reactions may ensue if high doses of both Cosmegen and radiation therapy are used, or if the patient is particularly sensitive to such combined therapy.*

Because of this potentiating effect, Cosmegen may be tried in radio-sensitive tumours not responding to doses of X-ray therapy that can be tolerated. Objective improvement in tumour size and activity may be observed when lower, better tolerated doses of both types of therapy are employed.

Isolation-perfusion technique: Cosmegen, alone or with other antineoplastic agents, has also been given by the isolation-perfusion technique, either as palliative treatment or as an adjunct to resection of a tumour. Some tumours that are considered resistant to chemotherapy and radiation therapy may respond when the drug is given by the perfusion technique. Neoplasms in which dactinomycin has been tried by this technique include various types of sarcoma, carcinoma and adenocarcinoma.

In some instances, tumours regressed, pain was relieved for variable periods, and surgery made possible. On other occasions, however, the outcome has been less favourable. Nevertheless, in selected cases, Cosmegen given by the perfusion technique may provide more effective palliation than when given systemically.

Dosage and administration Toxic reactions due to Cosmegen are frequent and may be severe, thus limiting the amount that may be given in many cases. However, the severity of toxicity varies markedly and is only partly dependent on the dosage used. Cosmegen must only be given in short courses.

The dosage of Cosmegen will vary with the tolerance of the patient, the size and location of the neoplasm, and the use of other forms of therapy. It may be necessary to reduce the usual dosage suggested below when other chemotherapy or X-ray therapy is used concurrently, or has been employed previously.

Intravenous use: Cosmegen is reconstituted by adding 1.1 ml of Water for Injections BP without preservative to the vial. For injection, 1.0 ml of the reconstituted solution, which will contain 0.5 mg of dactinomycin, is withdrawn into the syringe. Only Water for Injections BP (which does not contain preservatives) should be used. Other injection fluids may cause precipitation.

When reconstituted, the solution of dactinomycin can be added to an infusion solution of 5% dextrose injection or sodium chloride injection, either directly or into the tubing of a running intravenous infusion.

Since dactinomycin is extremely corrosive to soft tissue, precautions for materials of this nature should be observed. To avoid extravasation, the calculated dose of Cosmegen should be given through the tubing of a running intravenous infusion, so that when administration is completed, the tubing can be flushed immediately to avoid damage to the vein. Partial removal of dactinomycin from intravenous solutions by cellulose ester membrane filters used in some intravenous in-line filters has been reported.

If Cosmegen is to be injected directly into the vein without the use of an infusion, the 'two-needle' technique should be used. The calculated dose should be reconstituted and withdrawn from the vial with one sterile needle; direct injection into the vein should then be performed with another sterile needle.

Any unused portion of the solution must be discarded.

Adults: Usually 0.5 mg (500 mcg) a day for a maximum of five days, given intravenously.

Children: 0.015 mg (15 mcg) per kg body weight a day for a maximum of five days, given intravenously. Alternatively, a total dosage of 2.5 mg (2,500 mcg) per m² of body surface is given intravenously over a period of one week.

In both adults and children, a second course may be given, but not until at least two weeks have elapsed, and all evidence of toxicity has disappeared.

Isolation-perfusion technique: Administration by the isolation-perfusion technique offers certain advantages, provided leakage of the drug through the general circulation into other areas of the body is minimal. By this technique, dactinomycin is in continuous contact with the tumour for the duration of treatment. The dose may be increased well above that used by the systemic route, usually without adding to the danger of toxic effects. If the agent is confined to an isolated part, it should not interfere with the patient's defence mechanisms. Systemic absorption of toxic products from neoplastic tissue can be minimised by removing the perfusate when the procedure is finished.

The dosage schedules and the technique itself vary from one investigator to another; the published literature should, therefore, be consulted for details. In general, the following doses are suggested:

For a lower extremity or pelvis – 0.05 mg (50 mcg) per kg body weight.

For an upper extremity – 0.035 mg (35 mcg) per kg body weight.

It may be advisable to use lower doses in obese patients, or when previous chemotherapy or radiation therapy has been employed.

Contra-indications, warnings, etc

Contra-indications: If Cosmegen is given at or about the time of infection with chickenpox or herpes zoster, a severe generalised disease, which may be fatal, can occur.

Warning: Cosmegen should be administered only under the supervision of a physician who is experienced in the use of a cancer chemotherapeutic agent.

Precautions: Cosmegen, like all antineoplastic agents, is a toxic drug, and very careful and frequent observation of the patient for adverse reactions is necessary. These reactions may involve any tissue of the body. The possibility of an anaphylactoid reaction should be borne in mind.

As there is a greater frequency of toxic effects of dactinomycin in infants, Cosmegen should only be given to infants over the age of 6–12 months.

A variety of abnormalities of renal, hepatic and bone-marrow function have been reported in patients with neoplastic disease receiving dactinomycin. It is advisable to make frequent checks of renal, hepatic, and bone-marrow function.

An increased incidence of gastro-intestinal toxicity and bone-marrow depression has been reported when dactinomycin was given with X-ray therapy.

Particular caution is necessary when administering dactinomycin during the first two months after irradiation for the treatment of right-sided Wilms' tumour, since hepatomegaly and elevated SGOT levels have been seen.

Nausea and vomiting due to dactinomycin make it

necessary to give Cosmegen intermittently. It is extremely important to observe the patient daily for toxic side-effects when combined therapy is employed, since a full course of therapy is occasionally not tolerated. If stomatitis, diarrhoea, or severe haemopoietic depression appear during therapy, these drugs should be discontinued until the patient has recovered.

Recent reports indicate an increased incidence of second primary tumours following treatment with radiation and anti-neoplastic agents, such as dactinomycin. Multi-modal therapy creates the need for careful, long-term observation of cancer survivors.

Use in pregnancy: When use of Cosmegen during pregnancy is considered necessary, the danger to the foetus should be taken into account. There are published data showing teratogenic effects of dactinomycin in animals.

Nursing mothers: Although breast milk studies have not been performed in animals or humans, breast feeding should be stopped before beginning treatment with Cosmegen.

Side-effects: Toxic effects (except nausea and vomiting) do not usually become apparent until two to four days after a course of therapy is stopped, and may not reach a maximum before one to two weeks have elapsed. Deaths have been reported. However, side-effects are usually reversible on discontinuing therapy. They include the following:

General: Malaise, fatigue, lethargy, fever, myalgia, proctitis, hypocalcaemia.

Oral: Cheilitis, dysphagia, oesophagitis, ulcerative stomatitis, pharyngitis.

Gastro-intestinal: Anorexia, nausea, vomiting, abdominal pain, diarrhoea, gastro-intestinal ulceration. Nausea and vomiting, which occur early during the first few hours after administration, may be alleviated by giving anti-emetics.

Haematological: Anaemia (even to the point of aplastic anaemia, agranulocytosis, leucopenia, thrombocytopenia, pancytopenia, reticulocytopenia). Platelet and white blood cell counts should be done daily to detect severe haemopoietic depression. If either count shows a marked decrease, dactinomycin should be withheld until recovery occurs. This often takes up to three weeks.

Dermatological: Alopecia, skin eruptions, acne, flare-up of erythema or increased pigmentation of previously irradiated skin.

Soft tissues: Dactinomycin is extremely corrosive to soft tissues. If extravasation occurs during intravenous use, severe damage to soft tissues will occur. In at least one instance, this has led to contracture of the arms.

Side-effects relating especially to the isolation-perfusion technique: Complications of the perfusion technique are related mainly to the amount of drug that escapes into the systemic circulation and may consist of haemopoietic depression, increased susceptibility to infection, absorption of toxic products from massive destruction of neoplastic tissue, impaired wound healing, and superficial ulceration of the gastric mucosa. Other side-effects may include oedema of the extremity involved, damage to the soft tissues of the perfused area, and potentially venous thrombosis.

Treatment of overdosage: There is no known antidote. Treatment is symptomatic after Cosmegen is discontinued.

Pharmaceutical precautions Store in a cool, dry place, protected from light.

Legal category POM.

Package quantities Vials containing 0.5 mg dactinomycin with 20 mg mannitol.

Further information Generally, the actinomycins inhibit Gram-positive and Gram-negative bacteria and some fungi. However, the toxic properties of the actinomycins (including dactinomycin) in relation to antibacterial activity preclude their use as antibiotics in the treatment of infectious diseases.

Because the actinomycins are cytotoxic, they have an antineoplastic effect which has been demonstrated in experimental animals with various types of tumour implant. This cytotoxic action is the basis for their use in the palliative treatment of certain types of cancer.

Dactinomycin is minimally metabolised. Its plasma clearance half-life is 36 hours. It tends to concentrate in nucleated cells and does not cross the blood-brain barrier.

Product licence number 0025/5075.

CREMOSTREP*

Presentation Chocolate-peppermint-flavoured suspension containing, in each 5 ml, 500 mg Succinylsulphathiazole BP, 50 mg streptomycin (as Streptomycin Sulphate BP) and 500 mg Kaolin BP.

Uses For the treatment of mild bacterial diarrhoeas encountered in general practice.

Dosage and administration Cremostrep may be diluted with Syrup BP; the mixture should be used within 14 days.

Adults: The suggested dose is 20 ml two to four times a day before meals. Dosage should be adjusted according to response, and in more severe cases may have to be increased to as much as six 5 ml spoonfuls six times a day.

Infants and children: Dosage should be related to body weight and response. An example of an initial dosage would be one or two 5 ml spoonfuls three times a day. In acutely ill children, these dosages may be increased by 75% until the acute stage has been controlled.

Contra-indications, warnings, etc

Contra-indications: Intestinal obstruction, extensive ulceration of the bowel, diverticulosis (present or suspected), hypersensitivity to succinylsulphathiazole, sulphathiazole or streptomycin. Patients with porphyria should not be given sulphonamides, as these may precipitate an acute attack.

Use in pregnancy and newborn infants: Cremostrep should not be used in pregnancy at term, in premature infants or in newborn infants during the first week of life.

Precautions: Cremostrep should be used only after critical appraisal in patients with liver or renal damage, urinary obstruction or blood dyscrasias. Deaths have been reported from hypersensitivity reactions, agranulocytosis, aplastic anaemia and other blood dyscrasias associated with the systemic use of sulphonamides. When Cremostrep is taken intermittently or for long periods, the need for blood counts and liver and renal function checks should be considered.

Cremostrep should be used with caution in patients

with a history of significant allergies or of asthma. Exacerbation or activation of systemic lupus erythematosus has been reported with sulphonamides.

Succinylsulphathiazole may reduce faecal thiamine output and decrease vitamin K synthesis, leading to the need for supplementation. The action of succinylsulphathiazole may be delayed in the presence of extensive ulcerating lesions of the bowel. With extensive ulceration of the colon, absorption is slightly increased. Mineral oil interferes with the action of Cremostrep, as does watery diarrhoea or a hard stool. Purgatives should be avoided.

The adverse reactions reported with parenterally administered streptomycin have not been reported following its oral administration. However, if symptoms of vestibular dysfunction such as vertigo or tinnitus occur, therapy with Cremostrep should be stopped.

The use of antibiotics may cause resistant organisms to develop, so repeated evaluation of the patient is essential. If new infections appear during therapy, appropriate measures should be taken.

Side-effects: Systemic adverse reactions due to poorly absorbed succinylsulphathiazole are unlikely. As with other sulphonamides, however, the following reactions may occur: headache, malaise, anorexia, nausea, vomiting, hepatitis, pancreatitis, blood dyscrasias, neuropathy, drug fever, skin rash, injection of the conjunctiva and sclera, petechiae, purpura, haematuria and crystalluria.

Treatment of overdose: Emesis should be induced or gastric lavage performed. Depending on the circumstances, a cathartic or enema may be advisable. Fluids should be forced to hasten renal excretion of the sulphonamide. (In the presence of oliguria or anuria, fluids cannot be forced because of the danger of precipitating pulmonary oedema.) Sensitivity reactions and renal failure should be treated in the normal manner.

Pharmaceutical precautions Keep container well closed; store in a cool place, protected from light and freezing.

Cremostrep may be diluted with Syrup BP, the mixture should be used within 14 days.

Legal category POM.

Package quantities Bottles of 100 ml.

Further information Cremostrep combines the effect of two bacteriostatic agents, succinylsulphathiazole and streptomycin, with the adsorbent effect of kaolin. The bacteriostatic agents are both poorly absorbed from the intestine, and remain in high concentration in the bowel, exerting maximum effect at the site of infection. The kaolin is present in finely divided particles to give maximum contact with the intestinal mucosa.

Product licence number 0025/5060.

CUPRIMINE*

Presentation Yellow, opaque capsules, marked 'MSD 602', containing 250 mg Penicillamine BP.

Uses Orally effective chelating agent, recommended in Wilson's disease (hepatolenticular degeneration) to promote excretion of copper deposited in tissues. Also used in cystinuria to control excessive excretion of cystine, and in severe active rheumatoid arthritis.

Wilson's disease: Treatment has two objectives: control of the diet to minimise intake and absorption of copper;

promotion of the excretion of copper already deposited in the tissues. For the second objective, a copper chelating agent is used. Penicillamine is one that is orally effective.

Two types of patient require treatment for Wilson's disease: the symptomatic; and the asymptomatic, in whom the disease is likely to develop if left untreated.

In symptomatic patients, treatment usually produces marked neurological improvement, fading of Kayser-Fleischer rings, and gradual amelioration of hepatic dysfunction and psychic disturbances. Improvement may not be noticeable for one to three months, and during initial therapy with Cuprimine, neurological symptoms may occasionally become worse. Despite this, the drug should not be discontinued completely. Although temporary interruption may result in clinical improvement, it increases the risk of a sensitivity reaction developing.

In asymptomatic patients, daily treatment with Cuprimine appears to prevent signs and symptoms of the disease from developing.

Cystinuria: The normal daily output of cystine is 40–80 mg. In cystinuria this may exceed 1 g a day. At a rate of 500–600 mg a day, formation of stones is almost certain. Treatment is indicated when the output is more than 300 mg a day.

The conventional treatment of cystinuria is aimed at preventing stone formation by maintaining a large volume of alkaline urine (to keep as much cystine in solution as possible), and minimising the production of cystine (by a diet low in methionine, its major dietary precursor).

When these conventional measures are inadequate to control recurrent stone formation, Cuprimine may provide a useful additional treatment. If, for some reason, patients refuse to adhere to conventional therapy, Cuprimine may provide a useful substitute for it.

Cystine excretion can be kept at a near-normal level by administration of Cuprimine. This can hinder stone formation and the serious consequences of pyelonephritis and impaired renal function that develop in some patients.

Rheumatoid arthritis: Because Cuprimine can cause severe reactions, its use should be confined to patients with severe, active rheumatoid arthritis who have failed to respond to an adequate trial of conventional therapy. Other measures such as rest, physical therapy, salicylates and corticosteroids should be used with Cuprimine when indicated.

Dosage and administration *In Wilson's disease:* Cuprimine should be given four times a day, on an empty stomach: 30 minutes to one hour before meals, and at bedtime, at least two hours after the evening meal.

Optimal dosage can only be determined by measurement of urinary copper excretion. The urine must be collected in copper-free glassware, and should be quantitatively analysed for copper before and soon after initiation of therapy with Cuprimine. During therapy, the copper content of a 24-hour urine sample should be determined at approximately three-monthly intervals. A low-copper diet should keep copper absorption down to less than 1 mg a day. The patient should therefore be in negative copper balance if 0.5–1 mg of copper is present in a 24-hour urine sample.

In adults: The recommended initial dosage of Cuprimine is 1 g (4 capsules) a day. This may be increased if necessary, as indicated by the urinary copper determi-

nations, but it should seldom be necessary to exceed 2 g (8 capsules) a day. A dose of 2 g a day should not be continued for more than one year.

In patients unable to tolerate 1 g (4 capsules) a day initially, therapy should be reduced to a dosage of 250 mg (1 capsule) a day, and then increased gradually to the required amount. This should give closer control of the effects of the drug, and may help to reduce the incidence of side-effects.

In children: 20 mg/kg/day in divided doses before meals. Minimum dose 500 mg daily.

As far as possible, the daily diet should be composed of foods with a low copper content, and total daily intake of copper should not exceed 1 or 2 mg. Certain foods should be avoided completely; these include chocolate, nuts, shellfish, mushrooms, liver, molasses, broccoli, and cereals enriched with copper. If the patient's drinking water contains more than 0.1 ppm copper, distilled or demineralised water should be used.

In cystinuria: Cuprimine should be given in addition to conventional therapy.

For the treatment of stones, the adult dose is initially 750 mg/day rising to 2 g a day in divided doses.

Urine cystine levels of not more than 300 mg/litre should be established. Establish the lowest effective dose of penicillamine by quantitative amino-acid chromatography of the urine.

The dosage in children is not yet established, but should be adjusted to maintain urinary cystine levels below 200 mg/litre. The total daily amount is given as 4 divided doses. If 4 equal doses are not practicable, the larger portion should be given at bedtime. If side-effects necessitate a dosage reduction, it is important to retain the bedtime dose.

If dosage is initiated with 250 mg (1 capsule) a day, and then increased gradually to the required amount, closer control of the effects of Cuprimine and a reduction in side-effects may be obtained.

In addition to Cuprimine, patients should drink copiously. It is especially important to drink about a pint of fluid at bedtime, and another pint once during the night, when the urine is more concentrated and more acid than it is during the day. The total daily fluid intake should not be less than 6 pints. The greater the fluid intake, the lower the dosage of Cuprimine required. For prophylaxis against stones, the dose for adults is 250–750 mg at night. No prophylactic dosage has been established for children.

Urine estimations should be carried out weekly for the first 3 months of treatment, and thereafter, monthly. Renal function should be assessed monthly for 6 months, and 3 monthly thereafter.

Dosage must be individualised to that amount which limits cystine excretion to 100–200 mg a day in patients with no history of stones, and below 100 mg a day in those patients who have had stone formation and/or pain. In the determination of dosage, the inherent tubular defect, the patient's weight, age, rate of growth, diet and fluid intake must all be taken into consideration.

A useful qualitative measure of effective dosage is the standard nitroprusside-cyanide test, performed as follows:

Add 2 ml of freshly prepared 5% sodium cyanide solution to 5 ml of a 24-hour aliquot of protein-free urine. Allow to stand for 10 minutes. Add 5 drops of freshly prepared 5% sodium nitroprusside solution and mix. Cystine will turn the mixture magenta. If the result is negative, cystine excretion can be assumed to be less

than 100 mg per gram of creatinine. Treatment should be stopped if an increase in the original urinary cystine level is observed.

Although penicillamine is rarely excreted unchanged, it will also give a magenta colour in this test. If there is any doubt, a ferric chloride test will eliminate the possibility of a false positive result. Add drops of a 3% solution of ferric chloride to the urine. If there is any penicillamine present, the urine will immediately turn to a blue colour which quickly fades. Cystine does not produce this reaction.

Rheumatoid arthritis: Patients must be given Cuprimine on an empty stomach. The initial dose in adults is 250 mg (1 capsule) a day increasing at one to three monthly intervals by 250 mg (1 capsule) until patient response and tolerance indicate the correct dosage. If there is no discernible improvement and no signs of potentially serious toxicity with doses of 500–750 mg a day after two to three months, increase by 250 mg (1 capsule) a day at two to three monthly intervals until there is satisfactory remission, or signs of toxicity develop. If no improvement is seen with 1,000–1,500 mg (4–6 capsules) a day, it may be assumed that the patient will not respond, and Cuprimine should be discontinued.

Maintenance dosage may need readjustment during therapy. Many patients respond to 500–750 mg (2–3 capsules) a day, some patients may need less.

Changes in dosage levels may not be seen clinically or in ESR for two to three months.

In patients who experienced only partial response after six to nine months of therapy, the dosage may be increased by 250 mg a day at three-monthly intervals.

It is unusual to exceed 1,000 mg (4 capsules) a day, but 1,500 mg (6 capsules) a day has sometimes been required. Treatment should be discontinued if no benefit is obtained within 12 months.

Exacerbations of rheumatoid arthritis may occur in some patients during therapy despite an initial good response. These may be self-limiting and subside within 12 weeks. If the exacerbation continues, it is usually controlled by addition of a non-steroidal anti-inflammatory agent, and only if the patient shows a true 'escape' phenomenon should an increase in the dosage of Cuprimine be considered.

Migratory polyarthralgia due to penicillamine is difficult to differentiate from an exacerbation of rheumatitis. Discontinuance or a substantial reduction of Cuprimine will usually resolve the problem.

Although the optimum duration of therapy has not been determined, remission for six months or more indicates a gradual, step-wise reduction of dosage by 250 mg (1 capsule) a day at approximately three-monthly intervals.

Salicylates, non-steroidal anti-inflammatory drugs and corticosteroids may be used with Cuprimine. After improvement commences, analgesic and anti-inflammatory drugs may be slowly withdrawn as symptoms permit. Steroid withdrawal must be gradual, and Cuprimine continued for many months before steroids can be completely eliminated.

Dosages up to 500 mg (2 capsules) a day may be given as a single dose; higher dosages should be divided.

Use in children: The efficacy of Cuprimine in juvenile rheumatoid arthritis has not been established.

Contra-indications, warnings, etc

Contra-indications: Pregnancy (see use in pregnancy), and patients with a history or other evidence of renal

insufficiency or lupus erythematosus with rheumatoid arthritis. Patients with a history of penicillamine-related aplastic anaemia or agranulocytosis. Concomitant use in patients receiving gold therapy, anti-malarial drugs or cytotoxic drugs, oxyphenbutazone, or phenylbutazone. Hypersensitivity to penicillamine.

Precautions: Penicillamine has been associated with fatalities due to diseases such as aplastic anaemia, agranulocytosis, thrombocytopenia, Goodpasture's syndrome, and myasthenia gravis.

Because the hazard of serious haematological and renal side effects is always present with Cuprimine, routine urinalysis, white and differential blood cell counts, haemoglobin determination, and direct platelet counts must be carried out before starting therapy then every fortnight for at least the first six months and thereafter every month. Patients should be instructed to report promptly symptoms which might suggest granulocytopenia and/or thrombocytopenia, e.g. fever, sore throat, chills, bruising or bleeding. The above laboratory studies should be repeated promptly.

Leucopenia and thrombocytopenia have been reported in up to 5% of patients during penicillamine therapy. Leucopenia is of the granulocytic series and may, or may not, be associated with an increase in eosinophils. Penicillamine must be stopped if the WBC count is below 3,500. Thrombocytopenia may be idiosyncratic, with decreased or absent megakaryocytes in the marrow, when it is part of an aplastic anaemia. In other cases the thrombocytopenia is presumably on an immune basis since the number of megakaryocytes in the marrow has been reported to be normal or sometimes increased. A platelet count below 120,000, even in the absence of clinical bleeding, requires at least temporary withdrawal of penicillamine therapy. A progressive fall in either platelet count or WBC in three successive determinations, even though values are still within the normal range, also calls for at least temporary withdrawal. Therapy may be restarted at a lower dosage. Treatment should be permanently withdrawn if neutropenia or thrombocytopenia recurs.

Proteinuria has been reported to develop in 20–30% of patients, and haematuria may develop rarely. Both may be warning signs of membranous glomerulopathy which can progress to a nephrotic syndrome. Close observation of these patients is essential. In some the proteinuria disappears with continued therapy; in others, penicillamine must be discontinued. When a patient develops proteinuria or haematuria the physician must ascertain whether it is drug-induced or not.

Rheumatoid arthritis patients who develop moderate degrees of proteinuria may still be treated cautiously with penicillamine, provided that quantitative 24-hour urinary protein determinations are taken every one or two weeks. Penicillamine dosage should not be increased under these circumstances, and it should be stopped or reduced in patients with proteinuria over 1 g in 24 hours, or where the levels progressively increase. In some patients, proteinuria has been reported to clear following reduction in dosage.

In rheumatoid arthritis patients, penicillamine should be stopped if unexplained gross haematuria or persistent microscopic haematuria develops.

In patients with Wilson's disease or cystinuria, the risks of continued penicillamine therapy in patients with serious urinary abnormalities must be weighed against the expected benefits.

When penicillamine is used in cystinuria, an annual X-

ray for renal stones is advisable. Cystine stones form rapidly, sometimes within six months.

Urinary abnormalities may take up to one year or more to recover after penicillamine therapy has been stopped.

Because of rare reports of intrahepatic cholestasis and toxic hepatitis, liver function tests are advisable every six months for the duration of therapy.

Goodpasture's syndrome has occurred rarely. Penicillamine should be stopped immediately if abnormal urinary findings are associated with haemoptysis, and pulmonary infiltrates revealed on X-ray. Obliterative bronchiolitis has been reported rarely. The patient should be cautioned to report pulmonary symptoms such as exertional dyspnoea, unexplained cough or wheezing immediately. Pulmonary function studies should be considered at that time.

A myasthenic syndrome sometimes progressing to myasthenia gravis has been reported which, in the majority of cases, recedes after withdrawal of penicillamine.

Bullous lesions clinically indistinguishable from pemphigus have been seen with penicillamine therapy. If this dermatosis occurs, it should be treated with corticosteroids and penicillamine withdrawn. Once penicillamine is used to treat Wilson's disease or cystinuria, it should, as a rule, be continued on a daily basis. Restarting with penicillamine after only a few days interruption has caused sensitivity reactions.

Some patients may experience a marked febrile response to penicillamine, usually in the second to third week following initiation of therapy. This fever may be accompanied by a macular cutaneous eruption.

In the case of drug fever in patients with Wilson's disease or cystinuria, because no alternative treatment is available, penicillamine should be discontinued until the reaction subsides. After this, it should be reinstated in a small dosage that is gradually increased until the full dosage is reached. Systemic steroid therapy may be necessary, and is usually helpful in patients in whom toxic reactions develop a second or third time. In these patients, penicillamine therapy should be reintroduced before withdrawal of steroids.

However, if drug fever occurs in rheumatoid arthritis patients, because other treatments are available, penicillamine should be discontinued and another therapeutic alternative tried, since experience indicates that the febrile reaction to penicillamine will recur in a very high percentage of patients.

The skin and mucous membranes should be observed for allergic reactions. Early and late rashes have occurred. Early rash occurs during the first few months of treatment and is more common. It is usually a generalised pruritic, erythematous, maculopapular or morbilliform rash and resembles the allergic rash seen with other drugs. Early rash usually disappears within days after stopping penicillamine and seldom recurs when the drug is restarted at a lower dosage. Pruritus and early rash may often be controlled by the concomitant administration of antihistamines. Less commonly, a late rash may be seen, usually after six months or more of treatment, and requires withdrawal of penicillamine. It is usually on the trunk, is accompanied by intense pruritus, and is usually unresponsive to topical corticosteroid therapy. Late rash may take weeks to disappear after penicillamine is stopped and usually recurs if the drug is restarted.

The appearance of a drug eruption accompanied by fever, arthralgia, lymphadenopathy or other allergic manifestations usually requires discontinuation of penicillamine.

Certain patients will develop a positive antinuclear antibody (ANA) test and some of these may show a lupus erythematosus-like syndrome similar to drug-induced lupus associated with other drugs. The lupus erythematosus-like syndrome is not associated with hypocomplementaemia and may be present without nephropathy. The development of a positive ANA test does not require withdrawal of the drug; however, the physician should be aware that a lupus erythematosus-like syndrome may develop in the future.

Some patients may develop oral ulcerations which occasionally have the appearance of aphthous stomatitis. The stomatitis usually recurs when penicillamine is restarted but often clears on lowering the dosage. Although rare, cheilosis, glossitis and gingivostomatitis have also been reported. These oral lesions are frequently dose-related and may prevent further increase in penicillamine dosage, or even drug withdrawal.

Hypogeusia (a blunting or diminution in taste perception) has occurred in some patients. This may last two to three months or more and may develop into a total loss of taste; however, it is usually self-limited despite continued penicillamine treatment. Such taste impairment is rare in patients with Wilson's disease.

Penicillamine should not be given to patients who are currently receiving gold therapy, antimalarial or cytotoxic drugs, oxyphenbutazone or phenylbutazone, or any other drugs also associated with similar serious renal or haematological side-effects.

Patients withdrawn from gold therapy because of a major toxic reaction may be at a greater risk of reacting adversely to penicillamine; but the reaction may not be the same.

Patients who are allergic to penicillin may theoretically have cross-sensitivity to penicillamine. However, since penicillamine is now manufactured synthetically, there is no possibility of any drug reaction due to trace amounts of penicillin contaminating Cuprimine.

Because of their dietary restrictions, patients with Wilson's disease and cystinuria should be given 25 mg a day of pyridoxine during therapy, since penicillamine increases the requirement for this vitamin. Patients may also benefit from a multivitamin preparation, although there is no evidence that deficiency of any vitamin other than pyridoxine is associated with penicillamine. In Wilson's disease, multivitamin preparations must be copper-free.

Rheumatoid arthritis patients whose nutrition is impaired should also be given a daily supplement of pyridoxine. Mineral supplements should not be given, since they may block the response to penicillamine.

Iron deficiency may develop, especially in children and in menstruating women. In Wilson's disease, this deficiency may be compounded by a low copper diet which is probably also low in iron, with the effects of penicillamine on blood loss or growth. In cystinuria, a low methionine diet may contribute to iron deficiency, since it is necessarily low in protein.

If necessary, iron may be given in short courses, but a period of two hours should elapse between administration of penicillamine and iron, since orally administered iron has been shown to reduce the effects of penicillamine.

Penicillamine causes an increase in the amount of soluble collagen. This may be the cause of increased skin friability especially in areas subjected to pressure or trauma, such as shoulders, elbows, knees, toes, and buttocks. Extravasations of blood may occur and appear as bruising with external bleeding if the skin is broken, or

as vesicles containing dark blood. Neither type is progressive. There is no apparent association with bleeding elsewhere in the body and no coagulation defect has been found. Therapy with penicillamine may be continued despite these lesions. They may not recur if dosage is reduced. Other reported effects probably due to the action of penicillamine on collagen are excessive wrinkling of the skin and development of small, white papules at venepuncture and surgical sites.

The effects of penicillamine on collagen and elastin make it advisable to consider reducing the dosage to 250 mg (1 capsule) a day when surgery is contemplated. Starting full therapy with penicillamine should be delayed until wound healing is complete.

Use in pregnancy: Penicillamine has been shown to be teratogenic in rats when given in doses several times higher than the highest dose recommended for human use. Skeletal defects, cleft palates and foetal toxicity (resorptions) have been reported.

There are no controlled studies in pregnant women with Wilson's disease, but experience does not include any positive evidence of adverse effects on the foetus. Reported experience shows that continued treatment with penicillamine throughout pregnancy protects the mother against relapse of Wilson's disease, and that discontinuation of penicillamine has deleterious effects on the mother. It suggests that the drug does not increase the risks of foetal abnormalities, but it does not exclude the possibility of infrequent or subtle damage to the foetus.

If penicillamine is administered during pregnancy to patients with Wilson's disease, it is recommended that the daily dosage be limited to 1 g. If caesarian section is planned, the daily dosage should be limited to 250 mg during the last six weeks of pregnancy and post-operatively until wound healing is complete.

If possible, penicillamine should not be given during pregnancy to women with cystinuria. There is a report of a woman with cystinuria treated with 2 g a day of penicillamine during pregnancy who gave birth to a child with a generalised connective tissue defect that may have been caused by penicillamine. If stones continue to form in these patients, the benefits of therapy to the mother must be evaluated against the risk to the foetus.

Penicillamine should not be administered to rheumatoid arthritis patients who are pregnant and should be discontinued promptly in patients in whom pregnancy is suspected or diagnosed. Penicillamine should be used in women of childbearing potential with rheumatoid arthritis, only when the expected benefits outweigh possible hazards. Women of childbearing potential should be informed of the possible hazards of penicillamine to the developing foetus and should be advised to report promptly any missed menstrual periods or other indications of possible pregnancy.

There is a report that a woman with rheumatoid arthritis treated with less than one gram of penicillamine a day during pregnancy gave birth (caesarean delivery) to an infant with growth retardation, flattened face with broad nasal bridge, low set ears, short neck with loose skin folds, and unusually lax body skin.

Use in children: The efficacy of Cuprimine in juvenile rheumatoid arthritis has not been established.

Side-effects: Penicillamine causes many side-effects, some of which are potentially fatal. Therefore, it is mandatory that patients receiving penicillamine therapy remain under close medical supervision throughout the period of drug administration.

Reported incidences (%) for the most commonly occurring adverse reactions in *rheumatoid arthritis* patients are noted, based on 17 representative clinical trials reported in the literature (1,270 patients).

Allergic: Generalised pruritus, early and late rashes (5%), pemphigoid-type reactions, and drug eruptions which may be accompanied by fever, arthralgia, or lymphadenopathy have occurred. Some patients may show a lupus erythematosus-like syndrome similar to drug-induced produced by other pharmacological agents.

Urticaria and exfoliative dermatitis have occurred.

Thyroiditis has been reported but is extremely rare.

Some patients may develop a migratory polyarthralgia, often with objective synovitis.

Rarely, a Stevens Johnson-like syndrome or a rheumatoid arthritis type syndrome may occur.

Gastro-intestinal: Anorexia, epigastric pain, nausea, vomiting, or occasional diarrhoea may occur (17%).

Isolated cases of reactivated peptic ulcer, hepatic dysfunction, and pancreatitis have occurred. Intrahepatic cholestasis and toxic hepatitis have been reported rarely. There have been a few reports of increased serum alkaline phosphatase, lactic dehydrogenase, and positive cephalin flocculation and thymol turbidity tests.

Some patients may report a blunting, diminution, or total loss of taste perception (12%); or may develop oral ulceration. Although rare, cheilosis, glossitis, and gingivostomatitis have been reported.

Gastro-intestinal side-effects usually stop on withdrawing therapy.

Haematological: Penicillamine can cause bone marrow depression. Leucopenia (2%) and thrombocytopenia (4%) have occurred. Fatalities have been reported as a result of thrombocytopenia, agranulocytosis, and aplastic anaemia.

Thrombotic thrombocytopenic purpura, haemolytic anaemia, red cell aplasia, monocytosis, leucocytosis, eosinophilia, and thrombocytosis have also been reported.

Renal: Patients on penicillamine therapy may develop proteinuria (6%) and/or haematuria which, in some, may progress to the development of the nephrotic syndrome as a result of an immune complex membranous glomerulopathy.

Central nervous system: Tinnitus has been reported. Reversible optic neuritis has been reported following administration of DL-penicillamine (the racemic mixture) and may be related to pyridoxine deficiency.

Other: Side-effects that have been reported rarely include thrombophlebitis; hyperpyrexia; falling hair or alopecia; lichen planus; myasthenia gravis; polymyositis; dermatomyositis; mammary hyperplasia; elastosis perforans serpiginosa; toxic epidermal necrolysis; anetoderma (cutaneous macular atrophy); and Goodpasture's syndrome, a severe and ultimately fatal glomerulonephritis associated with intra-alveolar haemorrhage. Fatal renal vasculitis has also been reported. Allergic alveolitis, obliterative bronchiolitis, interstitial pneumonitis and pulmonary fibrosis have been reported in patients with severe rheumatoid arthritis, some of whom were receiving penicillamine. Bronchial asthma has also been reported.

Increased skin friability, excessive wrinkling of skin, and development of small white papules at venepuncture and surgical sites have been reported.

The chelating action of the drug may cause increased

excretion of other heavy metals such as zinc, mercury and lead.

Treatment of overdosage: There has been no experience with acute overdosage with penicillamine. Patients may be expected to be intolerant of a large dose and may vomit. Otherwise, emesis should be induced.

Treatment is symptomatic and further therapy with the drug should be discontinued.

Side-effects of the drug may be noted with overdosage. If an allergic reaction occurs, the patient may be treated with glucocorticoids. Iron and pyridoxine deficiency may also occur.

Pharmaceutical precautions Keep container well closed; store in a cool place, protected from light.

Legal category POM.

Package quantities Bottles of 50.

Further information Nil.

Product licence number 0025/5077.

DARANIDE*

Presentation Yellow, half-scored tablets, marked 'MSD 49', containing 50 mg Dichlorphenamide BP.

Uses Carbonic anhydrase inhibitor.

For chronic simple (open-angle) glaucoma and secondary glaucoma. May be useful for pre-operative control of intra-ocular tension in acute angle-closure glaucoma.

Dosage and administration Although Daranide can be used alone, it is usually more effective when given concurrently with miotics.

Initial adult dosage: Usually 2–4 tablets followed by 2 tablets every 12 hours.

Maintenance dosage: $\frac{1}{2}$ –1 tablet one to three times a day.

Dosage must be carefully adjusted to the individual requirements of each patient. In acute angle-closure glaucoma, Daranide may be administered with miotics and osmotic agents. If this does not reduce the intra-ocular tension rapidly, surgery may be mandatory.

Contra-indications, warnings, etc

Contra-indications: Hepatic insufficiency, renal failure, adrenocortical insufficiency, hyperchloraemic acidosis, depressed sodium or potassium levels. Should not be used in patients with severe pulmonary obstruction who are unable to increase their alveolar ventilation, since acidosis may be increased. Hypersensitivity to dichlorphenamide.

See also 'Use in pregnancy' under 'Precautions'.

Precautions: Daranide increases potassium excretion, and hypokalaemia may develop under the following circumstances: when diuresis is brisk; in the presence of severe cirrhosis; during concomitant therapy with steroids or ACTH; interference with adequate oral electrolyte intake. Digitalised patients are particularly sensitive to the effects of potassium depletion. Hypokalaemia may be treated by administration of potassium chloride or giving foods with a high potassium content.

Like all carbonic anhydrase inhibitors, high doses of Daranide cause some decrease in renal blood flow and glomerular filtration rate.

Daranide should be used with caution in the presence of severe degrees of respiratory acidosis.

Use in pregnancy: Studies with dichlorphenamide in rats have demonstrated teratogenic effects (skeletal anomalies) at high dosages. There is no evidence of these effects in humans; however, dichlorphenamide is not recommended for use in women of child bearing age or in pregnant patients, especially during the first trimester. If pregnancy is present or suspected, the benefits of using Daranide should be weighed against possible hazards to the foetus.

Side-effects: The side-effects characteristic of carbonic anhydrase inhibitors may occur. These include: gastro-intestinal disturbances (anorexia, nausea and vomiting); loss of weight; constipation; urinary frequency; renal colic; renal calculi; skin eruptions; pruritus; leucopenia; agranulocytosis; thrombocytopenia; headache; weakness; nervousness; globus hystericus; sedation; lassitude; depression; confusion; disorientation; dizziness; ataxia; tremor; tinnitus; paraesthesiae of hands, feet and tongue.

Treatment of overdosage: Supportive; the stomach should be emptied by emesis or gastric lavage. Fluids and electrolytes should, if necessary, be replenished. The most likely electrolyte disturbance is a hyperchloraemic acidosis that may respond to bicarbonate administration.

Pharmaceutical precautions Keep container well closed; store in a cool place, protected from light.

Legal category POM.

Package quantities Bottles of 100 and 500.

Further information In glaucoma, Daranide has a rapid onset of action, lowering the pressure within an hour. It reaches maximal effect in two to four hours, and is effective for six to twelve hours.

Product licence number 0025/5025.

DECADRON* INJECTION

Presentation A clear, colourless solution containing, in each millilitre, dexamethasone sodium phosphate equivalent to 4 mg dexamethasone phosphate or approximately 3.33 mg dexamethasone.

Uses Corticosteroid.

Systemic administration: Decadron Injection is recommended for systemic administration by intravenous or intramuscular injection when oral therapy is not feasible in the following conditions.

Adrenocortical insufficiency: Decadron Injection has predominantly glucocorticoid activity with low mineralocorticoid activity. It does not, therefore, offer complete replacement therapy, and must be supplemented with salt and/or deoxycortone. When so supplemented, Decadron Injection is indicated in the impairment of all adrenocortical activity, as in Addison's disease or following bilateral adrenalectomy, where replacement of both glucocorticoid and mineralocorticoid activity is required.

In the relative adrenocortical insufficiency that may occur following cessation of long-term therapy with suppressive doses of corticosteroids, mineralocorticoid secretion may be unimpaired. Replacement with a corticosteroid that acts predominantly as a glucocorticoid may be sufficient to restore adrenocortical function. When immediate support is mandatory, Decadron Injection may be effective within minutes after administration and can be life-saving.

Pre-operative and post-operative support: In patients undergoing bilateral adrenalectomy, or hypophysectomy, or any other surgical procedure when adrenocortical reserve is doubtful and in post-operative shock unresponsive to conventional therapy.

Non-suppurative thyroiditis.

Shock: Adjunctive treatment where high pharmacological doses are needed: severe shock of haemorrhagic, traumatic, surgical, or septic origin. Treatment is an adjunct to, and not a substitute for specific and supportive measures the patient may require.

Rheumatic disorders: As adjunctive therapy for short-term administration (to support the patient during an acute episode or exacerbation) in: post-traumatic osteoarthritis, synovitis of osteoarthritis, rheumatoid arthritis, including juvenile rheumatoid arthritis (some cases may require low-dose maintenance therapy), acute and subacute bursitis, epicondylitis, acute non-specific tenosynovitis, acute gouty arthritis, psoriatic arthritis, ankylosing spondylitis.

Collagen diseases: During an exacerbation or as maintenance therapy in selected cases of systemic lupus erythematosus and acute rheumatic carditis.

Dermatological diseases: Pemphigus, severe erythema multiforme (Stevens-Johnson syndrome), exfoliative dermatitis, bullous dermatitis herpetiformis, severe seborrhoeic dermatitis, severe psoriasis, mycosis fungoides.

Allergic states: Control of severe allergic conditions intractable to trials of conventional treatment in: bronchial asthma, contact dermatitis, atopic dermatitis, serum sickness, seasonal or perennial allergic rhinitis, drug hypersensitivity reactions, urticarial transfusion reactions; acute non-infectious laryngeal oedema, anaphylaxis (adrenaline is the drug of first choice).

Ophthalmic diseases: Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa, such as: allergic conjunctivitis, keratitis, allergic corneal marginal ulcers, herpes zoster ophthalmicus, iritis, iridocyclitis, chorioretinitis, diffuse posterior uveitis and choroiditis, optic neuritis, sympathetic ophthalmia, anterior segment inflammation.

Gastro-intestinal diseases: To support the patient during a critical period of disease in ulcerative colitis and regional enteritis (as systemic therapy).

Respiratory diseases: Symptomatic sarcoidosis, Löfller's syndrome not manageable by other means, berylliosis, fulminating or disseminated pulmonary tuberculosis (when accompanied by appropriate antituberculous chemotherapy), aspiration pneumonitis.

Haematological disorders: Acquired (auto-immune) haemolytic anaemia, idiopathic and secondary thrombocytopenic purpura in adults (intravenous only: intramuscular administration is contra-indicated), RBC anaemia, congenital hypoplastic anaemia.

Neoplastic diseases: For palliative management of: hypercalcaemia associated with cancer; leukaemias and lymphomas in adults; and acute leukaemias of childhood.

Oedematous states: To induce diuresis or remission of proteinuria in the nephrotic syndrome, without uraemia, of the idiopathic type or due to lupus erythematosus.

Cerebral oedema: Cerebral oedema associated with: primary or metastatic brain tumours; cerebrovascular accident (acute stroke) involving the cerebral cortex; neurosurgery; head injury or pseudotumour cerebri. Also

in the pre-operative preparation of patients with increased intracranial pressure secondary to brain tumours, and for palliation of patients with inoperable or recurrent brain neoplasms.

Use of Decadron Injection in cerebral oedema is not a substitute for careful neurological evaluation and definitive management such as neurosurgery or other specific therapy.

Miscellaneous: Tuberculous meningitis with subarachnoid block or impending block when accompanied by appropriate antituberculous chemotherapy, trichinosis with neurological or myocardial involvement.

Diagnostic testing of adrenocortical hyperfunction:

Local administration

By intrasynovial or soft tissue injection: As adjunctive therapy for short-term administration (to support the patient during an acute episode or exacerbation) in: synovitis of osteoarthritis, rheumatoid arthritis, acute and subacute bursitis, acute gouty arthritis, epicondylitis, acute non-specific tenosynovitis, post-traumatic osteoarthritis.

By intraleisional injection: Keloids; localised hypertrophic, infiltrated, inflammatory lesions of: lichen planus, psoriatic plaques, granuloma annulare, and lichen simplex chronicus (neurodermatitis), discoid lupus erythematosus, necrobiosis lipoidica diabetorum, alopecia areata, may also be useful in cystic tumours of an aponeurosis or tendon (ganglia).

Dosage and administration Decadron Injection is sensitive to heat and should not be autoclaved to sterilise the outside of the vial. Protect from freezing. It can be given without mixing or dilution, but if preferred, can be added without loss of potency to sodium chloride injection or dextrose injection or compatible blood for transfusion, and given by intravenous drip. The infusion mixture must be used within 24 hours, and the usual aseptic techniques for injections should be observed.

Intravenous and intramuscular injection:

General considerations: Generally, initial and maintenance dosages must be determined individually according to the disease under treatment and to the response of the patient.

The usual initial dosage is 0.5–20 mg (0.125–5 ml) a day. In situations of less severity, lower doses will generally suffice, while in certain patients, higher initial doses may be required.

Usually the parenteral dosage ranges are one-third to one-half the oral dose given every 12 hours. However, in certain overwhelming, acute, life-threatening situations, administration in dosages exceeding the usual dosages may be justified and may be in multiples of the oral dosages. In these circumstances, the slower rate of absorption by intramuscular administration should be recognised.

The initial dosage should be maintained or adjusted until a satisfactory response is noted. (If, after a reasonable time, there is a lack of satisfactory clinical response, Decadron Injection should be discontinued and the patient transferred to other appropriate therapy.) After a favourable response is noted, the proper maintenance dosage should be determined by decreasing the initial dosage by small amounts at appropriate intervals to the lowest dosage which will maintain an adequate clinical response. Constant monitoring is needed in regard to drug dosage. Included in the situations which may make dosage adjustments necessary are changes in

clinical status secondary to remissions or exacerbations in the disease process, the patient's individual drug responsiveness, and the effect of patient exposure to stressful situations not directly related to the disease under treatment (here it may be necessary to increase the dosage for a period consistent with the patient's condition). If the drug is to be stopped after it has been given for more than a few days, it should be withdrawn gradually rather than stopped abruptly.

Whenever possible, use intravenous route for the initial dose and for as many subsequent doses as are given while patient is in shock (because of the irregular rate of absorption of any medicament administered by any other route in such patients). When the blood pressure responds, use the intramuscular route until oral therapy can be substituted. For the comfort of the patient, not more than 2 ml should be injected intramuscularly at any one site.

In emergencies, the usual dose of Decadron Injection by intravenous or intramuscular injection is 1 ml–5 ml (4 mg–20 mg), depending on the severity of the condition (see also 'Shock'). This dose may be repeated until adequate response is discernible.

After initial improvement, single doses of 0.5 ml–1 ml (2 mg–4 mg) repeated as necessary, may be sufficient. The total daily dosage usually need not exceed 20 ml (80 mg), even in severe conditions.

When constant maximal effect is desired, dosage must be repeated at three-hour or four-hour intervals, or maintained by slow intravenous drip.

Intravenous and intramuscular injections are advised in acute illness. When the acute stage has passed, substitute oral steroid therapy as soon as feasible.

Shock (of haemorrhagic, traumatic, surgical or septic origin): Usually 2 to 6 mg/kg body weight as a single intravenous injection. This may be repeated in two to six hours if shock persists. Alternatively, this may be followed immediately by the same dose in an intravenous infusion. Therapy with Decadron Injection is an adjunct to, and not a replacement for conventional therapy.

Administration of these high doses should be continued only until the patient's condition has stabilised and usually no longer than 48–72 hours. Possible complications of prolonged therapy include adrenal suppression or gastro-intestinal ulcer.

Cerebral oedema: Associated with acute stroke: initially 10 mg (2.5 ml) intravenously, followed by 4 mg (1 ml) intramuscularly every six hours for ten days. Dosage should be tapered to zero over the ensuing seven days.

Associated with primary or metastatic brain tumour, neurosurgery, head injury, pseudotumour cerebri, pre-operative preparation of patients with increased intracranial pressure secondary to brain tumour: initially 10 mg (2.5 ml) intravenously, followed by 4 mg (1 ml) intramuscularly every six hours until symptoms of cerebral oedema subside. Response is usually noted within 12–24 hours; dosage may be reduced after two to four days and gradually discontinued over five to seven days.

High doses of Decadron Injection are recommended for initiating short-term intensive therapy for acute life-threatening cerebral oedema. Following the high loading dose schedule of the first day of therapy, the dose is scaled down over the seven- to ten-day period of intensive therapy and subsequently reduced to zero over the next seven to ten days. When maintenance therapy is required, substitute oral Decadron as soon as possible. (See table opposite.)

Suggested high dose schedule in cerebral oedema:

Adults:

Initial Dose	50 mg IV
1st day	8 mg IV every 2 hours
2nd day	8 mg IV every 2 hours
3rd day	8 mg IV every 2 hours
4th day	4 mg IV every 2 hours
5th–8th day	4 mg IV every 4 hours
Thereafter	decrease by daily reduction of 4 mg

Children (35 kg and over):

Initial Dose	25 mg IV
1st day	4 mg IV every 2 hours
2nd day	4 mg IV every 2 hours
3rd day	4 mg IV every 2 hours
4th day	4 mg IV every 4 hours
5th–8th day	4 mg IV every 6 hours
Thereafter	decrease by daily reduction of 2 mg

Children (below 35 kg):

Initial Dose	20 mg IV
1st day	4 mg IV every 3 hours
2nd day	4 mg IV every 3 hours
3rd day	4 mg IV every 3 hours
4th day	4 mg IV every 6 hours
5th–8th day	2 mg IV every 6 hours
Thereafter	decrease by daily reduction of 1 mg

Palliative management of recurrent or inoperable brain tumours: Maintenance therapy should be determined for each patient; 2 mg (0.5 ml) two or three times a day may be effective.

The smallest dosage necessary to control cerebral oedema should be used.

Dual therapy: In acute self-limiting allergic disorders or acute exacerbations of chronic allergic disorders, the following schedule combining oral and parenteral therapy is suggested:

First day	Decadron Injection, 4 mg–8 mg (1 ml–2 ml) intramuscularly
Second day	Two 0.5 mg Decadron Tablets twice a day
Third day	Two 0.5 mg Decadron Tablets twice a day
Fourth day	One 0.5 mg Decadron Tablet twice a day
Fifth day	One 0.5 mg Decadron Tablet twice a day
Sixth day	One 0.5 mg Decadron Tablet
Seventh day	One 0.5 mg Decadron Tablet
Eighth day	Reassessment day

(For information on Decadron Tablets, see separate entry.)

Intrasyovial, intralesional, and soft-tissue injection: In general, these injections are employed when only one or two joints or areas are affected.

Some of the usual single doses are:

Site of injection	Amount of dexamethasone phosphate
Large joints (e.g. knee)	2–4 mg (0.5–1 ml)
Small joints (e.g. interphalangeal, temporomandibular)	0.8–1 mg (0.2–0.25 ml)
Bursae	2–3 mg (0.5–0.75 ml)
Tendon sheaths	0.4–1 mg (0.1–0.25 ml)
Soft-tissue infiltration	2–6 mg (0.5–1.5 ml)
Ganglia	1–2 mg (0.25–0.5 ml)

Frequency of injection: once every three to five days to once every two to three weeks, depending on response.

Contra-indications, warnings, etc

Contra-indications: Systemic fungal infection (see 'Precautions' re amphotericin B); hypersensitivity to any component.

Precautions: Corticosteroids may exacerbate systemic fungal infections and therefore should not be used in the presence of such infections unless they are needed to control drug reactions due to amphotericin B. Moreover, there have been cases reported in which concomitant use of amphotericin B and hydrocortisone was followed by cardiac enlargement and congestive failure.

The lowest dosage that will control the condition under treatment should be used. Any reduction in dosage should be made gradually. When large doses are given, it may be advisable to give antacids between meals.

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, retention of salt and water, and increased excretion of potassium, but these effects are less likely to occur with synthetic derivatives, except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

The slower rate of absorption by intramuscular administration should be recognised.

In patients on corticosteroid therapy subjected to unusual stress, dosage should be increased before, during and after the stressful situation. Drug-induced secondary adrenocortical insufficiency may be minimised by gradual dosage reduction, but may persist for months after discontinuation of therapy. In any stressful situation during that period, therefore, corticosteroid therapy should be reinstated. If the patient is already receiving corticosteroids, the dosage may have to be increased. Salt and/or a mineralocorticoid should be given concurrently, since mineralocorticoid secretion may be impaired.

Stopping corticosteroids after prolonged therapy may cause withdrawal symptoms including fever, myalgia, arthralgia, and malaise. This may occur in patients even without evidence of adrenal insufficiency.

Because anaphylactoid reactions have occurred, rarely, in patients receiving parenteral corticosteroid therapy, appropriate precautions should be taken prior to administration, especially when the patient has a history of allergy to any drug.

Administration of live virus vaccines, including smallpox, is contra-indicated in individuals receiving immunosuppressive doses of corticosteroids. If inactivated viral or bacterial vaccines are administered to individuals receiving immunosuppressive doses of corticosteroids, the expected serum antibody response may not be obtained. However, immunisation procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e.g. for Addison's Disease.

Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinaemia.

The use of Decadron Injection in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate antituberculosis regimen. If the corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation may occur. During prolonged corticosteroid therapy, these patients should receive prophylactic chemotherapy.

Corticosteroids should be used with caution in: non-specific ulcerative colitis, if there is a probability of impending perforation, abscess, or other pyogenic infection; diverticulitis; fresh intestinal anastomoses; active or latent peptic ulcer; renal insufficiency; hypertension; osteoporosis; and myasthenia gravis. Signs of peritoneal irritation following gastro-intestinal perforation in patients receiving large doses of corticosteroids may be minimal or absent. Fat embolism has been reported as a possible complication of hypercortisone.

Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal ulceration.

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis. Corticosteroids may increase or decrease motility and number of spermatozoa in some patients.

Because phenytoin, phenobarbitone, ephedrine, and rifampicin may enhance the metabolic clearance of corticosteroids, resulting in decreased blood levels and reduced physiological activity, the dosage may have to be adjusted. These interactions may interfere with dexamethasone suppression tests which should be interpreted with caution during administration of these drugs.

The prothrombin time should be checked frequently in patients who are receiving corticosteroids and coumarin anticoagulants at the same time, because of reports that corticosteroids have altered the response to these anticoagulants. Studies have shown that the usual effect produced by adding corticosteroids is inhibition of response to coumarins, although there have been some conflicting reports of potentiation not substantiated by studies.

When corticosteroids are administered concomitantly with potassium-depleting diuretics, patients should be observed closely for development of hypokalaemia.

Corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance, and inability to localise infection. Moreover, corticosteroids may affect the nitroblue-tetrazolium test for bacterial infection and produce false negative results.

Corticosteroids may activate latent amoebiasis. Therefore, it is recommended that latent or active amoebiasis be ruled out before initiating corticosteroid therapy in any patient who has spent time in the tropics, or any patient with unexplained diarrhoea.

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes and severe depression, to frank psychotic manifestations. Also, existing instability or psychotic tendencies may be aggravated by corticosteroids.

Prolonged use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary infections due to fungi or viruses.

Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.

Intra-articular injection of a corticosteroid may produce systemic as well as local effects. Corticosteroids should not be injected into unstable joints.

Appropriate examination of joint fluid is necessary to exclude a septic process. A marked increase in pain accompanied by local swelling, further restriction of joint motion, fever, and malaise are suggestive of septic

arthritis. If this complication occurs and the diagnosis of sepsis is confirmed, appropriate antimicrobial therapy should be instituted. Local injection of a steroid into an infected site should be avoided.

Patients should understand the great importance of not over-using joints that are still diseased despite symptomatic improvement.

Frequent intra-articular injections may damage joint tissues.

Use in pregnancy and the nursing mother: Since adequate human reproduction studies have not been done with corticosteroids, their use in pregnancy or in women of child-bearing potential requires that the potential benefits be weighed against possible hazards to the mother and child or foetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Corticosteroids appear in breast milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other unwanted effects. Mothers taking pharmacological doses of corticosteroids should be advised not to nurse.

Side-effects: Fluid and electrolyte disturbances: Sodium retention, fluid retention, congestive heart failure in susceptible patients, potassium loss, hypokalaemic alkalosis, hypertension.

Musculoskeletal: Muscle weakness, steroid myopathy, loss of muscle mass, osteoporosis, vertebral compression fractures, aseptic necrosis of femoral and humeral heads, pathological fracture of long bones, tendon rupture.

Gastro-intestinal: Peptic ulcer and possible subsequent perforation and haemorrhage, perforation of the small and large bowel, particularly in patients with inflammatory bowel disease, pancreatitis, abdominal distension, ulcerative oesophagitis.

Dermatological: Impaired wound healing, thin fragile skin, petechiae and ecchymoses, erythema, increased sweating, possible suppression of skin tests, burning or tingling especially in the perineal area (after intravenous injection), other cutaneous reactions such as allergic dermatitis, urticaria, angioneurotic oedema.

Neurological: Convulsions, increased intracranial pressure with papilloedema (pseudotumour cerebri) usually after treatment, vertigo, headache.

Endocrine: Menstrual irregularities, development of Cushingoid state, suppression of growth in children, secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery or illness, decreased carbohydrate tolerance, manifestations of latent diabetes mellitus, increased requirements for insulin or oral hypoglycaemic agents in diabetes.

Ophthalmic: Posterior subcapsular cataracts, increased intra-ocular pressure, glaucoma, exophthalmos.

Metabolic: Negative nitrogen balance due to protein catabolism.

Other: Anaphylactoid or hypersensitivity reactions, thrombo-embolism, weight gain, increased appetite, nausea, malaise.

Additional side-effects related to parenteral corticosteroid therapy only: Rare instances of blindness associated with intralesional therapy around the face and head, hyperpigmentation or hypopigmentation, subcutaneous and cutaneous atrophy, sterile abscess, post-injection flare (following intra-articular use), Charcot-like arthropathy.

Treatment of overdosage: Anaphylactic and hypersensitivity reactions may be treated with adrenaline, positive-pressure artificial respiration and aminophylline. The patient should be kept warm and quiet.

Treatment is probably not indicated for reactions due to chronic poisoning unless the patient has a condition that would render him unusually susceptible to ill effects from corticosteroids. In this case, symptomatic treatment should be instituted as necessary.

Pharmaceutical precautions Keep in a cool place, protected from light and freezing. Only sodium chloride injection or dextrose injection should be used as diluent. Any infusion mixture must be used within 24 hours.

This product, like many steroid formulations, is sensitive to heat. Therefore, it should not be autoclaved when it is desirable to sterilise the exterior of the vial.

Legal category POM.

Package quantities Vials of 2 ml.

Further information Also available is Injection Decadron Shock-Pak containing, per millilitre, dexamethasone sodium phosphate equivalent to 20 mg dexamethasone, indicated exclusively for intravenous use as adjunctive therapy in severe shock. For information about this special high-dose form of Decadron Injection, see separate entry.

Decadron Injection is ready for immediate use. An adequate dose is contained in a small volume of vehicle, and small-bore needles can be used wherever appropriate.

Product licence number 0025/5045.

INJECTION DECADRON* SHOCK-PAK

Presentation An injection containing, per millilitre, dexamethasone sodium phosphate equivalent to 20 mg dexamethasone, as a colourless solution.

Uses Corticosteroid.

Only for the adjunctive treatment of shock where massive doses of corticosteroids are needed, e.g. severe shock or haemorrhagic, traumatic, surgical or septic origin. It is an adjunct to, and not a substitute for, specific or supportive measures that the patient may require, e.g. restoration of circulating blood volume, correction of fluid and electrolyte balance, oxygen, surgical measures and antibiotics.

Dosage and administration Injection Decadron Shock-Pak is for administration by the intravenous route only.

Intravenous injection in shock: Injection Decadron Shock-Pak can be used without mixing or diluting. Injection should be made slowly.

The usual dosage by intravenous injection is 2-6 mg/kg body weight given as a single intravenous injection. This may be repeated in two to six hours, if shock persists. As an alternative, the initial intravenous injection may be followed immediately by an intravenous infusion containing the same dose. (Although Injection Decadron Shock-Pak was not primarily designed for intravenous infusion, it can be added to sodium chloride injection, or to dextrose injection, and administered by intravenous drip without loss of potency. When the Shock-Pak is added to an infusion solution, the mixture must be used within 24 hours as infusion solutions do not contain preservatives.)

These dosages are large in comparison with the usual recommended dosages of dexamethasone sodium phosphate. They are, however, for emergency use in acute conditions needing massive doses of corticosteroid, and reflect the tendency in current medical practice to use such high doses in the treatment of shock.

Therapy with Injection Decadron Shock-Pak is an adjunct to, and not a replacement for, conventional therapy. Administration of high doses of corticosteroids should be continued only until the patient's condition has stabilised, and usually no longer than 48–72 hours. Prolonged therapy at such high doses should be avoided to prevent possible complications, such as adrenal suppression or gastro-intestinal ulceration.

Contra-indications, warnings, etc

Contra-indications: Systemic fungal infections; hypersensitivity to any component.

Precautions: Injection Decadron Shock-Pak is for adjunctive use in the treatment of shock, and therapy must be accompanied by the usual standard measures employed in its management.

This dosage form should be administered by the intravenous route only. It should be given only with full knowledge of the characteristic activity of, and the various responses to, corticosteroids. The pronounced hormonal effects associated with prolonged corticosteroid therapy will probably not be seen when this injection is used for short-term adjunctive therapy in shock.

Administration of high doses of corticosteroids should be continued only until the patient's condition has stabilised and usually no longer than 48–72 hours. In shock of septic origin, appropriate antibiotic therapy must be continued for as long as required.

Side-effects: Although adverse reactions associated with short-term corticosteroid therapy in high doses are uncommon, peptic ulceration may occur. However, for details of side-effects seen with prolonged dexamethasone therapy, please see previous entry on Injection Decadron. Some patients have reported transitory burning or tingling sensations, often in the perineal area, when intravenous injections of large doses of dexamethasone sodium phosphate were given. The usual aseptic techniques governing injections should be observed.

Treatment of overdosage: Anaphylactic and hypersensitivity reactions may be treated with adrenaline, positive-pressure artificial respiration and aminophylline. The patient should be kept warm and quiet.

Pharmaceutical precautions Injection Decadron Shock-Pak is sensitive to heat, and should not be autoclaved to sterilise the exterior of the vial. It should also be protected from freezing.

Only sodium chloride injection or dextrose injection should be used as diluents for infusion. Any infusion mixture must be used within 24 hours.

Legal category POM.

Package quantities Vials of 5 ml.

Further information Injection Decadron Shock-Pak is a special dosage form of dexamethasone sodium phosphate designed exclusively for intravenous use as adjunctive therapy in the treatment of severe shock. For other indications requiring an injectable steroid, Decadron Injection, a formulation containing, per millilitre, dexamethasone sodium phosphate equivalent to 4 mg

dexamethasone phosphate (approximately 3.33 mg dexamethasone), is available.

Product licence number 0025/0077.

DECADRON* TABLETS

Presentation Yellow, half-scored tablets, marked 'MSD 41', containing 0.5 mg Dexamethasone BP.

Pale blue, half-scored tablets, marked 'MSD 63', containing 0.75 mg Dexamethasone BP.

Uses Corticosteroid.

Allergic states: Severe or incapacitating allergies unresponsive to conventional treatment; seasonal or perennial allergic rhinitis, bronchial asthma, contact dermatitis, atopic dermatitis, serum sickness, drug hypersensitivity reactions.

Rheumatic disorders: As adjunctive therapy for short-term administration during an acute episode or exacerbation of: psoriatic arthritis, rheumatoid arthritis including juvenile rheumatoid arthritis (selected cases may require low-dosage maintenance therapy), ankylosing spondylitis, acute and subacute bursitis, acute non-specific tenosynovitis, acute gouty arthritis, post-traumatic osteoarthritis, synovitis of osteoarthritis, epicondylitis.

Dermatological diseases: Pemphigus, bullous dermatitis herpetiformis, severe erythema multiforme (Stevens-Johnson syndrome), exfoliative dermatitis, mycosis fungoides, severe psoriasis, severe seborrheic dermatitis.

Ophthalmic diseases: Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa, such as: allergic conjunctivitis, keratitis, allergic corneal marginal ulcers, herpes zoster ophthalmicus, iritis, iridocyclitis, chorioretinitis, diffuse posterior uveitis and choroiditis, optic neuritis, sympathetic ophthalmia, anterior segment inflammation.

Endocrine disorders: Primary or secondary adrenocortical insufficiency (the first choice is hydrocortisone or cortisone, but synthetic analogues may be used with mineralocorticoids where applicable; in infancy, mineralocorticoid supplementation is particularly important), congenital adrenal hyperplasia, non-suppurative thyroiditis, hypercalcaemia associated with cancer.

Respiratory diseases: Symptomatic sarcoidosis, Löf-ler's syndrome not manageable by other means, berylliosis, fulminating or disseminated pulmonary tuberculosis (when accompanied by appropriate concurrent antituberculous chemotherapy), aspiration pneumonia.

Haematological disorders: Idiopathic thrombocytopenic purpura in adults and secondary thrombocytopenia in adults, acquired (auto-immune) haemolytic anaemia, red blood cell anaemia, congenital hypoplastic anaemia.

Neoplastic diseases: Palliative management of leukaemias and lymphomas in adults, and of acute leukaemia in children.

Oedematous states: To induce a diuresis or remission of proteinuria in the nephrotic syndrome, without uraemia, of the idiopathic type or due to lupus erythematosus.

Cerebral oedema: In cerebral oedema associated with primary or metastatic brain tumours; in the pre-operative preparation of patients with increased intracranial pressure secondary to brain tumours; for the palliation of

symptoms in patients with inoperable or recurrent brain neoplasms; and in the management of cerebral oedema associated with neurosurgery. Some patients with cerebral oedema due to head injury or with benign intracranial hypertension (pseudotumour cerebri) may benefit from therapy with Decadron Tablets. It should be used as an adjunct to, and not a replacement for, definitive management such as neurosurgery or other specific therapy.

Gastro-intestinal diseases: During a critical period of the disease in: ulcerative colitis, regional enteritis.

Other indications: Tuberculous meningitis with subarachnoid block or impending block, used concurrently with appropriate antituberculous chemotherapy; trichinosis with neurological or myocardial involvement; during an exacerbation or as maintenance therapy in some cases of systemic lupus erythematosus and acute rheumatic carditis; for diagnostic testing of adrenocortical hyperfunction.

Dosage and administration *General considerations:* Therapy is governed by the following principles:

1. Dosage should be adjusted to the severity, prognosis and expected duration of the disease, and the response of the individual patient. For infants and children, the recommended dosages will usually have to be reduced, but dosage should be governed by the severity of the condition rather than by age or body weight.
2. Hormone therapy is an adjunct to conventional therapy and does not replace it. Appropriate conventional therapy should be instituted as indicated.
3. If therapy is continued for more than a few days, any decrease in dosage must be *gradual*.
4. Continued supervision of the patient after cessation of corticosteroid therapy is essential, since there may be a sudden reappearance of severe manifestations of the disease for which the patient was being treated.

In acute conditions where prompt relief is urgent, high dosages are permissible and may be mandatory for a short time.

In chronic conditions requiring long-term therapy, the lowest dosage which provides adequate (but not necessarily complete) relief should be used. If a high dosage is considered essential for prolonged periods, patients should be closely observed for any signs that might indicate that a reduction in dosage or discontinuation of corticosteroid therapy is necessary. Chronic conditions are subject to periods of spontaneous remission. When such periods occur, corticosteroids should be gradually discontinued.

Routine investigations, such as urine analysis, two-hour post-prandial blood sugar, determination of blood pressure and body weight, and a chest X-ray should be carried out at regular intervals if therapy is prolonged. Periodic determinations of serum potassium are advisable if high dosages are being used. Upper gastro-intestinal tract X-rays should be taken when treatment is prolonged, in patients with a history of ulcer, or when there is gastric distress.

Patients may be transferred to Decadron from other glucocorticoids with proper adjustment in dosage.

One 0.75 mg tablet of Decadron-75 will usually replace:

Methylprednisolone	
or triamcinolone	one 4 mg tablet
Prednisone or prednisolone	one 5 mg tablet
Hydrocortisone	one 20 mg tablet

Cortisone one 25 mg tablet

At equipotent anti-inflammatory doses, dexamethasone almost completely lacks the sodium-retaining property of hydrocortisone and its closely related derivatives.

Specific dosage recommendations: *In chronic, usually non-fatal diseases:* (e.g. endocrine and chronic rheumatic disorders, oedematous states, respiratory and gastro-intestinal diseases, some dermatological diseases and haematological disorders), therapy should be initiated with a low dosage (0.5–1 mg a day) which is gradually increased to the smallest amount that gives the desired degree of symptomatic relief.

When adequate suppression of symptoms is achieved, dosage should be maintained at the minimum amount capable of providing sufficient relief without excessive hormonal effects.

Dosage may be administered two, three, or four times a day. Regardless of the initial daily schedule, therapy is often successful on a twice-daily regime after the optimal maintenance dosage has been established.

In congenital adrenal hyperplasia: The usual daily dose is 0.5–1.5 mg.

In acute, non-fatal diseases: (e.g. allergic states, ophthalmic diseases, acute and subacute rheumatic disorders), the usual dosage is between 2 mg and 3 mg a day, but in some patients, higher dosages are necessary. Since these conditions are self-limiting, prolonged maintenance therapy is not usually necessary.

Dual therapy

In acute, self-limiting allergic disorders or acute exacerbations of chronic allergic disorders: (e.g. acute allergic rhinitis, acute attacks of seasonal allergic bronchial asthma, urticaria medicamentosa, and contact dermatoses), the following dosage schedule, which combines parenteral and oral therapy is suggested.

First day	Decadron Injection, 4 mg or 8 mg (1 ml or 2 ml) intramuscularly
Second day	Two 0.5 mg Decadron Tablets twice a day
Third day	Two 0.5 mg Decadron Tablets twice a day
Fourth day	One 0.5 mg Decadron Tablet twice a day
Fifth day	One 0.5 mg Decadron Tablet twice a day
Sixth day	One 0.5 mg Decadron Tablet
Seventh day	One 0.5 mg Decadron Tablet
Eighth day	Reassessment day

In chronic, potentially fatal diseases: Such as systemic lupus erythematosus, pemphigus, symptomatic sarcoidosis), the recommended initial dosage is from 2 mg to 4.5 mg a day; higher dosages are necessary in some patients. As soon as adequate relief is obtained, the dosage should be gradually reduced to the minimum amount that will produce the desired therapeutic effect.

In acute and life-threatening diseases: (e.g. acute rheumatic carditis, crisis of systemic lupus erythematosus, severe allergic reactions, pemphigus, neoplastic diseases), the initial dosage is between 4 mg and 10 mg a day, administered in at least 4 divided doses. In some patients, this dosage may have to be increased. As soon as control is attained, the dosage should be gradually reduced to the minimum that will maintain relief. When an extremely rapid onset of action is desired, Decadron Injection may be administered intravenously for the first 2 or 3 doses.

In severe allergic reactions: The therapy of first choice is

adrenaline. Decadron is useful as concurrent or supplementary therapy.

In cerebral oedema: Initial therapy is usually by Decadron Injection in acute conditions. When maintenance therapy is required, this should be changed to Decadron Tablets as soon as possible (see entry for Decadron Injection). For the palliative management of patients with recurrent or inoperable brain tumours, maintenance dosage should be calculated individually using Decadron Injection, or Decadron Tablets. A dosage of 2 mg two or three times a day may be effective. The smallest dosage necessary to control symptoms should always be used.

In the adrenogenital syndrome: Daily dosages of 0.5–1.5 mg may keep children in remission and prevent the recurrence of abnormal excretion of 17-ketosteroids.

As massive therapy in certain conditions: (e.g. acute leukaemia, the nephrotic syndrome and pemphigus), the recommended dosage is 10–15 mg a day. Patients receiving such a high dosage should be observed very closely for the appearance of severe reactions.

Dexamethasone suppression tests:

1. **Tests for Cushing's syndrome:** One milligram of Decadron is given orally at 11 p.m., then blood is drawn for plasma cortisol determination at 8 a.m. the following morning.

For greater accuracy, 0.5 mg Decadron is given orally every 6 hours for 48 hours. Twenty-four-hour urine collections are made for determination of 17-hydroxy-corticosteroid excretion.

2. **Test to distinguish Cushing's syndrome caused by pituitary ACTH excess from the syndrome induced by other causes:** Two milligrams of Decadron is given orally every 6 hours for 48 hours. Twenty-four-hour urine collections are made for determination of 17-hydroxy-corticosteroid excretion.

Contra-indications, warnings, etc

Contra-indications: Systemic fungal infections; hypersensitivity to the drug.

Precautions: The lowest dosage that will control the condition under treatment should be used. Any reduction in dosage should be made gradually.

When large doses are given, some authorities advise that corticosteroids be taken with meals, and antacids taken between meals.

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, retention of salt and water, and increased excretion of potassium, but these effects are less likely to occur with synthetic derivatives, except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

In patients on corticosteroid therapy subjected to unusual stress, dosage should be increased before, during and after the stressful situation. Drug-induced secondary adrenocortical insufficiency may result from too rapid withdrawal of corticosteroids and may be minimised by gradual dosage reduction, but may persist for months after discontinuation of therapy. In any stressful situation during that period, therefore, corticosteroid therapy should be reinstated. If the patient is already receiving corticosteroids, the dose may have to be increased. Salt and/or a mineralocorticoid should be given concurrently, since mineralocorticoid secretion may be impaired.

Stopping corticosteroids after prolonged therapy may cause withdrawal symptoms including fever, myalgia,

arthralgia, and malaise. This may occur in patients even without evidence of adrenal insufficiency.

Administration of live virus vaccines, including smallpox, is contra-indicated in individuals receiving immunosuppressive doses of corticosteroids. If inactivated viral or bacterial vaccines are administered to individuals receiving immunosuppressive doses of corticosteroids, the expected serum antibody response may not be obtained. However, patients who are receiving corticosteroids as replacement therapy, e.g. for Addison's disease, may be immunised.

Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinaemia.

The use of Decadron Tablets in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate antituberculous regimen. If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation of the disease is necessary as reactivation may occur. During prolonged corticosteroid therapy, these patients should receive prophylactic chemotherapy.

Corticosteroids should be used with caution in: non-specific ulcerative colitis; if there is a probability of impending perforation, abscess or other pyogenic infection; diverticulitis; fresh intestinal anastomosis; active or latent peptic ulcer; renal insufficiency; hypertension; osteoporosis; and myasthenia gravis. Signs of peritoneal irritation following gastro-intestinal perforation in patients receiving large doses of corticosteroids may be minimal or absent. Fat embolism has been reported as a possible complication of hypercortisnism.

Corticosteroids should be used cautiously in patients with ocular herpes simplex, because of possible corneal perforation.

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis.

Corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance and inability to localise infection in patients on corticosteroids. Moreover, corticosteroids may affect the nitroblue-tetrazolium test for bacterial infection and produce false negative results.

Corticosteroids may activate latent amoebiasis. Therefore, it is recommended that latent or active amoebiasis be ruled out before initiating corticosteroid therapy in any patient who has spent time in the tropics, or any patient with unexplained diarrhoea.

Various psychic derangements may appear in patients on corticosteroids, ranging from euphoria, insomnia, mood swings, personality changes and severe depression, to frank psychotic manifestations. Existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Prolonged use of corticosteroids may produce subcapsular cataracts, glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses.

Growth and development of infants and children who are on prolonged corticosteroid therapy should be carefully scrutinised.

Steroids may increase or decrease the motility and number of spermatozoa in some patients.

Because phenytoin, phenobarbitone, ephedrine, and rifampicin may enhance the metabolic clearance of corticosteroids, resulting in decreased blood levels and reduced physiological activity, the dosage of Decadron may have to be adjusted. These interactions may interfere

with dexamethasone suppression tests which should therefore be interpreted with caution during administration of these drugs.

The prothrombin time should be checked frequently in patients who are receiving corticosteroids and coumarin anticoagulants at the same time because of reports that corticosteroids have altered the response to these anticoagulants.

Studies have shown that the usual effect produced by adding corticosteroids is inhibition of response to coumarins, although there have been some conflicting reports of potentiation not substantiated by studies.

When corticosteroids are administered concomitantly with potassium-depleting diuretics, patients should be observed closely for development of hypokalaemia.

Use in pregnancy and nursing mothers: Since adequate human reproduction studies have not been conducted with corticosteroids, their use in pregnancy, or in women of child-bearing potential, requires that the anticipated benefits be weighed against the possible hazards to the mother and embryo or foetus. Infants born to mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism. Corticosteroids appear in breast milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other unwanted effects. Mothers taking pharmacological doses of corticosteroids should therefore be advised not to breast-feed.

Side-effects: Fluid and electrolyte disturbances: Sodium retention, fluid retention, congestive heart failure in susceptible patients, potassium loss, hypokalaemic alkalosis, hypertension.

Musculoskeletal effects: Muscle weakness, steroid myopathy, loss of muscle mass, osteoporosis, vertebral compression fractures, aseptic necrosis of femoral and humeral heads, pathological fracture of long bones, tendon rupture.

Gastro-intestinal: Peptic ulcer with possible perforation and haemorrhage, perforation of the small and large bowel particularly in patients with inflammatory bowel disease, pancreatitis, abdominal distension, ulcerative oesophagitis.

Dermatological: Impaired wound healing, thin fragile skin, petechiae and ecchymoses, erythema, increased sweating, suppressed reaction to skin tests, other cutaneous reactions such as allergic dermatitis, urticaria, angioneurotic oedema.

Neurological: Convulsions, vertigo, headache. Increased intracranial pressure with papilloedema (pseudotumour cerebri) may occur usually after treatment.

Endocrine: Menstrual irregularities, development of Cushingoid state, suppression of growth in children, secondary adrenocortical and pituitary unresponsiveness (particularly in times of stress as in trauma, surgery or illness), decreased carbohydrate tolerance, manifestations of latent diabetes mellitus, increased need for insulin or oral hypoglycaemic agents in diabetics.

Ophthalmic: Posterior subcapsular cataracts, increased intra-ocular pressure, glaucoma, exophthalmos.

Metabolic: Negative nitrogen balance due to protein catabolism.

Other: Hypersensitivity; thrombo-embolism; weight gain; increased appetite; nausea; malaise.

Treatment of overdose: Anaphylactic and hypersensitivity reactions may be treated with adrenaline, positive-pressure artificial respiration and aminophylline. The patient should be kept warm and quiet.

Treatment is probably not indicated for reactions due to chronic poisoning unless the patient has a condition that would render him unusually susceptible to ill effects from corticosteroids. In this case, the stomach should be emptied and symptomatic treatment should be instituted as necessary.

Pharmaceutical precautions Keep container well closed; store in a cool place, protected from light.

Legal category POM.

Package quantities 0.5 mg: Bottles of 100 and 500.
0.75 mg: Bottles of 100.

Further information Decadron is a potent glucocorticoid with little mineralocorticoid activity. It has considerable anti-inflammatory properties, but its effect on electrolyte metabolism is slight, and thus electrolyte imbalance is not normally a problem with Decadron. In low or average doses, Decadron does not usually cause elevation of blood pressure, salt and water retention, or excessive potassium excretion.

Product licence numbers

0.5 mg 0025/5046

0.75 mg 0025/5047

DEMSE[®] ▼

Presentation Available as, two-tone blue, opaque capsules, marked 'MSD 690', and 'DEMSE[®]', containing 250 mg metyrosine.

Uses The treatment of pheochromocytoma during: pre-operative preparation of patients for surgery; management of patients when surgery is contra-indicated; prolonged treatment of patients with malignant pheochromocytoma.

Demser is not recommended for the control of essential hypertension.

Dosage and administration *Adults and children over 12 years of age:* Initially, 1 capsule (250 mg) four times a day. This may be increased by 1 or 2 capsules (250 or 500 mg) daily to a maximum of 4 g daily in divided doses. When used pre-operatively, the optimum dosage should be given for at least five to seven days before surgery.

The optimum dosage range is usually between 8 and 12 capsules (2 to 3 g) a day, titrated by monitoring clinical symptoms and catecholamine excretion. In patients who are hypertensive, dosage should be adjusted to lower blood pressure and control symptoms; in patients whose blood pressure is normal, adjust dosage until the urinary excretion of catecholamines and/or vanillylmandelic acid is reduced by 50% or more.

It is recommended that an alpha-adrenergic blocking agent such as phenoxybenzamine be added if control with Demser is not adequate.

The use of Demser in children under twelve years of age has been limited, and a dosage recommendation cannot be made.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity.

Warnings: When Demser is used pre-operatively, especially in combination with alpha-adrenoceptor blocking agents, blood volume must be maintained during and after surgery to avoid hypotension and decreased perfusion of vital organs. During surgery, life-threatening

arrhythmias may occur requiring treatment with a beta-blocker or lignocaine. Blood pressure and ECG should be monitored continuously throughout surgery.

Demser does not eliminate the danger of arrhythmias or hypertensive crises occurring during manipulation of the tumour and additional alpha-blockade may be necessary.

Precautions: Crystalluria and urolithiasis have occurred in dogs; and crystalluria has been seen in a few patients. To minimise the risk, fluid intake should be sufficient to maintain a urine volume of 2,000 ml or more daily. Urine should be examined routinely, and if metyrosine crystals (needles or rods) are seen, fluid intake should be increased. If crystalluria persists, the dosage of Demser should be reduced or discontinued.

Caution should be observed in administering Demser to patients receiving phenothiazines or haloperidol because the extrapyramidal effects of these drugs can be expected to be potentiated by inhibition of catecholamine synthesis; this has been documented to date only for haloperidol.

No evidence of adverse effects on hepatic, haematological or other functions (except for a few instances of increased SGOT) has been seen during clinical trials. However, total experience in man is limited to approximately 300 patients, and few patients have been studied long-term. Therefore, suitable laboratory tests should be carried out periodically in patients on prolonged therapy, particularly those with impaired hepatic or renal function.

Demser may cause spurious increases in urinary catecholamine measurements.

Nursing mothers: It is not known whether Demser is excreted in human milk. Mothers who need Demser should stop nursing.

Pregnancy: Complete reproduction studies have not been performed in animals to determine whether Demser affects fertility in males or females, has teratogenic potential, or has other adverse effects on the foetus. There are no well-controlled studies of Demser in pregnant women. The use of Demser in pregnant women should be avoided, if possible, but may be appropriate when anticipated benefits outweigh the potential risks.

Adverse reactions: The most common adverse reaction to Demser is moderate to severe sedation, which has been observed in almost all patients. It occurs at both low and high dosages. Sedative effects begin within the first 24 hours of therapy, are maximal after two to three days, and tend to wane during the next few days. Sedation usually is not obvious after one week unless the dosage is increased, but at dosages greater than 2,000 mg/day some degree of sedation or fatigue may persist.

When receiving Demser, patients should be warned about engaging in activities requiring mental alertness and motor co-ordination, such as driving a motor vehicle or operating machinery. Demser may have additive effects with alcohol and other CNS depressants, e.g. hypnotics, sedatives, tranquilisers, anti-anxiety agents.

In most patients who experience sedation, temporary changes in sleep pattern occur following withdrawal of the drug. Changes consist of insomnia that may last for two or three days and feelings of increased alertness and ambition. Even patients who do not experience sedation while on Demser may report symptoms of psychic stimulation when the drug is discontinued.

Extrapyramidal signs such as drooling, speech difficulty and tremor have been reported in approximately

10% of patients, occasionally with trismus and frank parkinsonism.

Anxiety, depression, hallucinations, disorientation and confusion have occurred but may disappear on reduction of the dosage.

Diarrhoea occurs in about 10% of patients, and may be severe. Infrequently, slight swelling of the breast, galactorrhoea, nasal stuffiness, decreased salivation, dry mouth, headache, nausea, vomiting, abdominal pain, and impotence or failure of ejaculation may occur. Crystalluria transient dysuria and haematuria have been seen in a few patients. Eosinophilia, increased SGOT levels, peripheral oedema, and hypersensitivity such as urticaria and pharyngeal oedema has been reported rarely.

Treatment of overdosage: There is no clinical experience with overdosage; consequently, the signs, symptoms and treatment have not been identified.

Pharmaceutical precautions Store in a cool place, protected from light.

Legal category POM.

Package quantities Bottles of 100.

Further information Nil.

Product licence number 0025/0132.

DEPROPANEX*

Presentation Light amber, clear, saline solution of a chemically derived, protein-free, nitrogenous fraction obtained by an acid-alcohol treatment of mammalian pancreas. Phenol, 0.25%, is added as a preservative.

Uses Intermittent claudication: Because of its vasodilating and adrenaline-antagonising properties, Depropanex has produced favourable results in the treatment of intermittent claudication associated with arteriosclerotic disease and thrombo-angiitis. In some cases, a drop in systolic and diastolic blood pressures may be expected. Intermittent claudication is usually reduced following the use of the preparation. Patients with occlusive arterial disease, in whom intermittent claudication is the predominant symptom, are better able to withstand exertion while under treatment with Depropanex.

Renal and ureteral colic: Many patients with ureteral occlusion due to calculus, or spasm have benefited by relaxation of spasm and prompt relief of pain within a few minutes of treatment with pancreatic extract. Depropanex has been used with good results in ureteral and renal colic due to stone and kinking, to facilitate the use of a catheter beyond the ureteral stone, and in instrumental removal of calculi in the lower ureter.

Spastic ureteritis: Depropanex is a valuable anti-spasmodic agent in the treatment of spastic ureteritis when injected intramuscularly prior to introduction of the cystoscope and at intervals following dilatation. This pancreatic extract has also been used in preparation for intravenous pyelography. It reduces ureteral peristalsis and minimises gas formation in the intestinal tract.

Biliary colic: When used in conjunction with sedation, Depropanex has been found effective in the relief of the spasm, pain and distress of biliary colic.

Dysmenorrhoea: Since extensive clinical experience has shown that Depropanex is a valuable spasmolytic agent in peripheral vascular disease and in urology, it has been used in the treatment of a number of patients with severe

primary dysmenorrhoea to diminish the contractions of the menstruating uterus.

Surgery: Depropanex has been used successfully in the control of paralytic ileus following abdominal surgery. When this preparation was used routinely, patients had a more comfortable post-operative period with less nausea, vomiting, and abdominal distension than would ordinarily have been expected.

Ophthalmology: Depropanex has also been found to be of value in the treatment of certain ocular conditions where prolonged vasodilatation is desired. These include toxic amblyopia, resolving optic neuritis, and retrobulbar neuritis. The persistence of vasodilatation and the absence of undesirable side-effects are important advantages of Depropanex.

Dosage and administration Depropanex is to be administered by the intramuscular route only. Recommended dosages are given below:

In chronic vascular diseases: 2-3 ml every other day, depending on the severity of the condition and the response of the patient.

In acute contraction of smooth muscles, as in renal colic: 3-5 ml.

In preparation for pyelography: 4 ml injected intramuscularly ten minutes before intravenous administration of the dye.

For the treatment of primary dysmenorrhoea: 2-4 ml.

Following abdominal surgery: Good results have been obtained with 4 ml twice a day for three to five days post-operatively. The first 4 ml injection should be administered soon after the operation.

In certain ocular conditions where prolonged vasodilatation is desired: 1 ml twice a week should give favourable results.

Contra-indications, warnings, etc Depropanex is not recommended for intravenous administration. Injections of average doses may cause a decrease in systolic and diastolic pressures. Symptomatic hypotension may possibly occur after injection of large doses.

Treatment of overdosage: Generally symptomatic and supportive.

Pharmaceutical precautions No specific precautions required.

Legal category POM.

Package quantities Vials of 10 ml.

Further information Nil.

Product licence number 0025/5078.

DERMOGESIC*

Presentation Pink, non-greasy ointment containing, in each gram, 80 mg Calamine BP, 30 mg Benzocaine BP and 0.5 mg hexylated metacresol.

Uses Analgesic calamine ointment.

For relief of itching and skin irritations arising from allergic conditions, minor sunburn, insect bites and chafing.

Dosage and administration For external use only. Apply a small amount to the affected area two or three times a day. Before use, dry the affected surface thoroughly with clean gauze or cotton.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to ingredients, particularly benzocaine.

Precautions: Do not use in the eyes. Do not apply to large areas of the body. Not for prolonged use.

If sensitivity reactions appear, the use of Dermogesic should be discontinued. This product should be kept out of the reach of children.

Side-effects: None reported.

Treatment of overdosage: Not applicable.

Pharmaceutical precautions Store in a cool dry place, at temperatures below 30°C.

Legal category P.

Package quantities Tubes of 25 g.

Further information Nil.

Product licence number 0025/5063.

EDECIN*

Presentation White, half-scored tablets, marked 'MSD 90', containing 50 mg Ethacrynic Acid BP.

Injection, vials containing sodium ethacrylate equivalent to 50 mg ethacrynic acid, as a dry, lyophilised powder.

Uses Diuretic.

For use in patients requiring an agent with greater diuretic potential than those commonly employed. For oedema of:

Congestive heart failure, including chronic congestive heart failure accompanying arteriosclerotic heart disease, rheumatic heart disease, hypertensive cardiovascular disease, pulmonary heart disease or congenital heart disease; *pulmonary oedema* (in emergency, Edecrin Injection is recommended); *renal oedema*, including that of the nephrotic syndrome and other renal diseases where a diuretic is indicated, even in many patients with marked impairment of renal function (Edecrin should be discontinued immediately, however, if there is further deterioration in renal function); *hepatic cirrhosis with ascites* (it is usually desirable to initiate therapy in hospital); *oedema due to other causes* including ascites due to malignancy, idiopathic oedema and lymphoedema. In children (over 2 years old) with oedema due to the nephrotic syndrome or to congenital heart disease. (Edecrin Injection is not recommended for children.)

Edecrin Injection is useful in the treatment of acute pulmonary oedema and other conditions where urgent diuresis is required, or where patients are unable to swallow tablets.

Dosage and administration Dosage should be carefully regulated to prevent a more rapid or substantial diuresis than necessary. Response is usually closely related to the degree of oedema and to the dosage used; the presence and magnitude of aldosteronism largely determines the degree of potassium excretion. Excessive diuresis may be avoided if dosage increases are made by small amounts. Daily weighing of the patient under standard conditions and, where possible, serum electrolyte determinations will greatly contribute to the success of treatment.

Oral therapy: Usual initial adult dosage: 50 mg (1 tablet) a day given immediately after breakfast. When an urgent diuresis is essential, as in pulmonary oedema, an initial

dosage substantially higher than 50 mg will be necessary. (In cases of emergency, Edecrin Injection is recommended.)

Adjustment: Increase, as necessary, by amounts of 25–50 mg ($\frac{1}{2}$ –1 tablet) a day, to the lowest dosage which will produce a gradual weight loss (about $\frac{1}{2}$ –1 kg a day).

Effective dosage range: Usually 50–150 mg (1–3 tablets) a day. Patients with severe refractory oedema may need a higher dosage. This should be achieved gradually, and in no case should exceed 400 mg (8 tablets) a day. When the total daily requirement is higher than 50 mg, it should be divided into 2 doses after meals.

Maintenance dosage: This should be adjusted to fit the changing needs of the patient. It is often less than the initial effective dosage. Treatment may be maintained by continuous or intermittent therapy. Intermittent therapy can usually be used without loss of therapeutic response. Edecrin may be administered on alternate days, or preferably for two- to three-day periods alternating with two or three days' rest, allowing more time for readjustment of any electrolyte imbalance.

Replacement of other diuretics: Transfer to Edecrin from other diuretic agents may be by simple substitution, as long as the recommended dosage schedule is followed.

Continuous or intermittent use of Edecrin may eliminate the need for injections or mercurials.

Children: Initially 25 mg ($\frac{1}{2}$ tablet) taken immediately after breakfast. If necessary, this should be carefully increased by 25 mg ($\frac{1}{2}$ tablet) a day until an effective dosage is achieved. A dosage for infants (under 2 years) has not been established.

Other considerations: Larger doses of Edecrin may be necessary to produce effective diuresis in renal oedema than in congestive failure. Edecrin has additive effects when used with other diuretics. It may potentiate the effect of carbonic anhydrase inhibitors, increasing sodium and potassium excretion. If Edecrin is given to patients already receiving a carbonic anhydrase inhibitor, the initial dose and increments should be only 25 mg ($\frac{1}{2}$ tablet).

In severely oedematous patients. Edecrin may occasionally cause a massive diuresis with resultant imbalance. The dosage, therefore, must be carefully regulated.

Parenteral therapy: Usual adult intravenous dose: 50 mg, or 0.5–1 mg/kg of body weight. Some patients with renal oedema may require larger doses. Single intravenous doses of up to 100 mg have been used in critical situations.

To reconstitute the dry material, 50 ml of isotonic saline or 5% dextrose is added to the vial. (Some 5% dextrose injection solutions have a pH below 5. If such a preparation is used as diluent, the resulting solution may be cloudy or opalescent. The use of such a solution is not recommended.) The solution may be given slowly through the tubing of a running infusion, or by direct intravenous injection over several minutes. If repeated injections are necessary, the site of injections should be rotated to avoid possible thrombophlebitis. Edecrin Injection should not be given subcutaneously or intramuscularly because of local pain and irritation.

Edecrin Injection should not be mixed with whole blood or blood derivatives. If it is desired to administer it at the same time as a blood transfusion, it should be given independently.

Children: As paediatric experience with Edecrin Injection is limited, it is not recommended for children.

Contra-indications, warnings, etc

Contra-indications: Anuria, infants (under 2 years). For 'Use in pregnancy and the nursing mother' see 'Precautions'. Hypersensitivity to any component of Edecrin.

Precautions: Edecrin should be given with caution to patients with advanced cirrhosis of the liver, particularly those with a history of episodes of electrolyte imbalance or hepatic encephalopathy. Edecrin may precipitate hepatic coma and death.

The effects of Edecrin on electrolytes are based on its renal pharmacology and are usually dose related. To minimise the possibility of profound electrolyte and water loss, therapy should be initiated with a low dosage and this carefully adjusted as necessary, intermittent dosage should be used where possible and the patient weighed regularly throughout treatment. If diuresis is excessive, Edecrin should be withdrawn until homeostasis is restored. When excessive electrolyte loss occurs, the imbalance should be corrected or the administration of Edecrin should be temporarily suspended.

Frequent serum electrolyte, alkali reserve and blood urea determinations should be made early in therapy, and periodically thereafter while active diuresis is taking place. Any electrolyte abnormality should be corrected or the drug temporarily withdrawn. If increasing electrolyte imbalance, azotaemia and/or oliguria occur during treatment of severe progressive renal disease, the diuretic should be discontinued.

Too vigorous a diuresis may induce an acute hypotensive episode. In elderly cardiac patients, severe diuresis may cause a rapid contraction of plasma volume and haemoconcentration which should be avoided to prevent the possible development of such thromboembolic episodes as cerebral thrombosis or pulmonary embolism.

Potassium supplements or a generous intake of potassium-rich foods is often advisable during treatment with Edecrin in patients receiving potassium-depleting steroids, and in patients receiving digitalis where hypokalaemia may precipitate digitalis toxicity. When metabolic alkalosis may be anticipated (e.g. in cirrhosis with ascites), a potassium-conserving agent or potassium chloride may mitigate or prevent hypokalaemia.

Weakness, muscle cramps, paraesthesiae, thirst, anorexia, and signs of hyponatraemia, hypokalaemia and/or hypochloraemic alkalosis may follow vigorous or excessive diuresis or be accentuated by rigid salt restriction. Rarely, tetany has been reported following vigorous diuresis.

Note: Symptoms and signs which might indicate ulceration or obstruction of the small bowel in patients taking tablets or capsules containing potassium salts are indications for stopping treatment with such preparations immediately.

The chance of the chloruretic effect of Edecrin giving rise to bicarbonate retention and metabolic alkalosis may be corrected by giving chloride (ammonium or arginine chloride). Ammonium chloride should not be given to cirrhotic patients.

A reasonable salt intake will usually prevent hyponatraemia and hypochloraemia. However, cirrhotic patients usually require at least moderate salt restriction during diuretic therapy. Hypoproteinaemia may reduce the response to Edecrin and the use of salt-poor albumin considered.

A few patients on Edecrin have had a sudden onset of profuse, watery diarrhoea. If this occurs, and all other causative factors are ruled out, Edecrin should be discontinued and not readministered.

When Edecrin is given to patients receiving antihypertensive agents, the dosage of these agents may require adjustment; orthostatic hypotension may occur. The value and safety of Edecrin itself in the treatment of hypertension has not been established.

Edecrin has little or no effect on glomerular filtration rate or renal blood flow, except immediately after a pronounced reduction in plasma volume following rapid diuresis.

An increase in blood urea may occur. Although transient, it may usually be readily reversed by discontinuing Edecrin.

The concurrent use of such drugs as aminoglycosides with Edecrin should be avoided because of the risk of increasing their ototoxic potential.

Several drugs, including Edecrin, have been shown to displace warfarin from plasma protein. In patients receiving both types of drug, a reduction in the dosage of the anticoagulant may therefore be required.

Lithium should generally not be given to patients receiving diuretics, since the risk of lithium toxicity is very high in such patients.

Edecrin may increase the risk of gastric haemorrhage associated with corticosteroid treatment.

Use in pregnancy and the nursing mother: Edecrin is not recommended in pregnant patients. If administration in confirmed or suspected pregnancy is considered, the benefits should be weighed against possible hazards to the foetus. Safety and efficacy for use in toxæmia of pregnancy have not been established. Successive generation studies on laboratory animals have shown no foetal abnormalities. Edecrin is contra-indicated in nursing mothers. If its use is deemed essential, the patient should stop nursing.

Side-effects: Gastro-intestinal upsets include anorexia, malaise, abdominal discomfort or pain, dysphagia, nausea, vomiting and diarrhoea. They have occurred more frequently with large doses or after one to three months of continuous therapy. A few patients have had sudden onset of profuse, watery diarrhoea. Gastro-intestinal bleeding has occurred in some patients.

Reversible hyperuricaemia and decreased urinary urate excretion may occur. Acute gout may be precipitated. Acute symptomatic hypoglycaemia with convulsions occurred in two uraemic patients who received doses higher than those recommended.

Hyperglycaemia has occurred in a few patients, most of whom had decompensated cirrhosis of the liver. Rarely, acute pancreatitis has been reported in patients receiving diuretics, including Edecrin.

Jaundice, abnormal results of liver function tests, agranulocytosis, severe neutropenia and Henoch-Schönlein purpura (in rheumatic heart disease), have been reported rarely in seriously ill patients receiving several drugs including Edecrin. Thrombocytopenia has been reported rarely.

A number of possibly drug-related deaths have occurred in critically ill patients refractory to other diuretics. These have generally fallen into two categories: patients with severe myocardial disease who were receiving digitalis and presumably developed acute hypokalaemia with fatal arrhythmias; patients with severely decompensated hepatic cirrhosis with ascites, with or without accompanying encephalopathy, who were in electrolyte imbalance and died following intensification of the electrolyte deficit.

Skin rash, headache, fever, rigors, blurred vision, fatigue, apprehension and confusion have occurred

infrequently. Rarely, haematuria has been reported. Deafness, tinnitus and vertigo with a sense of fullness in the ears, have occurred, most frequently in patients with severe impairment of renal function. These symptoms have been associated most often with intravenous administration and with doses in excess of those recommended. The deafness has usually been reversible and temporary (1-24 hours), but in some critically ill patients, the hearing loss has been permanent. A number of these patients were also receiving drugs previously known to be ototoxic.

Edecrin Injection has occasionally caused local irritation and pain due to extravasation of injected fluid.

Treatment of overdosage: Symptomatic and supportive; no specific antidote. Emesis should be induced or gastric lavage performed. Dehydration, electrolyte imbalance, hepatic coma and hypotension should be corrected by standard methods. If respiration is impaired, oxygen or artificial respiration should be given.

Pharmaceutical precautions Keep tablet container well closed. Store tablets and injection in a cool place, protected from light. Injection: to reconstitute the lyophilised material, 50 ml of isotonic saline or 5% dextrose is added to the vial. (Some 5% dextrose injection solutions have a pH below 5. If such a preparation is used as diluent, the resulting solution may be cloudy. The use of such a solution is not recommended.) Any unused reconstituted solution should be discarded after 24 hours.

Legal category POM.

Package quantities *Tablets:* Bottles of 100 and 500.

Injection: Vials containing sodium ethacrylate equivalent to 50 mg ethacrynic acid.

Further information Onset of action is usually apparent within 30 minutes of oral administration, peak effect is attained in about two hours, and diuresis lasts for six to eight hours. Onset of action is usually observed within five minutes after intravenous injection.

Product licence numbers

Tablets 0025/5006

Injection 0025/5007

HYDROCORTONE* CREAM AND OINTMENT

Presentation Hydrocortone is available as a non-greasy cream containing, in each gram, 10 mg Hydrocortisone Acetate BP, and as a greasy ointment containing, in each gram, 10 mg Hydrocortisone BP, each in packs of 15 g.

Uses Relief of the inflammatory manifestations of corticosteroid-responsive dermatoses.

Dosage and administration A small quantity of Hydrocortone is applied to the affected skin three or four times a day after gently cleansing the area. Before Hydrocortone is used in the ear, the aural canal should be thoroughly cleaned and sponged dry. A thin coating of the cream or ointment should be applied to the affected canal area three or four times a day.

Contra-indications, warnings, etc

Contra-indications: Tuberculosis of the skin, fungal infections, chickenpox, vaccinia, herpes simplex; known hypersensitivity to any component of the cream or ointment. Hydrocortone should not be used in the ear if the drum is perforated.

Precautions: If irritation develops, appropriate therapy should be substituted.

In the presence of an infection, an appropriate antifungal or antibacterial agent should be used, and if the infection does not respond quickly, treatment with Hydrocortone should be discontinued until the infection has been adequately controlled.

If extensive areas are treated with Hydrocortone, there will be increased systemic absorption of the corticosteroid and suitable precautions should be taken, particularly in children. The use of occlusive dressings with Hydrocortone is not recommended. In infants, continuous long-term topical administration of corticosteroids should be avoided; adrenal suppression can occur, even when occlusive dressings are not employed. Hydrocortone is not recommended for ophthalmic use. When applied to the eyelid or skin near the eyes, Hydrocortone may enter the eye, and prolonged ocular exposure may cause steroid glaucoma.

Use in pregnancy: Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Side-effects: Local side-effects reported with corticosteroids are burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae, and miliaria. Contact sensitivity to a particular dressing may occur.

Treatment of overdosage: Not applicable.

Pharmaceutical precautions Keep in a cool place.

Legal category POM.

Package quantities Cream 1%: Tubes containing 15 g.

Ointment 1%: Tubes containing 15 g.

Further information Nil.

Product licence numbers

Cream 0025/5051

Ointment 0025/5052

HYDROCORTONE* TABLETS

Presentation White, half-scored tablets, marked 'MSD 619', containing 10 mg Hydrocortisone BP. White, half-scored tablets, marked 'MSD 625', containing 20 mg Hydrocortisone BP.

Uses Corticosteroid.

Allergic states: Control of severe or incapacitating allergic conditions not responsive to adequate trials of conventional treatment: seasonal or perennial allergic rhinitis, bronchial asthma, contact dermatitis, atopic dermatitis, serum sickness, drug hypersensitivity reactions.

Rheumatic disorders: As adjunctive therapy for short-term administration during an acute episode or exacerbation of: psoriatic arthritis, rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy), ankylosing spondylitis, acute and subacute bursitis, acute non-specific tenosynovitis, acute gouty arthritis, post-

traumatic osteoarthritis, synovitis of osteoarthritis, epicondylitis.

Dermatological diseases: Pemphigus, bullous dermatitis herpetiformis, severe erythema multiforme (Stevens-Johnson syndrome), exfoliative dermatitis, mycosis fungoides, severe psoriasis, severe seborrhoeic dermatitis.

Ophthalmic diseases: Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as: allergic conjunctivitis, keratitis, allergic corneal marginal ulcers, herpes zoster ophthalmicus, iritis and iridocyclitis, chorioretinitis, anterior segment inflammation, diffuse posterior uveitis and choroiditis, optic neuritis, sympathetic ophthalmia.

Endocrine disorders: Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisone is the first choice; synthetic analogues may be used in conjunction with mineralocorticoids where applicable; in infancy mineralocorticoid supplementation is of particular importance), congenital adrenal hyperplasia, non-suppurative thyroiditis, hypercalcaemia associated with cancer.

Respiratory diseases: Symptomatic sarcoidosis, Löf-ler's syndrome not manageable by other means, berylliosis, fulminating or disseminated pulmonary tuberculosis when accompanied by appropriate antituberculous chemotherapy, aspiration pneumonitis.

Haematological disorders: Idiopathic thrombocytopenic purpura in adults, secondary thrombocytopenia in adults, acquired (auto-immune) haemolytic anaemia, erythroblastopenia (RBC anaemia), congenital (erythroid) hypoplastic anaemia.

Neoplastic diseases: For palliative management of: leukaemias and lymphomas in adults, acute leukaemia of childhood.

Oedematous states: To induce a diuresis or remission of proteinuria in the nephrotic syndrome without uraemia, of the idiopathic type or that due to lupus erythematosus.

Gastro-intestinal diseases: During a critical period of the disease in: ulcerative colitis, regional enteritis.

Miscellaneous: Tuberculous meningitis with subarachnoid block or impending block, when accompanied by appropriate antituberculous chemotherapy. Trichinosis with neurological or myocardial involvement. During an exacerbation or as maintenance therapy in selected cases of: systemic lupus erythematosus, acute rheumatic carditis, systemic dermatomyositis (polymyositis).

Dosage and administration *General considerations:* Therapy is governed by the following principles:

1. Dosage must be determined for each patient according to the severity, prognosis and expected duration of the disease and the response to Hydrocortone. For infants and children, the recommended dosages usually will have to be reduced, but dosage should be dictated by the severity of the condition rather than by age or body weight.

2. Corticosteroid therapy is an adjunct to, not a replacement for, conventional therapy, which should be instituted as indicated.

3. Dosage must be decreased or therapy gradually discontinued when Hydrocortone has been taken for more than a few days.

4. Continued supervision of the patient after cessation of corticosteroid therapy is essential, as there may be sudden reappearance of severe manifestations of the disease for which the patient was being treated.

In acute conditions where prompt relief is urgent, large doses are permissible and may be mandatory for a short period.

In chronic conditions requiring long-term therapy, the lowest dosage that provides adequate, but not necessarily complete, relief should be used. If a high dosage for prolonged periods is considered essential, patients must be observed closely for signs that might indicate that a reduction in dosage or withdrawal of the corticosteroid is necessary. Chronic conditions are subject to periods of spontaneous remission. When such periods occur, corticosteroids should be gradually discontinued.

Routine laboratory studies such as urine analysis, two-hour post-prandial blood sugar, determinations of blood pressure and body weight, and a chest X-ray should be carried out at regular intervals during prolonged therapy. Periodic determinations of serum potassium are advisable if large dosages are being used. Upper gastrointestinal tract X-rays should be taken when treatment is prolonged, in patients with history of ulcer, or when there is gastric distress.

The daily dosage should be divided into 3 or 4 doses.

Specific dosage recommendations: In chronic, usually non-fatal diseases, including endocrine and chronic rheumatic disorders, oedematous states, respiratory and gastro-intestinal diseases, some dermatological diseases and haematological disorders, therapy should be started with a low dosage (20–40 mg a day) and gradually increased to the smallest amount that gives the desired degree of symptomatic relief.

When symptoms have been suppressed adequately, dosage should be maintained at the minimum amount capable of providing sufficient relief without excessive hormonal effects.

In chronic adrenocortical insufficiency, 10–20 mg a day, or occasionally more, with 4–6 g of sodium chloride or 1–3 mg of desoxycorticosterone acetate. When immediate support is mandatory, one of the soluble adrenocortical hormone preparations (e.g. Decadron® Injection, dexamethasone sodium phosphate, MSD), which may be effective within minutes after parenteral administration, can be life-saving.

In congenital adrenal hyperplasia, the usual daily dosage is 10–30 mg.

In acute, non-fatal diseases, including allergic states, ophthalmic diseases, acute and subacute rheumatic disorders, dosage ranges between 60 and 120 mg a day; however, higher dosages are necessary in some patients. Since the course of these conditions is self-limiting, prolonged maintenance therapy is not usually necessary.

In chronic, potentially fatal diseases such as systemic lupus erythematosus, pemphigus, symptomatic sarcoidosis, the recommended initial dosage is 60–120 mg a day; higher dosages are necessary in some patients. As soon as adequate relief is obtained, the dosage should be reduced gradually to the minimum amount that will produce the desired therapeutic effect.

When the disease is acute and life-threatening (e.g. acute rheumatic carditis, crisis of systemic lupus erythematosus, severe allergic reactions, pemphigus, neoplastic diseases), the initial dosage is between 100 and 240 mg a day, administered in at least 4 divided doses; this dosage may have to be increased in some patients to establish control. As soon as control is attained, the dosage should be reduced gradually to the minimum amount that will maintain relief.

When an extremely rapid onset of action is desired, Decadron Injection may be administered intravenously for the first 2 or 3 doses.

Adrenaline is the drug of first choice in severe allergic reactions. Hydrocortone Tablets are useful either concurrently or as supplementary therapy.

As massive therapy in certain conditions, such as acute leukaemia, the nephrotic syndrome, and pemphigus, the recommended dosage is 90 mg or more a day. Patients receiving such a high dosage must be observed very closely for the appearance of severe reactions.

Contra-indications, warnings, etc

Contra-indications: Systemic fungal infections. Hypersensitivity to the drug.

Precautions: The lowest possible dosage of corticosteroid should be used to control the condition under treatment, and when reduction in dosage is possible, the reduction should be gradual.

Average and large dosages of hydrocortisone or cortisone can cause elevation of blood pressure, salt and water retention, and increase excretion of potassium. These effects are less likely to occur with the synthetic derivatives except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

When large doses are given, some authorities advise that corticosteroids be taken with meals and antacids taken between meals.

In patients on corticosteroid therapy subjected to unusual stress, increased dosage of rapidly acting corticosteroids before, during and after the stressful situation is indicated.

Drug-induced secondary adrenocortical insufficiency may result from too rapid withdrawal of corticosteroids and may be minimised by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstated. If the patient is receiving steroids already, the dosage may have to be increased. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

Stopping corticosteroids after prolonged therapy may cause withdrawal symptoms including fever, myalgia, arthralgia, and malaise. This may occur in patients even without evidence of adrenal insufficiency.

Administration of live virus vaccines, including smallpox, is contra-indicated in individuals receiving immunosuppressive doses of corticosteroids. If inactivated viral or bacterial vaccines are administered to individuals receiving immunosuppressive doses of corticosteroids, the expected serum antibody response may not be obtained. However, immunisation procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e.g. for Addison's disease.

Acetylsalicylic acid should be used cautiously in conjunction with corticosteroids in hypoprothrombinaemia.

The use of Hydrocortone Tablets in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate antituberculous regimen. If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged

corticosteroid therapy, these patients should receive prophylactic chemotherapy.

Corticosteroids should be used with caution in: non-specific ulcerative colitis if there is a probability of impending perforation, abscess or other pyogenic infection; diverticulitis; fresh intestinal anastomoses; active or latent peptic ulcer; renal insufficiency; hypertension; osteoporosis; and myasthenia gravis. Signs of peritoneal irritation following gastro-intestinal perforation in patients receiving large doses of corticosteroids may be minimal or absent. Fat embolism has been reported as a possible complication of hypercortisolemia.

Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.

There is an enhanced effect of corticosteroids on patients with hypothyroidism and in those with cirrhosis.

Corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance and inability to localise infection when corticosteroids are used.

Moreover, corticosteroids may affect the nitroblue-tetrazolium test for bacterial infection and produce false negative results.

Corticosteroids may activate latent amoebiasis. Therefore it is recommended that latent or active amoebiasis be ruled out before initiating corticosteroid therapy in any patient who has spent time in the tropics or any patient with unexplained diarrhoea.

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes and severe depression, to frank psychotic manifestations. Also, existing emotional instability of psychotic tendencies may be aggravated by corticosteroids.

Prolonged use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses.

Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.

Corticosteroids may increase or decrease motility and number of spermatozoa in some patients.

Phenytoin, ephedrine, phenobarbitone and rifampicin may enhance the metabolic clearance of corticosteroids, resulting in decreased blood levels and lessened physiological activity, thus requiring adjustment in corticosteroid dosage.

The prothrombin time should be checked frequently in patients who are receiving corticosteroids and coumarin anticoagulants at the same time because of reports that corticosteroids have altered the response to these anticoagulants. Studies have shown that the usual effect produced by adding corticosteroids is inhibition of response to coumarins, although there have been some conflicting reports of potentiation not substantiated by studies.

When corticosteroids are administered concomitantly with potassium-depleting diuretics, patients should be observed closely for development of hypokalaemia.

Use in pregnancy and nursing mothers: Since adequate human reproduction studies have not been done with corticosteroids, the use of these drugs in pregnancy, or in women of child-bearing potential requires that the possible benefits of the drug be weighed against the potential hazards to the mother and embryo or foetus.

Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Corticosteroids appear in breast milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other unwanted effects. Mothers taking pharmacological doses of corticosteroids should be advised not to nurse.

Side-effects: *Fluid and electrolyte disturbances:* Sodium retention, fluid retention, congestive heart failure in susceptible patients, potassium loss, hypokalaemic alkalosis, hypertension.

Musculoskeletal effects: Muscle weakness, steroid myopathy, loss of muscle mass, osteoporosis, vertebral compression fractures, aseptic necrosis of femoral and humeral heads, pathological fracture of long bones, tendon rupture.

Gastro-intestinal: Peptic ulcer with possible perforation and haemorrhage, perforation of the small and large bowel particularly in patients with inflammatory bowel disease, pancreatitis, abdominal distension, ulcerative oesophagitis.

Dermatological: Impaired wound healing, thin fragile skin, petechiae and ecchymoses, erythema, increased sweating, may suppress reactions to skin tests, other cutaneous reactions such as allergic dermatitis, urticaria, angioneurotic oedema.

Neurological: Convulsions, increased intracranial pressure with papilloedema (pseudotumour cerebri) usually after treatment, vertigo, headache.

Endocrine: Menstrual irregularities, development of Cushingoid state, suppression of growth in children, secondary adrenocortical and pituitary unresponsiveness (particularly in times of stress, as in trauma, surgery, or illness), decreased carbohydrate tolerance, manifestations of latent diabetes mellitus, increased requirements for insulin or oral hypoglycaemic agents in diabetics.

Ophthalmic: Posterior subcapsular cataracts, increased intra-ocular pressure, glaucoma, exophthalmos.

Metabolic: Negative nitrogen balance due to protein catabolism.

Other: Hypersensitivity, thromboembolism, weight gain, increased appetite, nausea, malaise.

Treatment of overdosage: Anaphylactic and hypersensitivity reactions may be treated with adrenaline, positive-pressure artificial respiration and aminophylline. The patient should be kept warm and quiet.

Treatment is probably not indicated for reactions due to chronic poisoning unless the patient has a condition that would render him unusually susceptible to ill effects from corticosteroids. In this case, symptomatic treatment should be instituted as necessary.

Pharmaceutical precautions Keep container well closed, store in a cool place, protected from light.

Legal category POM.

Package quantities 10 mg: Bottles of 100.

20 mg: Bottles of 100.

Further information Nil.

Product licence numbers

10 mg 0025/5053

20 mg 0025/5054

HYDRODERM*

Presentation A white, translucent ointment contain-

ing, in each gram, 10 mg Hydrocortisone BP, 5 mg Neomycin Sulphate BP and 1,000 units Bacitracin Zinc BP, in an emollient base.

Uses Topical corticosteroid with topical antibiotics.

Hydroderm is recommended for treatment of the following skin disorders when they are threatened with infection caused by organisms sensitive to neomycin or bacitracin: allergic dermatoses (such as contact dermatitis), eczematoid dermatitis, atopic dermatitis (allergic eczema), infantile eczema (but see 'Precautions'), food eczema, neurodermatitis, pruritus with lichenification, seborrhoeic dermatitis, non-specific anogenital pruritus, miliaria, intertrigo, otitis externa (but not where the drum is perforated), acute actinic dermatitis, including severe sunburn and insect bites.

Dosage and administration A small amount of Hydroderm should be applied to the affected area two or three times a day. The area to be treated should be carefully cleansed before application, so that the possibility of introducing infection is minimised. Hydroderm should be applied gently to avoid damage to the skin. Before using Hydroderm in the ear, ensure that the eardrum is intact, and that the aural canal is thoroughly clean and sponged dry. A thin coating of Hydroderm should be applied to the affected surface of the ear with a cotton-tipped applicator two or three times a day. When a favourable response is obtained, the number of daily applications of Hydroderm may be reduced to one or two, and eventually therapy may be discontinued.

Contra-indications, warnings, etc

Contra-indications: Tuberculosis of the skin, chickenpox, herpes simplex, vaccinia, or fungal infections; sensitivity to any of the components of Hydroderm. The ointment should not be used in the ear if the drum is perforated.

Precautions: Hydroderm should not be used ophthalmically.

Ototoxicity and nephrotoxicity have been reported following the topical application of neomycin where systemic absorption was possible. Prolonged use of Hydroderm should therefore be avoided on such lesions as extensive burns, trophic ulceration or infected wounds where absorption of neomycin is possible.

Topical corticosteroids may mask or enhance incipient infection. If any infection does not respond promptly, treatment with Hydroderm should be discontinued until the infection has been controlled by other means. If a new infection resistant to neomycin or bacitracin appears during therapy, it should be controlled by appropriate measures.

A few individuals may be sensitive to one or more components of Hydroderm, and therapy should always be stopped if this occurs. Sensitivity to neomycin may occur, especially if the skin is abraded. Several reports indicate an increase in the number of persons sensitive to neomycin.

The use of occlusive dressings with Hydroderm is not recommended. In infants, continuous long-term topical administration of corticosteroids should be avoided. Adrenal suppression can occur, even when occlusive dressings are not employed.

Use in pregnancy: Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Side-effects: Burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, and hypopigmentation. Perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae, and miliaria may also occur.

Treatment of overdosage: Not applicable.

Pharmaceutical precautions Keep in a cool place.

Legal category POM.

Package quantities Tubes of 5 g and 15 g.

Further information Hydroderm combines the anti-inflammatory, anti-allergic and antipruritic effects of a topical corticosteroid with the antibacterial action of two topically effective antibiotics.

Product licence number 0025/5055.

HYDROMET*

Presentation Salmon-pink, film-coated tablets, marked 'MSD 423', containing Methyldopa BP equivalent to 250 mg anhydrous methyldopa, and 15 mg Hydrochlorothiazide BP.

Uses Antihypertensive.

A highly effective combination of methyldopa and hydrochlorothiazide, two antihypertensive agents with complementary properties for the treatment of hypertension.

Dosage and administration *Initial dosage:* Usually 1 tablet twice a day for two days.

Adjustment: Upwards or downwards. Preferably at intervals of at least two days, until an adequate response is obtained.

The maximum recommended daily dosage of the components is 3 g of methyldopa and 200 mg hydrochlorothiazide.

Many patients experience sedation for two or three days when therapy with Hydromet is started or when the dose is increased. When increasing the dosage, therefore, it may be desirable to increase the evening dose first.

General considerations: Methyldopa is largely excreted by the kidney and patients with impaired kidney function may respond to smaller doses of Hydromet. Syncope in older patients may be related to an increased sensitivity and advanced arteriosclerotic vascular disease. This may be avoided by lower doses of Hydromet.

Withdrawal of Hydromet is followed by return of hypertension usually within 48 hours. This is not complicated by an overshoot of blood pressure.

Therapy with Hydromet may be initiated in most patients already on treatment with other antihypertensive agents by terminating these antihypertensive medications, gradually if required (see manufacturer's recommendations on stopping these drugs). Following such previous antihypertensive therapy, Hydromet should be limited to an initial dose of 1 tablet daily and increased as required at intervals of not less than two days.

When Hydromet is given to patients on other antihypertensives, the dose of these agents may need to be adjusted to effect a smooth transition.

Contra-indications, warnings, etc

Contra-indications: Active liver disease (such as acute hepatitis and active cirrhosis); anuria; known sensitivity to methyldopa or hydrochlorothiazide, including hepatic

disorders associated with previous methyldopa therapy. See 'Precautions' for use in pregnancy and the nursing mother.

Precautions: The precautions relating to the use of Hydromet are generally those of its components.

Methyldopa: Acquired haemolytic anaemia has occurred rarely. Should symptoms suggest anaemia, haemoglobin and/or haematocrit determinations should be made. If anaemia is confirmed, tests should be done for haemolysis. If haemolytic anaemia is present, Hydromet should be discontinued. Stopping therapy, with or without corticosteroids, has usually brought prompt remission. Rarely, however, deaths have occurred.

Some patients on continued therapy with methyldopa develop a positive direct Coombs test. From the reports of different investigators, the incidence averages between 10% and 20%. A positive Coombs reaction rarely develops in the first six months of therapy, and if it has not developed within 12 months, it is unlikely to do so later on continuing therapy. Development is also dose-related, the lowest incidence occurring in patients receiving 1 g or less of methyldopa per day. The test becomes negative usually within weeks to months after methyldopa is discontinued.

Prior knowledge of a positive Coombs reaction will aid in evaluation of cross-matching for transfusions. If a patient with a positive Coombs reaction shows an incompatible minor cross-match, an indirect Coombs test should be performed. If this is negative, transfusion with blood otherwise compatible in the major cross-match may be carried out. If positive, the advisability of transfusion should be determined by a haematologist.

Reversible leucopenia, with primary effect on granulocytes, has been reported rarely. The granulocyte count returned promptly to normal on discontinuing therapy. Reversible thrombocytopenia has occurred rarely.

Occasionally, fever has occurred within the first three weeks of therapy, sometimes associated with eosinophilia or abnormalities in liver function tests. Jaundice, with or without fever, also may occur. Its onset is usually within the first two or three months of therapy. In some patients the findings are consistent with those of cholestasis. Rare cases of fatal hepatic necrosis have been reported. Liver biopsy performed in several patients with liver dysfunction showed a microscopic focal necrosis compatible with drug hypersensitivity.

Liver function tests, and a total and differential white blood cell count, are advisable at intervals during the first six to twelve weeks of therapy, or whenever an unexplained fever occurs. Should fever, abnormality in liver function, or jaundice occur, therapy should be withdrawn. If related to methyldopa, the temperature and abnormalities in liver function have characteristically reverted to normal when methyldopa has been discontinued. Methyldopa should not be reinstated in these patients. Methyldopa should be used with caution in patients with a history of previous liver disease or dysfunction.

When methyldopa is used with other antihypertensive drugs, potentiation of antihypertensive action may occur. The progress of patients should be carefully followed to detect side reactions or unusual manifestations of drug idiosyncrasy.

Patients may require reduced doses of anaesthetics when on methyldopa. If hypotension does occur during anaesthesia, it can usually be controlled by vasopressors. The adrenergic receptors remain sensitive during treatment with methyldopa.

Dialysis removes methyldopa; therefore, hypertension may recur after this procedure.

Rarely, involuntary choreoathetotic movements have been observed during therapy with methyldopa in patients with severe bilateral cerebrovascular disease. Should these movements occur, therapy should be discontinued.

Interference with laboratory tests: Methyldopa may interfere with the measurement of urinary uric acid by the phosphotungstate method, serum creatinine by the alkaline picrate method, and SGOT by colorimetric method. Interference with spectrophotometric methods for SGOT analysis has not been reported.

As methyldopa fluoresces at the same wavelengths as catecholamines, spuriously high amounts of urinary catecholamines may be reported, giving rise to a false-positive diagnosis of phaeochromocytoma.

It is important to recognise this phenomenon before a patient with a possible phaeochromocytoma is subjected to surgery. Methyldopa does not interfere with measurement of VMA (vanillylmandelic acid) by those methods which convert VMA to vanillin. Methyldopa is not recommended for the treatment of patients with phaeochromocytoma.

Rarely, when urine is exposed to air after voiding, it may darken because of breakdown of methyldopa or its metabolites.

Hydrochlorothiazide: Azotaemia may be precipitated or increased by hydrochlorothiazide. Cumulative effects of hydrochlorothiazide may develop in patients with impaired renal function. If increasing azotaemia and oliguria occur during treatment of severe progressive renal disease, Hydromet should be discontinued.

Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance or of serum ammonia may precipitate hepatic coma.

Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma.

Hydrochlorothiazide adds to or potentiates the action of other antihypertensive agents. Potentiation occurs with ganglion or adrenergic blocking drugs.

The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

Patients should be carefully monitored for signs of fluid and electrolyte imbalance (hyponatraemia, hypomagnesaemia, hypochlorhaemic alkalosis and hypokalaemia). It is particularly important to make serum and urine electrolyte determinations if the patient is vomiting excessively or receiving parenteral fluids. Warning signs are dryness of the mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia and gastro-intestinal disturbance.

Hypokalaemia may develop, especially with brisk diuresis, when severe cirrhosis is present, or during concurrent steroid or ACTH administration. Interference with adequate electrolyte intake will contribute to hypokalaemia. Hypokalaemia can sensitise or exaggerate the response of the heart to the toxic effects of digitalis (e.g. increased ventricular irritability).

Hypokalaemia may be avoided or treated by giving potassium chloride or foods with a high potassium content. (Note that symptoms and signs which might indicate ulceration or obstruction of the small bowel in patients taking tablets or capsules containing potassium salts are indications for stopping treatment with such preparations immediately.)

Any chloride deficit is generally mild and does not usually require specific treatment except under unusual circumstances (as in liver or renal disease). Dilutional hyponatraemia may occur in oedematous patients in hot weather; except in rare instances when hyponatraemia is life-threatening, appropriate therapy is water restriction rather than administration of salt. In actual salt depletion, appropriate replacement is the therapy of choice.

Thiazides may increase responsiveness to tubocurarine. The antihypertensive effect of the thiazide may be enhanced in the post-sympathectomy patient. Hydrochlorothiazide may decrease arterial responsiveness to noradrenaline, but not enough to prevent noradrenaline being therapeutically useful. Orthostatic hypotension may occur, and may be potentiated by alcohol, barbiturates or narcotics.

Thiazides may decrease serum protein-bound iodine levels without signs of thyroid disturbance.

Calcium excretion is decreased by hydrochlorothiazide. Pathological changes in the parathyroid glands, with hypercalcaemia and hypophosphataemia, have been observed in a few patients on prolonged thiazide therapy.

The common complications of hyperparathyroidism such as renal lithiasis, bone resorption and peptic ulceration have not been seen. Thiazides should be discontinued before testing parathyroid function.

Hyperuricaemia may occur, or gout may be precipitated, in certain patients receiving thiazide therapy.

Insulin requirements in diabetic patients may be increased, decreased or unchanged. Latent diabetes mellitus may become manifest during thiazide administration.

Lithium should generally not be given to patients receiving diuretics, since the risk of lithium toxicity is very high in such patients.

Use of Hydromet in pregnancy and the nursing mother: Methyldopa has been used under close medical and obstetric supervision for the treatment of hypertension during pregnancy. There was no clinical evidence that methyldopa caused foetal abnormalities or affected the neonate. Methyldopa does cross the placental barrier and appears in cord blood and breast milk. Although no obvious teratogenic effects have been reported, the possibility of foetal injury cannot be excluded.

Thiazides also cross the placental barrier and appear in cord blood. Use of any drug in women who are or may become pregnant requires that anticipated benefits be weighed against possible risks. Hazards include foetal or neonatal jaundice, thrombocytopenia and possibly other adverse reactions which have occurred in the adult.

Thiazides also appear in breast milk. If use of Hydromet is deemed essential, the patient should stop nursing.

Side-effects: The side-effects of Hydromet are generally those of its components; combination of methyldopa and hydrochlorothiazide has not produced any additional side-effects.

Methyldopa: Significant side-effects due to methyldopa have been infrequent and this agent is usually well tolerated.

Sedation, usually transient, may occur initially or when the dosage is increased. Other early transient effects which may occur are headache, asthenia and weakness.

Central nervous system: Sedation (usually transient headache, asthenia or weakness), paraesthesiae, parkinsonism, Bell's Palsy, involuntary choreoathetotic movements. Psychic disturbances including nightmares, im-

paired mental activity and reversible mild psychoses or depression. Dizziness, light-headedness, and symptoms of cerebrovascular insufficiency (may be due to lowering of blood pressure).

Cardiovascular: Bradycardia, aggravation of angina pectoris. Orthostatic hypotension (decrease daily dosage). Oedema (and weight gain) usually relieved by use of a diuretic. (Discontinue methyldopa if oedema progresses or signs of heart failure appear.)

Gastro-intestinal: Nausea, vomiting, distension, constipation, flatus, diarrhoea, colitis, mild dryness of the mouth, sore or 'black' tongue, pancreatitis, salivary gland inflammation.

Haematological: Positive Coombs test, haemolytic anaemia, bone-marrow depression, leucopenia, granulocytopenia, thrombocytopenia. Positive tests for anti-nuclear antibody, LE cells, and rheumatoid factor.

Allergic: Drug-related fever and abnormal liver function tests with jaundice and hepatocellular damage (see 'Precautions'), lupus-like syndrome, myocarditis.

Dermatological: Rash as in eczema or lichenoid eruption, toxic epidermal necrolysis.

Other: Nasal stuffiness, rise in blood urea, breast enlargement, gynaecomastia, lactation, impotence, decreased libido, mild arthralgia, myalgia.

Hydrochlorothiazide: Gastro-intestinal system: Anorexia, gastric irritation, nausea, vomiting, cramps, diarrhoea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis, salivary gland inflammation.

Central nervous system: Dizziness, vertigo, paraesthesiae, headache, yellow vision.

Haematological: Leucopenia, agranulocytosis, thrombocytopenia, aplastic anaemia, haemolytic anaemia.

Cardiovascular: Orthostatic hypotension (may be aggravated by alcohol, barbiturates or narcotics).

Hypersensitivity: Purpura, photosensitivity, rash, urticaria, necrotising angitis (vasculitis, cutaneous vasculitis), fever, respiratory distress including pneumonitis, anaphylactic reactions.

Other: Hyperglycaemia, glycosuria, hyperuricaemia, muscle spasm, weakness restlessness, transient blurred vision.

Whenever side-effects are moderate to severe, dosage should be reduced or therapy withdrawn.

Treatment of overdosage: No specific antidote. If ingestion is recent, emesis may be induced or gastric lavage performed. When ingestion has been earlier, infusions may be helpful to promote urinary excretion. Otherwise, management is symptomatic treatment with special attention to cardiac rate and output, blood volume, electrolyte balance, dehydration, paralytic ileus, urinary function, hepatic coma and cerebral activity. Sympathomimetic agents may be indicated. Oxygen or artificial respiration may be required if breathing is impaired. If chronic overdosage is suspected, Hydromet should be discontinued.

Pharmaceutical precautions Keep container well closed; store in a cool place, protected from light.

Legal category POM.

Package quantities Bottles of 100 and 500.

Further information Hydromet reduces both supine and standing blood pressure. Symptomatic postural hypotension, exercise hypotension and diurnal blood pressure variations rarely occur. By adjustment of

dosage, morning hypotension can be prevented without sacrificing control of afternoon blood pressure.

Product licence number 0025/5008.

HYDROSALURIC*

Presentation White, half-scored tablets, marked 'MSD 42', containing 25 mg Hydrochlorothiazide BP.

White, half-scored tablets, marked 'MSD 105', containing 50 mg Hydrochlorothiazide BP.

Uses Diuretic and antihypertensive.

Oedema associated with congestive heart failure, hepatic cirrhosis, premenstrual tension, drug-induced oedema and oedema due to various forms of renal dysfunction, i.e. the nephrotic syndrome, acute glomerulonephritis, chronic renal failure. Hypertension, either alone or as an adjunct to other antihypertensive drugs such as Aldomet* (methyldopa, MSD) or Blocadren* (timolol maleate, MSD).

Dosage and administration Dosage should be determined on an individual basis, and the lowest dosage necessary to achieve the desired result should be used.

Adults – for diuresis: Usually 50–100 mg once or twice a day. Many patients respond to intermittent therapy; for example, every other day, or three to five days a week. Intermittent therapy is less likely to produce excessive diuretic response with resulting undesirable electrolyte imbalance.

In oedema accompanying premenstrual tension: 25–50 mg once or twice a day, from the first morning of symptoms until the onset of the menses.

Adults – for control of hypertension: Usual starting dosage, 50 mg or 100 mg a day as a single or divided dose, increased or decreased according to response. Rarely some patients may require up to 200 mg daily in divided doses.

Thiazides may add to or potentiate the action of other antihypertensives. If HydroSaluric is used with other antihypertensive agents, it may be necessary to reduce the dosage of such agents so as to prevent an excessive drop in blood pressure.

Infants and children: Usually 2.5 mg per kg body weight a day, given in two doses. Infants under 6 months may need up to 3.5 mg per kg a day, in two doses. Infants up to 2 years of age may be given 12.5–37.5 mg of HydroSaluric a day in two doses. Children from 2 to 12 years of age may be given 37.5–100 mg a day in two doses. Dosage in both age groups should be based on body weight.

Contra-indications, warnings, etc

Contra-indications: Anuria, known hypersensitivity to hydrochlorothiazide. See also 'Use in pregnancy and the nursing mother', under 'Precautions'.

Precautions: Azotaemia may be precipitated or increased by HydroSaluric. Cumulative effects of hydrochlorothiazide may develop in patients with impaired renal function. If increasing azotaemia and oliguria occur during treatment of severe progressive renal disease, HydroSaluric should be discontinued.

Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance, or of serum ammonia, may precipitate hepatic coma.

Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma.

HydroSaluric adds to or potentiates the action of other antihypertensive agents. Potentiation occurs with ganglion or adrenergic blocking drugs.

The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

Patients should be carefully monitored for signs of fluid and electrolyte imbalance (hyponatraemia, hypochloraemic alkalosis, hypomagnesaemia and hypokalaemia). It is particularly important to make serum and urine electrolyte determinations if the patient is vomiting excessively or receiving parenteral fluids. Warning signs, irrespective of cause, are dryness of the mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia and gastro-intestinal disturbances.

Hypokalaemia may develop, especially with brisk diuresis, when severe cirrhosis is present, or during concurrent steroid or ACTH administration. Interference with adequate electrolyte intake will contribute to hypokalaemia. Hypokalaemia can sensitise or exaggerate the response of the heart to the toxic effects of digitalis (e.g. increased ventricular irritability).

Hypokalaemia may be avoided or treated in the adult by concurrent use of Midamor* (amiloride hydrochloride) a potassium-conserving agent. It also may be avoided by giving potassium chloride or foods with a high potassium content. (Note that symptoms and signs which might indicate ulceration or obstruction of the small bowel in patients taking tablets or capsules containing potassium salts are indications for stopping treatment with such preparations immediately.)

Any chloride deficit is generally mild and does not usually require specific treatment except under unusual circumstances (as in liver or renal disease). Dilutional hyponatraemia may occur in oedematous patients in hot weather; appropriate therapy is water restriction rather than administration of salt except in rare instances when hyponatraemia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice.

Thiazides may increase responsiveness to tubocurarine. The antihypertensive effect of the thiazide may be enhanced in the post-sympathectomy patient.

Hydrochlorothiazide may decrease arterial responsiveness to noradrenaline, but not enough to prevent noradrenaline being therapeutically useful. Orthostatic hypotension may occur, and may be potentiated by alcohol, barbiturates or narcotics.

Thiazides may decrease serum protein-bound iodine levels without signs of thyroid disturbance.

Calcium excretion is decreased by HydroSaluric.

Pathological changes in the parathyroid glands, with hypercalcaemia and hypophosphataemia, have been observed in a few patients on prolonged thiazide therapy. The common complications of hyperparathyroidism, such as renal lithiasis, bone resorption and peptic ulceration, have not been seen. Thiazides should be discontinued before carrying out tests for parathyroid function.

Hyperuricaemia may occur, or gout may be precipitated, in certain patients receiving thiazide therapy.

Insulin requirements in diabetic patients may be increased, decreased or unchanged. Latent diabetes mellitus may become manifest during thiazide administration.

Lithium should generally not be given to patients receiving diuretics, since the risk of lithium toxicity is very high in such patients.

Use in pregnancy and the nursing mother: Thiazides appear in breast milk. If use of the drug is deemed essential, the patient should stop nursing. Thiazides cross the placental barrier and appear in cord blood. The use of HydroSaluric when pregnancy is present or suspected requires, therefore, that the benefits of the drug be weighed against possible hazards to the foetus. These hazards include foetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. The routine use of diuretics in otherwise healthy pregnant women with or without mild oedema is not indicated.

Side-effects: Gastro-intestinal system: Anorexia, gastric irritation, nausea, vomiting, cramps, diarrhoea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis, salivary gland inflammation.

Central nervous system: Dizziness, vertigo, paraesthesiae, headache, yellow vision.

Haematological: Leucopenia, agranulocytosis, thrombocytopenia, aplastic anaemia, haemolytic anaemia.

Cardiovascular: Orthostatic hypotension (may be aggravated by alcohol, barbiturates, or narcotics).

Hypersensitivity: Purpura, photosensitivity, rash, urticaria, necrotising angitis (vasculitis, cutaneous vasculitis), fever, respiratory distress including pneumonitis, anaphylactic reactions.

Other: Hyperglycaemia, glycosuria, hyperuricaemia, muscle spasm, weakness, restlessness, transient blurred vision.

Whenever side-effects are moderate to severe, thiazide dosage should be reduced or therapy withdrawn.

Treatment of overdose: Symptomatic and supportive; no specific antidote. If ingestion is recent the stomach should be emptied by emesis or gastric lavage. Dehydration, electrolyte imbalance, hepatic coma and hypotension should be corrected by standard methods. For impaired respiration, oxygen or artificial respiration should be given.

Pharmaceutical precautions Keep container tightly closed; store in a cool place, protected from light.

Legal category POM.

Package quantities 25 mg: Bottles of 100 and 500. 50 mg: Bottles of 100 and 500.

Further information Diuresis begins within two hours following administration, is at a peak after four hours and persists for six to twelve hours. No rigid dietary salt restriction required.

Product licence numbers

25 mg 0025/5009

50 mg 0025/5010

INVERSINE®

Presentation Yellow, half-scored tablets, marked 'MSD 52', containing 2.5 mg mecamlamine hydrochloride.

White, quarter-scored tablets, marked 'MSD 120', containing 10 mg mecamlamine hydrochloride.

Uses Ganglion-blocking antihypertensive agent.

For moderately severe to severe essential hypertension, and selected cases of malignant hypertension.

Dosage and administration The usual initial dosage is 2.5 mg twice a day. This is modified by amounts of 2.5 mg at intervals of not less than two days, until the

desired blood pressure response is obtained. One criterion of an adequate dose is that it is just less than the amount which produces signs of mild postural hypotension. Close supervision of the patient and critical adjustment of dosage are essential for successful treatment; blood pressure readings during dosage adjustment should be taken in the erect position.

The average daily dosage of Inversine is 25 mg, usually in three divided doses. In some cases, however, as little as 2.5 mg once a day may be sufficient to control hypertension. In severe or urgent cases, it may be necessary to give larger increments than 2.5 mg, at shorter intervals than two days. Partial tolerance may develop and necessitate an increase in the dosage of Inversine.

Administration of Inversine after meals may result in more gradual absorption of medication and give smoother control of high blood pressure. The timing of administration in relation to meals should be consistent. Because response to antihypertensive drugs is greatest in the early morning, the midday and evening doses should be larger than the morning dose, which should be relatively small and may even be omitted in some instances.

Replacement of other ganglion-blocking agents: Inversine may be substituted for other ganglion-blocking agents and the following procedure is suggested. The total daily dosage of other agents is reduced by 25%, and this replaced by 25% of an equivalent daily dose of Inversine given in divided doses (10 mg of Inversine is approximately equivalent to 100 mg pentolinium tartrate, or 1,000 mg hexamethonium chloride). Further substitution of Inversine for the other agents is made at five- to seven-day intervals in 25% increments, and thus complete conversion is achieved within three or four weeks. Daily supervision is essential during the period of conversion, and adjustment is dosage must be carefully regulated because all ganglion-blocking agents have a wide dosage range and individual patient response is variable. One to four weeks after complete conversion, a further evaluation of dosage should be made to determine the patient's maintenance requirements.

Concurrent administration with other antihypertensive agents: When Inversine is given with other antihypertensive drugs, the dosages of both Inversine and the other agents should be reduced to avoid excessive response. However, when thiazides are administered concomitantly, they should be given in their usual dosages, and the dosage of Inversine at least halved.

Contra-indications, warnings, etc

Contra-indications: Should not be used for mild or labile hypertension. Contra-indicated in coronary insufficiency or recent myocardial infarction, uraemia, patients with chronic pyelonephritis receiving antibiotics and sulphonamides, glaucoma, organic pyloric stenosis or hypersensitivity. Should be used with great discretion, if at all, when elevated or rising blood urea level indicates renal insufficiency.

Precautions: Should be used only when a potent ganglion-blocking agent is needed. Hypertension is liable to return if antihypertensive therapy is suddenly withdrawn. This may occur abruptly in patients with malignant hypertension and some others, and may cause fatal cerebrovascular accidents or acute congestive heart failure. Inversine should be withdrawn gradually, and other antihypertensive therapy must usually be substituted. Sometimes, however, the effects of Inversine may last from hours to days after it has been discontinued.

Careful evaluation of the patient, especially his renal and cardiovascular system, is necessary. When renal, cerebral or coronary blood flow is deficient, any additional impairment, which might result from added hypotension, must be avoided. Inversine should be used with caution in marked cerebral and coronary arteriosclerosis, or after a recent cerebral accident.

The action of mecamlamine may be potentiated by excessive heat, fever, infection, haemorrhage, pregnancy, anaesthesia, surgery, vigorous exercise, other antihypertensive agents, alcohol, and salt depletion due to diminished intake or increased excretion from diarrhoea, vomiting, excessive sweating or diuretics. Sodium intake should not be restricted during therapy, but the dosage of Inversine should be adjusted if necessary.

Caution is required in prostatic hypertrophy, bladder neck obstruction and urethral stricture, because urinary retention may occur. Frequent loose bowel movements with abdominal distension and decreased borborygmi may be the first signs of paralytic ileus. If these are present, Inversine should be withdrawn immediately and remedial steps taken.

Constipation may be prevented by giving a parasympathomimetic agent such as pilocarpine or neostigmine with each dose of Inversine. It should be treated with cream of magnesia or similar laxative, but not with bulk laxatives.

Postural hypotension due to excessive response may be corrected by reducing the dosage of Inversine.

Side-effects: Anorexia, dry mouth and glossitis, nausea, vomiting, constipation (sometimes preceded by small, frequent, liquid stools), ileus, weakness, fatigue, sedation, orthostatic dizziness and syncope, paraesthesiae, dilated pupils, blurred vision, decreased libido, impotence and urinary retention.

Interstitial pulmonary oedema and fibrosis have been reported after blood pressure reduction with potent antihypertensive agents, including mecamlamine hydrochloride.

Mecamlamine, a secondary amine, readily penetrates the brain, and thus may produce CNS effects.

Tremor, choreiform movements, mental aberrations and convulsions occur rarely, most often with high dosages and in patients with cerebral or renal insufficiency.

Treatment of overdosage: Pressor amines may be used to counteract excessive hypotension. Since patients on ganglion-blocking agents are more than normally reactive to pressor amines, small doses of these amines are recommended, in order to avoid excessive response.

Pharmaceutical precautions Keep container well closed; store in a cool place, protected from light.

Legal category POM.

Package quantities 2.5 mg: Bottles of 100.
10 mg: Bottles of 100.

Further information Inversine reduces blood pressure in both normotensive and hypertensive individuals. It is almost completely absorbed from the gastrointestinal tract, resulting in consistent lowering of blood pressure in most patients with hypertensive cardiovascular disease. Its onset of action is gradual (half to two hours), and its effect is long-lasting (usually six to twelve hours or longer). Although the antihypertensive effect is primarily orthostatic, the supine blood pressure is also reduced significantly.

Product licence numbers

2.5 mg 0025/5027
10 mg 0025/5028

MANNITOL

Presentation A clear, colourless, sterile solution containing, in each 50 ml, 12.5 g Mannitol BP.

Uses Mannitol Injection is indicated for promotion of diuresis, in the prevention and/or treatment of the oliguric phase of acute renal failure before irreversible renal failure becomes established; reduction of intracranial pressure and treatment of cerebral oedema by reducing brain mass; reduction of elevated intra-ocular pressure when the pressure cannot be lowered by other means; promoting the urinary excretion of toxic substances.

Mannitol Solution is indicated as an irrigating solution in transurethral prostatic resection, or other transurethral surgical procedures.

Dosage and administration Mannitol should only be injected intravenously. Total dosage, concentration and rate of administration is governed by the nature and severity of the condition being treated, fluid requirements and urinary output. The usual adult dosage ranges from 50–200 g in 24 hours, but in most instances an adequate response is achieved at a dosage of approximately 100 g in 24 hours. The rate is usually adjusted to maintain an adequate urine flow (at least 30–50 ml an hour).

Test dose: In marked oliguria or inadequate renal function, a test dose of Mannitol should be given to determine diuretic response, the dose may be approximately 0.2 g/kg (about 50 ml of a 25% solution) infused in three to five minutes to produce an adequate urine flow (at least 30–50 ml/hr). If the flow of urine does not increase within two or three hours, a second test dose may be given. If the response is still inadequate, the patient should be re-evaluated and further test doses of Mannitol should not be attempted.

Prevention of oliguria: 50–100 g of Mannitol as a 5–25% solution may be given during surgery, immediately postoperatively, or following trauma. The concentration and amount will depend on the fluid requirements of the patient. Following suspected or actual haemolytic-transfusion reactions, 20 g of Mannitol may be given over a five-minute period to provoke diuresis. If diuresis does not occur, the 20 mg dose may be repeated. If there is an adequate urine flow (30–50 ml per hour), then intravenous fluids containing not more than 50–75 mEq of sodium per litre should be given in sufficient volume to match the desired urine flow (100 ml/hour) until fluids can be taken orally.

Treatment of oliguria: 50–100 g of Mannitol as a 15–25% solution.

Reduction of intracranial pressure, cerebral oedema, or intra-ocular pressure: A 25% solution of Mannitol is recommended since its effectiveness depends on establishing intravascular hyperosmolarity. Used before or during surgery, a total dose of 1.5–2 g/kg can be given over 30–60 minutes. Careful evaluation must be made of the circulatory and renal reserve prior to and during use of Mannitol at this relatively high dose and rapid infusion rate. Careful attention must be paid to fluid and electrolyte balance, bodyweight and total input and output before and after infusion of Mannitol. Evidence

of reduced cerebrospinal fluid pressure may be observed within 15 minutes of starting the infusion.

Maximal reduction of intra-ocular pressure occurs 30–60 minutes after injection.

Urinary excretion of toxic substances: 5–25% solutions of Mannitol may be used as an infusion for as long as indicated if the level of urinary output remains high. The concentration will depend on fluid requirement and urinary output. Intravenous water and electrolytes must be given to replace the loss of these substances in the urine, sweat and expired air. If benefits are not seen after 200 g of Mannitol has been given, it should be discontinued.

For urological irrigation: A 2.5% solution is recommended to minimise the haemolytic effect of water alone, the entrance of haemolysed blood into the circulation, and the resulting haemoglobinaemia which is considered a major factor in producing serious renal complications.

Note: If crystals are present in Mannitol 25% sterile solution dissolve only by one of these two methods: (1) heat water bath to 80°C; remove it from heat and immerse ampoule (for 15–20 minutes) or (2) autoclave for 20 minutes at 120°C (15 psi). As soon as cool enough to handle, shake gently several times. Allow to cool to body temperature before use. Do not use ampoule if crystals are present.

Preparation of dilutions:

For intravenous injection

Concentration preparation

Test dose – use as supplied (25%)

Add one 50 ml ampoule		} of 5% Dextrose Injection or in a clinically appropriate electrolyte solution
5%	to 200 ml	
10%	to 75 ml	
15%	to 33.3 ml	
20%	to 12.5 ml	
25%	Use as supplied	

For urological irrigation

2.5% Add two 50 ml ampoules to 900 ml of Water for Injections BP

Contra-indications, warnings, etc

Contra-indications: Well-established anuria due to severe renal disease. Severe pulmonary congestion, frank pulmonary oedema or severe congestive heart failure. Active intracranial bleeding except during craniotomy. Severe dehydration.

After therapy with Mannitol is started, progressive renal damage or dysfunction (including increasing oliguria and azotaemia), and progressive heart failure or pulmonary congestion.

Precautions: Careful checking of the patient's electrolytes is important to avoid depletion.

Closely monitor the urine output of the patient and discontinue Mannitol infusion promptly if output is low. Inadequate urine output results in accumulation of Mannitol, expansion of extra-cellular fluid volume and could result in water intoxication or congestive heart failure. Renal function must be closely monitored during Mannitol infusion.

Mannitol must be used with caution in patients with significant cardiopulmonary or renal dysfunction. Irriga-

tion with Mannitol in transurethral prostatectomy may alter cardiopulmonary and renal dynamics.

Carefully evaluate the cardiovascular status of the patient before using Mannitol intravenously, or before or during transurethral resection since expansion of extra-cellular fluid may lead to fulminating congestive heart failure.

By sustaining diuresis, Mannitol may obscure and intensify inadequate hydration or hypovolaemia.

Never add Mannitol to whole blood. If it is essential to transfuse Mannitol with blood, at least 20 mEq of sodium chloride should be added to each litre of Mannitol to avoid pseudo-agglutination.

The contents of opened containers should be used promptly, and any unused contents discarded.

Use in pregnancy: Mannitol is not recommended in pregnancy. Use of any drug in women of childbearing potential requires that anticipated benefits be weighed against possible hazards.

Use in children: Dosage requirements for children of 12 years of age and less are not established.

Side-effects: The following reactions may occur: pulmonary oedema, oedema, hypertension, hypotension, tachycardia, angina-like chest pains; electrolyte imbalance, acidosis, dryness of mouth, thirst, urinary retention, blurred vision, thrombophlebitis, chills, fever, urticaria; convulsions, nausea, vomiting, headache, dizziness, osmotic nephrosis, diarrhoea, rhinitis, arm pain, skin necrosis, and fluid imbalance.

Treatment of overdose: No specific antidote. Normal supportive measures should be taken.

Pharmaceutical precautions No special requirements.

Legal category POM.

Package quantities Vials of 50 ml.

Further information Nil.

Product licence number 0025/5079.

MEFOXIN* INJECTION ▼

Presentation In vials containing 1 g or 2 g of cefoxitin as the sodium salt. Each gram of cefoxitin contains approximately 2.3 mEq sodium.

Uses Mefoxin is a broad-spectrum bactericidal antibiotic indicated for the treatment of infections caused by susceptible strains of Gram-positive and Gram-negative pathogens both aerobic and anaerobic.

Mefoxin has been clinically effective not only in infections due to antibiotic-sensitive organisms, but also in infections due to organisms resistant to one or more of the following antibacterial agents: penicillin, ampicillin, carbenicillin, tetracyclines, erythromycin, chloramphenicol, cephalosporins, kanamycin, gentamicin, tobramycin, and sulphamethoxazole-trimethoprim.

Many Gram-negative pathogens are resistant to penicillins and cephalosporins through the action of the beta-lactamases which are produced by these pathogens. Mefoxin is remarkably stable in the presence of these bacterial beta-lactamases, both penicillinases and cephalosporinases. Hence, the clinical efficacy of Mefoxin extends to many infections caused by such pathogens.

Mefoxin is indicated for the treatment of the following infections caused by sensitive bacteria: peritonitis and

examethonium, reserpine, chlorthalidopoxide, ephedrine and erythromycin. Because of the small number of reported incidents the clinical significance of the interactions remains uncertain. Probably the most important are those involving cimetidine, erythromycin and frusemide; which may result in impaired theophylline elimination and hence an increase in plasma theophylline levels.

Pharmaceutical precautions The capsules should be stored in a cool dry place and the containers kept tightly closed.

Legal category P.

Package quantities Slo-phyllin capsules 60 mg, 25 mg, and 250 mg. Securitainers containing 100 capsules.

Further information Nil.

Product licence numbers

lo-phyllin Capsules 60 mg	0161/0021
lo-phyllin Capsules 125 mg	0161/0019
lo-phyllin Capsules 250 mg	0161/0020

ONI-SLO* ▼

Representation Capsules containing isosorbide dinitrate in a timed release formulation which provides a prolonged therapeutic effect.

60 mg Capsules: Size No. 3 transparent pink capsules with a clear colourless cap, filled with off-white almost spherical pellets. Each capsule contains 20 mg isosorbide dinitrate.

40 mg Capsules: Size No. 2 transparent red capsule with a clear colourless cap, filled with off-white almost spherical pellets. Each capsule contains 40 mg isosorbide dinitrate.

Uses For the prophylactic treatment of angina pectoris.

Dosage and administration Dosage should be adjusted according to the response obtained by the individual patient and the severity of the anginal pain.

Adults: 40–120 mg daily in divided doses, generally morning and evening. Eight hourly administration may be found necessary in severe cases.

Initially the lowest dose is generally recommended. This should be increased gradually until the maximum therapeutic effect is achieved. Severe cases may require 20 mg daily. Gradual reduction of dosage after long-term therapy is recommended whenever possible.

Children: There is no recommended dose for children.

Contra-indications, warnings, etc

Hypersensitivity to this drug; shock, marked hypotension; Angina caused by hypertrophic obstructive cardiomyopathy, (nitrates may exaggerate outflow obstruction).

Precautions: Not recommended during pregnancy or for nursing mothers. As with other nitrates, tolerance to this drug and cross-tolerance to other nitrates/nitrites may occur. The hypotensive effect may be enhanced by alcohol.

Adverse Reactions: These are common to all nitrates used for the treatment of angina pectoris. Cutaneous vasodilatation with flushing, tachycardia and occasionally unexplained bradycardia. Headache may occur initially, but is less likely if the dose is increased gradually. Analgesics may be useful. Postural hypotension which may cause cerebral ischaemia and present as transient episodes of dizziness and weakness.

This drug can act as a physiological antagonist to noradrenaline, acetylcholine, histamine and many other agents.

Overdosage – Signs and Symptoms: As with all nitrates large doses may cause flushing of the face, severe headache, a feeling of suffocation, hypotension and fainting. Rarely, cyanosis and methaemoglobinaemia may occur. In a few patients there may be a reaction comparable to shock, with nausea, vomiting, weakness, sweating and syncope.

Overdosage – treatment: Recovery often occurs without special treatment. Hypotension may be corrected by elevation of the legs to promote venous return.

In the event of more severe overdosage symptomatic treatment is required. Gastric lavage may be required but should only be considered after careful assessment of the patient's condition, in particular the level of consciousness, and the time since ingestion which should be no more than four hours.

Pharmaceutical precautions Store in a cool dry place protected from light. Shelf life 3 years.

Legal category P.

Package quantities Securitainers containing 100 capsules.

Further information Nil.

Product licence numbers

Soni-Slo 20 mg	0161/0024
Soni-Slo 40 mg	0161/0026.

***Trade Mark**



AGIOLAX*

Presentation Brown, sugar-coated granules, each 100 grams of which contains: Seeds of *Plantago Ovata* 54.2 g, *Senna Pods* 12.4 g.

Uses For the relief of constipation.

It is particularly suitable for bowel regulation in bed-ridden patients and pregnant women. It is also useful in facilitating pain-free evacuation in patients with haemorrhoids.

Dosage and administration Agiolax should be placed dry on the tongue and, without chewing or crushing, swallowed with a glass of water or warm drink.

Adults and children over 12 years: One or two standard 5 ml teaspoonfuls before breakfast and after supper. In obstinate cases, up to two standard 5 ml teaspoonfuls every six hours for 1 to 3 days.

Children (5 to 12 years): Half the adult dosage.

Contra-indications, warnings, etc Should not be used in cases of intestinal obstruction.

Treatment of overdose: Excessive use of purgatives may produce excessive loss of water and electrolytic loss. Treat symptomatically with careful attention to body electrolytes, particularly potassium.

Pharmaceutical precautions No special storage precautions required.

Legal category P.

Package quantities Containers of 100 grams and 250 grams.

Further information Special note for diabetics: Each heaped standard 5 ml teaspoonful contains approximately 5 g of Agiolax equivalent to 0.9 g of sucrose.

Product licence number 4638/0001.

ANANASE* FORTE

Presentation Orange yellow, enteric-coated tablets each containing Bromelain Concentrate equivalent to 100,000 Rorer Units of activity.

Uses Ananase Forte is a proteolytic enzyme for use in the treatment of inflammatory oedema associated with:

Soft tissue trauma – contusions, lacerations, sprains, strains, haematomas, dislocations, fractures, burns.

Post-operative tissue reactions – as in general orthopaedic, ocular, oral and gynaecological surgery.

Skin conditions – cellulitis, furunculosis.

Ulceration – varicose, decubitus, diabetic.

Dosage and administration Usual adult dose is 1 tablet four times daily, taken orally.

Children's dosage is at the discretion of the physician.

Contra-indications, warnings, etc Contra-indi-

cated in patients with known sensitivity to the drug or to pineapple or its products.

Ananase Forte should be used with caution in patients with abnormalities of the blood-clotting mechanism such as haemophilia, or with severe hepatic or renal disease.

Patients on anticoagulant therapy should be observed carefully because of possible potentiation of the anticoagulant effect.

Side-effects are seldom observed. Sensitivity manifested by skin rash has occurred. There has been no report of anaphylactic reaction. Cases of metrorrhagia and menorrhagia may possibly be related to the drug. Nausea, vomiting or diarrhoea are rare. In the event of any adverse reaction, the drug should be discontinued.

Treatment of overdose: Symptomatic treatment observing closely blood clotting factors.

Pharmaceutical precautions Can be stored at room temperature.

Legal category P.

Package quantities Securitainers of 25 and 250 tablets.

Further information Ananase Forte is intended to supplement and augment standard therapeutic procedures for reduction of inflammation and oedema, to ease pain, speed healing and accelerate tissue repair. It contains a concentrate of proteolytic enzymes derived from the pineapple plant. While the mode of action of proteolytic enzymes has not been finally established, it is probable that depolymerisation of fibrin and permeability modifications of venules and lymphatics underlie the action.

Product licence number 0050/5005.

AURALTONE*

Presentation A clear, colourless or very pale yellow liquid, odourless and very hygroscopic. It contains:

Phenazone BPC 5.0% w/v

Benzocaine BP 1.0% w/v

Uses For the treatment of acute otitis media, inflammatory conditions of the tympanic membrane and generally for the relief of ear-ache.

Dosage and administration For external use.

It is administered to the ear with the dropper provided.

In the absence of specific instructions from the physician fill the affected ear with Auraltone and plug the ear lightly with dry cotton wool.

Contra-indications, warnings, etc *Phenazon*

toxic effects: Phenazone is liable to give rise to skin eruptions and in susceptible individuals even small dose may have this effect.

Warning: Keep out of the reach of children.

Pharmaceutical precautions Keep in a cool, dry place, tightly capped. Do not warm or use with wet resins.

Legal category P.

Package quantities 15 ml in a bottle fitted with a rubber cap.

Further information Nil.

Product licence number 0208/5000.

RONCHOTONE*

Presentation A damson-coloured liquid with an odour of oranges, and bitter characteristic taste. Each 5 ml contains the following active ingredients:

phedrine Hydrochloride BP	22.89 mg
sodium Salicylate BP	91.85 mg
caffeine BP	86.50 mg
sodium Iodide BP	57.04 mg
incture of Belladonna BP	0.52 ml

he content of total alkaloids of belladonna herb calculated as hyoscyamine is 0.16 mg.

Uses Indicated in the treatment of asthma and bronchitis.

It is a respiratory stimulant, bronchodilator, expectorant and antispasmodic.

Dosage and administration *For oral administration*
adults: Up to three 5 ml spoonfuls (15 ml) in asthma and one or two 5 ml spoonfuls (5–10 ml) in bronchitis. These doses may be repeated every four hours.

Contra-indications, warnings, etc *Precautions:* *phedrine hydrochloride:* The use of ephedrine is contra-indicated in the presence of coronary thrombosis, hypertension and thyrotoxicosis. It should be given with caution to patients with organic heart disease, cardiac compensation or angina of effort, and in patients receiving digitalis. In patients with prostatic enlargement, may increase difficulty with micturition.

Ephedrine should not be given to patients being treated with a monoamine oxidase inhibitor or within 14 weeks of stopping such treatment.

sodium salicylate: Sodium salicylate should be given cautiously to patients on a low-sodium diet: it is contra-indicated in the presence of severe renal disease.

The precautions of sodium salicylate are the same as for aspirin. Therefore it should be cautiously employed, at all, in patients prone to dyspepsia or known to have a lesion of the gastric mucosa. It should not be administered to patients with haemophilia or to those with an intolerance to aspirin. Caution is necessary when renal function is impaired and, particularly in children, when the patient is dehydrated.

It may enhance the activity of coumarin anticoagulants and hypoglycaemic agents. The activity of methotrexate may be markedly enhanced and its toxicity increased. The toxicity of sulphonamides may also be increased. It diminishes the effects of uricosuric agents such as probenecid and sulphapyrazole. Barbiturates and other sedatives may mask the respiratory symptoms of aspirin overdose and have been reported to enhance its toxicity.

caffeine: Caffeine should be given with care to patients with a history of peptic ulceration.

Sodium iodide: Sodium iodide should generally not be given in pulmonary tuberculosis as it may convert a dormant into an active disease.

Caution is necessary if preparations containing iodides are taken for prolonged periods and such preparations should not be taken regularly during pregnancy. The administration of preparations containing iodides interferes with tests of thyroid function.

Tincture of belladonna: Atropine and other parasympatholytics should not be given to patients with closed-angle glaucoma or to patients with a narrow angle between the iris and cornea, since its use may increase the intra-ocular pressure.

Caution should be observed when drugs of this group are administered to patients with prostatic enlargement, coronary insufficiency or cardiac failure. Tachycardia may result from vagal inhibition and induce angina of effort in patients with coronary heart disease. They are contra-indicated in patients suffering from paralytic ileus.

The effects of atropine and other parasympatholytics may be enhanced by the concomitant administration of other drugs with parasympatholytic properties, such as some antihistamines and phenothiazines and tricyclic antidepressants.

Warning: *Keep out of the reach of children.*

Treatment of overdose: Gastric lavage and saline purgative. For overstimulation sedation may be required (e.g. chlorpromazine 50–100 mg i.m.). To control tachycardia, propranolol 2.5–5.0 mg i.v., except in asthmatics where practolol may be more suitable.

Pharmaceutical precautions Keep container tightly closed.

Legal category POM.

Package quantities 100 ml and 500 ml.

Further information Nil.

Product licence number 0208/5001.

COPHOLCO*

Presentation A dark brown syrupy linctus, odour and taste of aniseed. Each 5 ml contains the following active ingredients:

Pholcodine BP	5.63 mg (0.113% w/v)
Terpin Hydrate BPC (1968)	2.82 mg
Menthol BP	1.41 mg
Cineole BPC	0.0026 ml

Uses For the relief of cough in laryngitis, tracheitis and for all unproductive and 'ticklish' coughs.

Dosage and administration *For oral administration.*

Children over 5 years: Half to one 5 ml spoonful without water four or five times daily.

Adults: Two 5 ml spoonfuls without water four or five times daily.

Contra-indications, warnings, etc *Pholcodine toxic effects:* Nausea and drowsiness occasionally occur.

Terpin hydrate toxic effects: Epigastric pain may follow the administration of terpin hydrate on an empty stomach.

Warning: *Keep out of the reach of children.*

Treatment of overdose: Gastric lavage within two hours. Afterwards symptomatic treatment as required.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities 100 ml, 500 ml and 2 litres.

Further information Nil.

Product licence number 0208/5002.

COPHOLCOIDS*

Presentation Blackish, hard, sugar coated pastilles. Odour and taste of aniseed. Each pastille contains:

Pholcodine BP	4.0 mg (0.20% w/w)
Terpin Hydrate BPC (1968)	16.0 mg
Menthol BP	2.0 mg
Cineole BPC	0.004 ml

Uses Copholcoids are for the relief of cough in laryngitis, tracheitis and all unproductive and 'ticklish' coughs.

Dosage and administration For oral administration. *Children over 5 years:* Suck 1 pastille three times daily at four hourly intervals.

Adults: Suck 1 or 2 pastilles three or four times daily according to the severity of the condition.

Contra-indications, warnings, etc *Pholcodine toxic effects:* Nausea and drowsiness occasionally occur.

Terpin hydrate toxic effects: Epigastric pain may follow the administration of terpin hydrate on an empty stomach.

Warning: keep out of the reach of children.

Treatment of overdose: Gastric lavage within two hours. Afterwards symptomatic treatment as required.

Pharmaceutical precautions Store in a cool, dry place.

Legal category P.

Package quantities Cartons containing 50 g.

Further information Nil.

Product licence number 0208/5003.

MAALOX* SUSPENSION AND TABLETS

Presentation White peppermint-flavoured suspension. Each 5 ml contains:

Dried Aluminium Hydroxide Gel BP	220 mg
Magnesium Hydroxide BPC	195 mg

White peppermint-flavoured tablet containing:

Dried Aluminium Hydroxide Gel BP	400 mg
Magnesium Hydroxide BPC	400 mg

Uses Antacid therapy in gastric and duodenal ulcer, gastritis, heartburn and gastric hyperacidity.

Dosage and administration Maalox is administered orally and can be taken with milk or water if required.

Usual adult doses are: 10–20 ml taken 20 minutes to one hour after meals and at bedtime, or as required. One or two tablets well chewed, 20 minutes to one hour after meals and at bedtime, or as required.

Contra-indications, warnings, etc Maalox should not be used in patients who are severely debilitated or suffering from kidney failure.

Maalox will inhibit absorption of tetracyclines and vitamins if taken concurrently. Gastro-intestinal side effects are uncommon.

Treatment of overdose: Serious symptoms are unlikely following overdose.

Pharmaceutical precautions The suspension may be kept from freezing and the bottle kept tightly closed.

Legal category GSL.

Package quantities Suspension: Glass bottles 118 ml and 300 ml

Tablets: Cartons containing 20 and 50 strip-pack tablets.

Further information Maalox is a highly palatable balanced combination of two reliable antacids and has minimal gastro-intestinal side-effects. It is therefore especially suitable when prolonged therapy is necessary.

Product licence numbers

Suspension 0050/5002

Tablets 0050/5003

MAALOX* PLUS SUSPENSION AND TABLETS

Presentation White lemon/cream flavoured suspension. Each 5 ml contains the equivalent of:

Dried Aluminium Hydroxide Gel BP	220 mg
Magnesium Hydroxide BPC	195 mg
Simethicone	25 mg

Pale yellow tablet of diameter 0.625 inch with Maalox Plus embossed on one side. Each tablet contains:

Dried Aluminium Hydroxide Gel BP	200 mg
Magnesium Hydroxide BPC	200 mg
Simethicone	25 mg

Uses As an antacid/antiflatulent for relief of hyperacidity and/or flatulence associated with all gastric disorders of a functional or organic nature.

Dosage and administration Maalox Plus suspension and tablets are for oral administration and can be taken with milk or water if required.

Adult doses: 10–20 ml four times a day, taken two minutes to one hour after meals and at bedtime, or as required.

Two to four tablets well chewed, four times a day taken twenty minutes to one hour after meals and at bedtime, or as required.

Contra-indications, warnings, etc Maalox Plus should not be used in patients who are severely debilitated or suffering from kidney failure.

Maalox Plus will inhibit absorption of tetracyclines and vitamins if taken concurrently.

Gastro-intestinal side-effects are uncommon.

Treatment of overdose: Serious symptoms are unlikely following overdose.

Pharmaceutical precautions The suspension may be kept from freezing and the bottle kept tightly closed.

Legal category GSL.

Package quantities

Suspension: Glass bottle of 118 ml and 300 ml.

Tablets: Carton containing 20 and 50 strip-pack tablets.

Further information Maalox Plus is a highly palatable, balanced combination of two reliable antacids together with a potent antifatulent. The antacids are balanced such that gastro-intestinal side-effects (constipation and diarrhoea) are minimal. It is therefore especially suitable when prolonged therapy is necessary. The dimethicone disperses gastric foam and assists eructation of gases. It accelerates the penetration of antacids throughout the gastric contents and provides mucosal protection from the effects of excess acid.

Product licence numbers

Suspension 3384/0002
Tablets 3384/0001

NEURODYNE® CAPSULES

Presentation No. 0 white hard gelatin capsules, marked 'NEURODYNE' containing a white odourless powder. Each capsule contains:

Paracetamol BP 500 mg
Codeine Phosphate BP 8 mg

Uses For the relief of pain in neuralgia, neuritis, rheumatism, sciatica, dysmenorrhoea, etc., and in the treatment of influenza.

Dosage and administration For oral administration. *For adults only:* 1 or 2 capsules to be taken every three or four hours.

Contra-indications, warnings, etc *Paracetamol toxic effects:* Side-effects of paracetamol are usually mild, though haematological reactions have been reported. Skin eruptions have also occurred.

Symptoms of overdosage include vomiting, gastrointestinal haemorrhage, liver damage, cerebral oedema and renal tubular necrosis.

Hyperglycaemia and hypoglycaemia have been reported after overdosage with paracetamol and hypoglycaemia has followed a therapeutic dose in a child.

Precautions: Paracetamol should be given with care to patients with impaired kidney or liver function. It may enhance the activity of coumarin anticoagulants.

Codeine phosphate toxic effects: The commonest side-effects of therapeutic doses of codeine are constipation, nausea and vomiting, dizziness and drowsiness, but these are less common than with morphine.

Poisoning with codeine produces central stimulation with exhilaration and, in children, convulsions, followed by vomiting, drowsiness, respiratory depression and cyanosis and coma.

Very rare skin rashes may occur in patients hypersensitive to codeine.

Precautions: Codeine should be given with caution to patients with severe respiratory depression. The depressant effects of codeine may be enhanced by the concurrent administration of sedatives and tranquillisers.

Warning: *Keep out of the reach of children.*

Treatment of overdosage: Gastric lavage and saline purgative. Assist respiration if necessary. Observe closely for signs of paracetamol liver toxicity.

Pharmaceutical precautions Keep in a tightly closed container and store in a cool, dry place.

Legal category P.

Package quantities Bottles containing 100 and 250 capsules.

Further information Nil.

Product licence number 0208/5004.

PHYTOCIL® CREAM

Presentation A white, semi-translucent, homogeneous cream with the odour of menthol. It contains:

1-Phenoxypropan-2-ol	2.0% w/w
Salicylic Acid BP	1.5% w/w
2-p-Chlorophenoxyethanol	1.0% w/w
Menthol BP	1.0% w/w

Uses For the treatment of tinea pedis, tinea cruris, tinea circinata and other fungal infections of the skin.

Dosage and administration For external use only. Apply sufficient to treat the affected area of the skin twice or three times a day.

Contra-indications, warnings, etc No side-effects reported.

Warning: *Keep out of the reach of children.*

Pharmaceutical precautions Store in a cool, dry place.

Legal category P.

Package quantities Tubes containing 25 g.

Further information Nil.

Product licence number 0208/5005.

PHYTOCIL® POWDER

Presentation A fine uniform white powder with a sweetish odour, characteristic of the phenoxetols. It contains:

Zinc Undecenoate BP	5.8% w/w
1-Phenoxypropan-2-ol	2.0% w/w
2-p-Chlorophenoxyethanol	1.0% w/w

Uses For the treatment of tinea pedis, tinea cruris, tinea circinata and other fungal infections of the skin.

Dosage and administration For external use only. Apply to the affected areas of the skin twice daily and also dust into hosiery and shoes.

Contra-indications, warnings, etc No side-effects reported.

Warning: *Keep out of the reach of children.*

Pharmaceutical precautions Store in dry place.

Legal category P.

Package quantities Powder tins containing 50 g.

Further information Nil.

Product licence number 0208/5006.

SECADERM® SALVE

Presentation A green, translucent ointment with the odour of phenol, terebene and melaleuca oil. It contains:

Resin BP	26.0% w/w
Turpentine Oil BP	6.00% w/w

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RORER PHARMACEUTICALS

Melaleuca Oil BPC (1949)	5.60% w/w
Terebene	5.25% w/w
Phenol BP	2.40% w/w

Warning: Keep out of the reach of children.

Pharmaceutical precautions Store in a cool

Legal category GSL.

Uses Indicated in the relief and treatment of boils, abscesses, whitlow, bunions and chilblains.

Package quantities Tubes containing 15 g.

Dosage and administration For external use only.

Further information Nil.

Apply once or twice daily to the affected parts and cover with a light dressing of gauze.

Product licence number 0208/5007.

Contra-indications, warnings, etc No side-effects reported.

** Trade Mark*

ACTINAC*

Presentation Actinac is presented as a pale yellow dry powder, together with a solvent for the preparation of a lotion. Each gram of powder contains:

chloramphenicol BP	40 mg
hydrocortisone Acetate BP	40 mg
utoxyethyl nicotinate	24 mg
llantoin	24 mg
recipitated Sulphur BPC	320 mg

The solvent is Purified Water BP, containing an approved preservative perfume and bacteriostat.

Uses Actinac is for use in the topical treatment of acne vulgaris and other acneiform conditions. It is formulated to control local infection and suppress inflammation with consequent scarring effects.

Dosage and administration The lotion should be prepared according to the manufacturer's literature and applied with cotton wool or lint night and morning for the first four days and only at night thereafter. In order to prevent recurrence, treatment should be continued for three nights after the lesions have disappeared.

Contra-indications, warnings, etc Actinac is contra-indicated in patients who have a known hypersensitivity to any of the ingredients.

Avoid Actinac coming into contact with the eyes and mouth.

Early in the course of treatment, erythema may occur at the site of application and the patient may experience sensation of warmth due to the vasodilator action of the nicotinate. In the unlikely event of a severe reaction, the patient is instructed to consult the doctor before further use of Actinac.

In pregnant animals, administration of corticosteroids can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods. It is advisable to remove jewellery before applying the lotion.

Pharmaceutical precautions Store cool. The lotion when constituted will remain active for 21 days. Any portion remaining after this time must be discarded and a fresh supply of lotion prepared.

Legal category POM.

Package quantities Each pack of Actinac contains two bottles of powder (each 5 g), two bottles of solvent (each 16 ml) and an instruction leaflet for the patient.

Further information Nil.

Product licence number 0109/0037.

ALTACITE*

Presentation Altacite is available as white, buttermint-

flavoured tablets marked 'altacite' and 'ROUSSEL', and as an aqueous suspension, slightly off-white, viscous and flavoured with peppermint.

Each tablet and each 5 ml of suspension contains 500 mg of hydrotalcite.

Uses Antacid, buffering in the optimum range of pH 3-5 for over two hours.

Altacite is indicated for symptomatic relief in the following conditions: peptic ulceration; dyspepsia; hyperacidity; gastritis; heartburn, especially when associated with reflux oesophagitis or hiatus hernia, and heartburn in pregnancy.

Dosage and administration *Adults:* 2 tablets or 10 ml of suspension between meals and at bedtime or as directed by a physician.

Children (6-12 years): Half the adult dose.

The tablets should be chewed or crushed before swallowing.

Contra-indications, warnings, etc There are no contra-indications to Altacite but it is probably wise to avoid any drug, including antacids, during the first trimester of pregnancy. As with other compounds containing aluminium or magnesium, Altacite may reduce intestinal absorption of tetracycline. Side-effects are uncommon. Diarrhoea and vomiting have been reported but have ceased on withdrawal of therapy.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities *Altacite Tablets:* Carton of 12 blister strips each containing 10 tablets.

Altacite Suspension: Polypropylene bottle containing 500 ml.

Further information There is no evidence of absorption of Altacite in man. Investigations in healthy human volunteers have shown no elevation of serum aluminium or magnesium levels on administering Altacite at therapeutic dosage for a continuous period of 28 days.

The sodium content of Altacite is 0.22 mmol per tablet or 5 ml of suspension.

Product licence numbers

Altacite Tablets	0109/0040
Altacite Suspension	0109/0041

ALTACITE PLUS*

Presentation *Suspension:* Viscous, slightly off-white aqueous suspension, flavoured with spearmint. Each 5 ml of suspension contains 500 mg of hydrotalcite and 125 mg of activated dimethicone.

Tablets: Round, white to off-white peppermint flavoured tablets marked R364 on one side and  on the reverse. Each tablet contains 500 mg hydrotalcite and 250 mg activated dimethicone.

Uses Altacite Plus has antacid, mucosal protective and anti-flatulent properties. As an antacid, Altacite Plus buffers in the optimal range of pH 3-5 for over two hours.

It is indicated for symptomatic relief in the following conditions: dyspepsia; flatulence and abdominal distension; hyperacidity; gastritis; peptic ulceration; heartburn, especially when associated with oesophagitis or hiatus hernia, and heartburn in pregnancy.

Dosage and administration *Adults*: 10 ml suspension or 2 tablets between meals and at bedtime or as directed by the physician.

Children: (8-12 years): Half the adult dose.

The tablets should be chewed or crushed before swallowing.

Contra-indications, warnings, etc There are no known contra-indications to Altacite Plus, but it is probably wise to avoid any drug, including antacids, during the first trimester of pregnancy. As with other compounds containing aluminium or magnesium, Altacite Plus may reduce intestinal absorption of tetracycline. Side-effects are uncommon. Diarrhoea and vomiting have been reported but have ceased on withdrawal of therapy.

Pharmaceutical precautions Store in a cool, dry place.

Legal category P.

Package quantities *Altacite Plus Suspension*: Polypropylene bottle containing 500 ml.

Altacite Plus Tablets: Carton of five polypropylene tubes, each tube containing 20 tablets.

Further information There is no evidence of absorption of hydrotalcite in man. Investigations in healthy human volunteers have shown no elevation of serum aluminium or magnesium levels on administration of hydrotalcite at therapeutic dosage for a continuous period of 28 days.

The sodium content of Altacite Plus suspension is 0.078 mmol/5 ml and of Altacite Plus tablets 0.046 mmol/tablet.

Product licence numbers

Altacite Plus Suspension	0109/0062
Altacite Plus Tablets	0109/0056.

CIDOMYCIN® GENTAMICIN INJECTION BP GENTAMICIN INTRATHECAL INJECTION GENTAMICIN SULPHATE BP

Presentation Cidomycin for parenteral use is available as:

Cidomycin Injectable in 2 ml vials or ampoules each containing the equivalent of 80 mg gentamicin base as sulphate.

Cidomycin Injectable Paediatric in 2 ml vials each containing the equivalent of 20 mg gentamicin base as sulphate.

Cidomycin Intrathecal Injectable in 1 ml ampoules each containing 5 mg gentamicin base as sulphate.

Cidomycin Sterile Powder is whitish in colour and is available in packs of 1 g (base activity).

Uses Gentamicin is an aminoglycoside antibiotic with broad-spectrum bactericidal activity. It is usually active against most strains of the following organisms: *Escherichia coli*, *Klebsiella spp.*, *Proteus spp.* (indole positive and indole negative), *Pseudomonas aeruginosa*, staphylococci, *Enterobacter spp.*, *Citrobacter spp.* and *Providencia spp.*

Gentamicin injection and gentamicin paediatric injection are indicated in urinary-tract infections, chest infections, bacteraemia, septicaemia, infections following burns, infected traumatic or surgical wounds and other systemic infections due to sensitive organisms.

Gentamicin intrathecal injection is indicated as supplement to systemic therapy in bacterial meningitis, ventriculitis and other bacterial infections of the central nervous system.

Gentamicin sterile powder prepared as a steril injection may be used for serious intra-ocular infection and prophylactically prior to intra-ocular surgery.

Dosage and administration *Gentamicin injection* *Adults: Serious infections*: If renal function is not impaired, 5 mg/kg daily in divided doses at six- or eight hourly intervals. The total daily dose may be subsequently increased or decreased as clinically indicated.

Systemic infections: 80 mg eight-hourly for 7-10 days is usually an effective dose. If body weight is less than 60 kg, 60 mg eight hourly should be used.

Urinary-tract infections: As 'systemic infections'. Or, if renal function is not impaired, 160 mg once daily may be used.

Children: Up to 2 weeks of age: 3 mg/kg 12-hourly.

2 weeks to 12 years: 2 mg/kg eight-hourly.

Assay of peak serum levels gives confirmation of adequacy of dosage and also serves to detect levels above 10 mg/l, at which the possibility of ototoxicity should be considered.

Gentamicin is excreted by simple glomerular filtration and therefore is given in reduced dosage in cases of renal impairment. The following table may be useful when treating adults.

Blood urea		Creatinine clearance (GFR)	Dose and frequency of administration
(mg/100 ml)	(mmol/l)		
<40	6-7	>70	80 mg 8-hourly
40-100	6-17	30-70	80 mg 12-hourly
100-200	17-34	10-30	80 mg* daily
>200	>34	5-10	80 mg* every 48 hours
Twice-weekly intermittent haemodialysis		<5	80 mg* after dialysis

*60 mg if body weight <60 kg. Frequency of dosage in hours may also be approximated as serum creatinine (mg%) $\times$ eight or in SI units, as serum creatinine (mmol/l) divided by 11. If these dosage guides are used peak serum levels must be measured. Peak levels of gentamicin occur approximately one hour after intra-muscular injection and 15 minutes after bolus intravenous injection. Trough levels are measured just prior to the next injection.

The recommended dose and precautions for intramuscular and intravenous administration are identical. Gentamicin when given intravenously should be injected

irectly into a vein or into the drip set tubing over no less than three minutes. If administered by infusion, this should be over no longer than 20 minutes and in no greater volume of fluid than 100 ml.

Gentamicin intrathecal injection: Bacterial meningitis and ventriculitis: the starting dose of gentamicin intrathecal injection for both children and adults is 1 mg daily, intrathecally or intraventricularly, together with 1 mg/kg every eight hours intramuscularly. The MIC of the infecting organism in the CSF should be assessed and, if necessary, the intrathecal/intraventricular dose increased to 5 mg daily, whilst keeping the intramuscular dose at 1 mg/kg eight-hourly. Treatment should be continued for at least seven days but longer if necessary. Periodic serum and CSF gentamicin assays should be carried out to ensure that adequate antibiotic levels are maintained and that serum and CSF levels do not exceed 0 mg/l.

Gentamicin sterile powder: Serious bacterial ocular infections and prophylaxis prior to intra-ocular surgery: gentamicin sulphate equivalent to 20–40 mg base should be injected subconjunctivally once or twice daily until infection subsides. This may require continuation of therapy for two or more days. In the majority of cases concomitant intramuscular therapy is not required. This dosage regime is suitable for children and adults.

Contra-indications, warnings, etc Gentamicin should not be used to treat infections during the first trimester of pregnancy, except when the clinician deems it advisable as in life-threatening infections. Neither should it be used if there is a history of sensitivity to the antibiotic. Ototoxicity in the form of vestibular damage hearing loss has seldom been manifest) has been recorded following the use of gentamicin. In most cases it occurred in the presence of impaired renal function following higher dosage or more prolonged administration than that recommended. In some patients with impaired renal function there has been a transient rise in blood-urea-nitrogen which has usually reverted to normal during or following cessation of therapy. It is important to adjust the frequency of dosage according to the degree of renal function (see table).

There is evidence that any potential nephrotoxicity of cephalosporins, and in particular of cephaloridine, may be increased in the presence of gentamicin. Consequently if this combination is used monitoring of kidney function is advised. Concurrent administration of gentamicin and other potentially ototoxic or nephrotoxic drugs should be avoided.

Neuromuscular blockade and respiratory paralysis have been reported from administration of aminoglycosides to patients who have received curare-type muscle relaxants during anaesthesia.

Pharmaceutical precautions Gentamicin is a remarkably stable antibiotic and does not require refrigeration. Avoid freezing.

In general gentamicin injection should not be mixed. In particular the following are incompatible in mixed solution with gentamicin injection: penicillins, cephalosporins, erythromycin, Lipiphysan, heparins, sodium bicarbonate.† Dilution in the body will obviate the danger of physical and chemical incompatibility and enable gentamicin to be given concurrently with the drugs listed above either as a bolus injection into the drip tubing,

Carbon dioxide may be liberated on addition of the two solutions. Normally this will dissolve in the solution but under some circumstances small bubbles may form.

with adequate flushing, or at separate sites. In the case of carbenicillin, administration should only be at a separate site.

Legal category POM.

Package quantities *Cidomycin Injectable:* Packs of 25 × 2 ml vials or ampoules.

Cidomycin Injectable Paediatric: Packs of 5 × 2 ml vials.

Cidomycin Intrathecal Injectable: Packs of 5 × 1 ml ampoules.

Cidomycin Sterile Powder: Bottles containing 1 g.

Further information Nil.

Product licence numbers

Cidomycin Injectable	0109/5065
Cidomycin Injectable Paediatric	0109/5066
Cidomycin Sterile Powder	0109/5067
Cidomycin Intrathecal Injectable	0109/0052

CIDOMYCIN* (TOPICAL)

Presentation Available as a white cream which contains gentamicin sulphate in a water-miscible base and as a translucent ointment in a petroleum base. Each gram of ointment or cream contains gentamicin sulphate equivalent to 3 mg gentamicin base.

Uses Cidomycin is a wide-spectrum antibiotic and the ointment and cream are recommended for the treatment of primary and secondary skin infections due to susceptible bacteria.

Primary infections: Impetigo contagiosa, superficial folliculitis, ecthyma, furunculosis, sycosis barbae and pyoderma gangrenosum.

Secondary infections: Infected, contact, seborrhoeic, and eczematoid dermatitis, pustular acne, infected burns and wounds, ulcers and paronychia.

Dosage and administration A small amount of ointment or cream should be applied to the lesions three or four times daily or as prescribed. If necessary this may be covered with a dressing.

Contra-indications, warnings, etc Cidomycin is contra-indicated when there is a known hypersensitivity to any ingredient of the preparation.

Precautions: If irritation, sensitisation or super-infection develop, treatment with Cidomycin should be discontinued and appropriate therapy instituted.

Pharmaceutical precautions Store cool. In order to preserve their antibacterial activity Cidomycin Cream and Ointment should not be diluted by the addition of excipient.

Legal category POM.

Package quantities *Cidomycin cream:* Tubes of 15 g and 30 g.

Cidomycin ointment: Tubes of 15 g and 30 g.

Further information Nil.

Product licence numbers

Cidomycin Cream	0109/5063
Cidomycin Ointment	0109/5064

CLAFORAN* ▼

Presentation Claforan is available in vials containing 500 mg, 1 g or 2 g of cefotaxime as cefotaxime sodium.

Claforan is a white to slightly creamy powder which, when dissolved in Water for Injections BP forms a straw coloured solution suitable for intravenous or intramuscular administration. Variations in the intensity of colour of the freshly prepared solution do not indicate change in potency or safety.

Uses

Properties: Claforan is a broad spectrum bactericidal cephalosporin antibiotic. Claforan is exceptionally active in vitro against Gram-negative organisms sensitive or resistant to first or second generation cephalosporins. It is similar to other cephalosporins in activity against Gram-positive bacteria.

Indications: Claforan is indicated in the treatment of the following infections either before the infecting organism has been identified or when caused by bacteria of established sensitivity.

Septicaemia

Respiratory tract infections: acute and chronic bronchitis, bacterial pneumonia, infected bronchiectasis, lung abscess and post-operative chest infections.

Urinary tract infections: acute and chronic pyelonephritis, cystitis and asymptomatic bacteriuria.

Soft tissue infections: cellulitis, peritonitis and wound infections.

Bone and joint infections: osteomyelitis, septic arthritis.

Obstetric and gynaecological infections: pelvic inflammatory disease.

Gonorrhoea: particularly if penicillin-resistant.

Other bacterial infections: meningitis and other sensitive infections suitable for parenteral antibiotic therapy.

Bacteriology: The following organisms have shown in vitro sensitivity to Claforan.

Gram-positive: Staphylococci, including coagulase-positive, coagulase-negative and penicillinase-producing strains. Beta-haemolytic and other streptococci such as *Streptococcus mitis* (*viridans*). Many strains of enterococci, e.g. *Streptococcus faecalis*, are relatively resistant. *Streptococcus* (*Diplococcus*) *pneumoniae*. *Clostridium* spp.

Gram-negative: *Escherichia coli*
Haemophilus influenzae including ampicillin-resistant strains

Klebsiella spp.

Proteus spp. both indole-positive and indole-negative

Enterobacter spp.

Neisseria spp. including β -lactamase producing strains of *N. gonorrhoeae*

Salmonella spp. including *Salm. typhi*

Shigella spp.

Providencia spp.

Serratia spp.

Citrobacter spp.

Claforan has frequently exhibited useful in vitro activity against *Pseudomonas* and *Bacteroides* species although some strains of *Bacteroides fragilis* are resistant.

There is in vitro evidence of synergy between Claforan and aminoglycoside antibiotics such as gentamicin against some species of Gram-negative bacteria including some strains of *Pseudomonas*. No in vitro antagonism has been noted. In severe infections caused by *Pseudomonas* spp. the concurrent use of an aminoglycoside antibiotic may be indicated.

Dosage and administration Claforan may be administered intravenously or intramuscularly. Dosage, route

and frequency of administration should be determined by severity of infection, sensitivity of causative organism and condition of the patient. Therapy may be started before the result of sensitivity tests are known.

Adults: The recommended dosage for moderate infections is 1 g every 12 hours (twice daily). However dosage may be varied according to the severity of the infection, sensitivity of causative organisms and condition of the patient.

In severe infections the recommended dosage may be increased up to 12 g daily given in 3 or 4 divided doses. For infections caused by sensitive *Pseudomonas* spp. daily doses of more than 6 g are usually required.

Children: The usual dosage is 100–150 mg/kg/day in 2 to 4 divided doses. In very severe infections up to 200 mg/kg/day, in divided doses, may be required.

Neonates: The recommended dosage is 50 mg/kg/day in 2 to 4 divided doses. In severe infections, 150–200 mg/kg/day, in divided doses, have been given.

Dosage in gonorrhoea: A single injection of 1 g should be administered intramuscularly or intravenously.

Dosage in renal impairment: Because of extra-renal elimination, it is only necessary to reduce the dosage of Claforan in severe renal failure (GFR < 5 ml/min). After an initial loading dose of 1 g, the daily dose should be halved without change in the frequency of dosing, e.g. 1 g 12 hourly becomes 0.5 g 12 hourly, 1 g 8 hourly becomes 0.5 g 8 hourly, 2 g 8 hourly becomes 1 g 8 hourly, etc. As in all other patients, dosage may require further adjustment according to the course of the infection and the general condition of the patient.

Intravenous and intramuscular administration: Dissolve Claforan in Water for Injections BP as shown below. Shake well until dissolved and then withdraw the entire contents of the vial into the syringe and use immediately.

Vial size	Volume of Water for Injections to be added
500 mg	2 ml
1 g	4 ml
2 g	10 ml

Intravenous infusion: Claforan may be administered by intravenous infusion. 1–2 g are dissolved in 40–100 ml of Water for Injections BP or in the infusion fluids listed under Pharmaceutical precautions. The prepared infusion should be administered over 20–60 minutes.

Contra-indications, warnings, etc

Contra-indications: Known allergy to cephalosporins.

Precautions: Cephalosporin antibiotics may usually be given safely to patients who are hypersensitive to penicillins, although cross reactions have been reported. Special care is indicated in patients who have had an anaphylactic response to penicillin.

Patients with severe renal dysfunction – see 'Dosage and administration'.

Cephalosporin antibiotics at high dosage should be given with caution to patients receiving aminoglycoside antibiotics or potent diuretics such as frusemide as these combinations are thought to have an adverse effect on renal function. However, at the recommended doses, enhancement of nephrotoxicity is unlikely to be a problem with Claforan.

Interference with laboratory tests: A false-positive reaction to glucose may occur with reducing substances but not with the use of specific glucose oxidase methods.

Pregnancy: Although studies in animals have not shown an adverse effect on the developing foetus, the safety of claforan in human pregnancy has not been established. Consequently, claforan should not be administered during pregnancy especially during the first trimester, without carefully weighing the expected benefits against the possible risks.

Lactation: Claforan is excreted in the milk.

Side effects: Adverse reactions to claforan have occurred relatively infrequently and have generally been mild and transient. Effects reported include diarrhoea, candidiasis, rashes, fever, eosinophilia, leukopenia and transient rises in liver transaminase and alkaline phosphatase.

Transient pain may be experienced at the site of injection. This is more likely to occur with higher doses. Occasionally, phlebitis has been reported in patients receiving intravenous claforan. However, this has rarely been a cause for discontinuation of treatment.

Overdosage: Serum levels of claforan may be reduced by peritoneal dialysis or haemodialysis.

Pharmaceutical precautions The dry powder in vials should be stored away from heat and protected from light. Whilst it is preferable to use only freshly prepared solutions for both intravenous and intramuscular injection, claforan is compatible with several commonly used intravenous infusion fluids and will retain satisfactory potency for up to 24 hours refrigerated in the following:

Water for Injections BP
Sodium Chloride Injection BP
5% Dextrose Injection BP
Dextrose and Sodium Chloride Injection BP
Compound Sodium Lactate Injection BP (Ringer-Lactate Injection).

After 24 hours any unused solution should be discarded.

Claforan is also compatible with 1% lignocaine. Freshly prepared solutions should be used.

Some increase in colour of prepared solutions may occur on storage. However, provided the recommended storage conditions are observed, this does not indicate change in potency or safety.

Legal category POM.

Package quantities Individually packed vials containing 500 mg or 1 g cefotaxime as cefotaxime sodium for use by intramuscular or intravenous injection) in packs of 10.

Individually packed vials containing 2 g cefotaxime as cefotaxime sodium (for intravenous use only) in packs of 10.

Further information Each gram of claforan contains approximately 48 mg (2.09 mmol) of sodium. Claforan has been used with other beta-lactam antibiotics such as carbenicillin in the treatment of neutropenic patients. Claforan may also be administered separately with metronidazole in the treatment of mixed infections caused by anaerobic and aerobic organisms.

Claforan usually passes the blood-brain barrier in levels above the MIC of common sensitive pathogens when the meninges are inflamed.

The laboratory abbreviation for cefotaxime is CTX.

Product licence number 0109/0074

LANITOP®

Presentation Lanitop tablets contain 0.1 mg digoxin. The tablets are round (6 mm diameter), yellow and with a score line. They are engraved one side with LAN on the left side and TOP on the right side of the breakline.

Lanitop Intravenous Injection contains 0.2 mg digoxin in each 2 ml ampoule.

Uses Lanitop is indicated in all cases in which digitalis therapy is required, e.g. congestive heart failure and certain cardiac arrhythmias, especially atrial fibrillation.

Dosage and administration The dosage of Lanitop is the same whether given orally or i.v. The two routes of administration are therefore interchangeable at any time during treatment.

Dosage is dependent upon the glycoside requirement of the heart in individual patients. It has been shown that 95% of patients may be treated successfully, using the following schedule.

1. **Adults and children over 14:** *Digitalisation:* 2 tablets twice daily (or 2 ampoules i.v. daily if oral administration is impossible) for three to five days.

Maintenance: 1 tablet two or three times daily (or 1–1½ ampoules i.v. daily if oral administration is impossible).

In emergencies a more rapid digitalisation may be achieved by giving: 2 tablets three times daily for two to four days.

If the immediate onset of action is critical, the first dose may be given i.v. (1 ampoule).

If oral administration is impossible rapid digitalisation may be achieved by giving 1 ampoule i.v. three times daily for two to four days.

2. **Infants and children under 14 years:** Digitalisation may be effected by using 0.01 mg/kg repeated six-hourly until therapeutic result is obtained, 2–4 doses usually being sufficient. Maintenance is usually achieved with 0.01 mg/kg daily, which should be adjusted as necessary.

Contra-indications, warnings, etc All cardiac glycosides are contra-indicated in digitalis intoxication, hypercalcaemia and before electro-cardioversion. Special care should be taken if the patient is already receiving or has recently been receiving a cardiac glycoside. In addition, glycoside therapy may be contra-indicated or may require additional therapeutic measures in manifest hypokalaemia, disorders of atrio-ventricular conduction and in pathological bradycardia, depending on its severity.

Parenteral administration of calcium, particularly simultaneously, should be avoided during any glycoside therapy.

Lanitop should be accorded the same precautions as all other cardiac glycosides when administered intravenously.

As with all digitalis therapy, gastric disturbance, arrhythmias and visual disturbances may occur, particularly in those patients who are hypersensitive to glycosides or who have an electrolyte imbalance such as that caused by diuretic therapy.

A reduced glycoside requirement may be expected in the elderly and when there is renal insufficiency. The recommended doses may produce evidence of toxicity in patients with acute myocardial infarction, severe pulmonary disease, advanced liver failure, and in premature infants.

Teratogenic studies have been conducted in animals without adverse effects. However, the likely benefit from the administration of Lanitop should be weighed against possible adverse effects during the first trimester of pregnancy.

Treatment of overdosage: Gastric lavage should be given and the ECG monitored. Potassium should be administered for hypokalaemia and glucose and insulin for hyperkalaemia; atropine for bradycardia, antiarrhythmic agents such as disopyramide or lignocaine for tachycardia and arrhythmia.

Pharmaceutical precautions Store in a cool dry place. Protect from light.

Legal category POM.

Package quantities *Lanitop Tablets*: Bottles of 100.

Lanitop Injection: Boxes of 5 × 2 ml ampoules.

Further information Absorption of Lanitop is rapid (5–20 minutes) and virtually complete. Its duration of action is similar to that of digoxin. These characteristics fulfil the pharmacokinetic requirements of an ideal cardiac glycoside.

The stated dosages are less than those normally used when digoxin is administered. Under steady state conditions 0.3 mg Lanitop daily is therapeutically equivalent to 0.5 mg of digoxin daily.

Product licence numbers

Lanitop Tablets 0109/0053

Lanitop Injection 0109/0054

MOLIPAXIN* ▼

Presentation Molipaxin (trazodone hydrochloride) is available as: Molipaxin 50 mg. Size No. 3, opaque violet/green capsules printed R365B and . Each capsule contains 50 mg trazodone hydrochloride.

Molipaxin 100 mg. Size No. 2, opaque violet/fawn capsules printed R365C and . Each capsule contains 100 mg trazodone hydrochloride.

Uses *Properties:* Molipaxin is a potent antidepressant. It also has anxiety reducing activity. Molipaxin is a triazolopyridine derivative chemically unrelated to known tricyclic, tetracyclic and other antidepressant agents. It has negligible effect on noradrenaline re-uptake mechanisms. Whilst the mode of action of Molipaxin is not known precisely, its antidepressant activity may concern noradrenergic potentiation by mechanisms other than uptake blockade. A central anti-serotonin effect may account for the drug's anxiety reducing properties.

Indications: Relief of symptoms in all types of depression including depression accompanied by anxiety. Symptoms of depression likely to respond in the first week of treatment include depressed mood, insomnia, suicidal thoughts, anxiety, somatic symptoms and hypochondriasis.

Dosage and administration Molipaxin may be administered as a single bedtime dose or in divided doses after food. Symptomatic relief may be seen during the initial week, with optimum antidepressant effects typically evident within two weeks.

Adults: According to severity, treatment should be initiated at 100 or 150 mg per day and then increased to 200 or 300 mg per day, respectively, at the end of the

first week. In exceptionally severe depression, dosage may be further increased to a maximum of 600 mg per day in divided doses. However, the usual maintenance dose in patients with moderate-to-severe depression is 300 mg per day. In cases of mild depression, as seen in general practice, the usual maintenance dose is 200 mg per day.

Sedative effects, although usually well tolerated on continued medication, may suggest administration of, or the major portion of the usual daily doses at bedtime.

In elderly and frail patients the recommended starting dosage is 100 mg per day in divided doses increasing thereafter according to clinical progress. In general, single doses above 100 mg should be avoided in these patients.

In conformity with current psychiatric opinion, it is suggested that Molipaxin be continued for several months after remission. Cessation of Molipaxin treatment should be gradual.

Children: There are insufficient data to recommend the use of Molipaxin in children.

Contra-indications, warnings, etc

Contra-indications: None.

Precautions: As with all other drugs acting on the central nervous system, patients should be warned against the risks of handling machinery and driving.

Although no untoward effects have been reported, Molipaxin may enhance the effects of muscle relaxants and volatile anaesthetics. Similar considerations apply to combined administration with sedative and antidepressant drugs, including alcohol. Molipaxin has been well tolerated in depressed schizophrenic patients receiving standard phenothiazine therapy and also in depressed parkinsonian patients receiving therapy with levodopa.

Interactions between Molipaxin and monoamine oxidase inhibitors have not been reported. However, on grounds of clinical caution, Molipaxin is not recommended for concurrent administration with monoamine oxidase inhibitors or within two weeks of terminating treatment with these compounds.

Since Molipaxin is only a very weak inhibitor of noradrenaline re-uptake and does not modify the blood pressure response to tyramine, interference with the hypotensive action of guanethidine-like compounds is unlikely. However, studies in laboratory animals suggest that Molipaxin may inhibit most of the acute actions of clonidine. In the case of other types of antihypertensive drug, although no clinical interactions have been reported, the possibility of potentiation should be considered.

Current clinical experience suggests that Molipaxin does not cause seizures. Nevertheless, care should be exercised when administering Molipaxin to patients suffering from epilepsy, avoiding in particular, abrupt increases or decreases in dosage.

Molipaxin should be administered with care in patients with severe hepatic or renal disease.

Pregnancy and lactation: Although studies in animals have not shown any direct teratogenic effect, the safety of Molipaxin in human pregnancy has not been established. On basic principles, therefore, its use during the first trimester should be avoided. The possibility of Molipaxin being excreted in the milk should also be considered in nursing mothers.

Side-effects: Molipaxin is a sedative antidepressant and drowsiness sometimes experienced during the first day of treatment usually disappears on continued therapy.

c-like symptoms is not

been reported even in
or periods in excess of
ms, most of which are
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all numbers of patients
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ardia, tachycardia, pos-
fiarrhoea, blurred vision,
insomnia and skin rash.
; antidote to Molipaxin.
l as quickly as possible.
ic and supportive in the
ve sedation.

; No special storage

in 50 mg and 100 mg
ips of 20 each in pack

ntrast to the tricyclic
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urinary hesitancy have
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or pulmonary disease.

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Dosage and administration *Sofradex Drops: In the ear:* 2 or 3 drops should be instilled into the ear three or four times daily; alternatively, a gauze wick kept saturated with the drops should be inserted into the external auditory meatus.

In the eye: For rapid effect, 1 or 2 drops every one or two hours should be instilled in acute conditions (generally for two, or three days), reducing to 1 or 2 drops three or four times daily.

Sofradex Ointment: In the ear: Sofradex should be applied twice or thrice daily, and especially at bedtime, to the meatus, concha or over the pinna and to adjacent skin areas if extension to these parts has occurred.

In the eye: 2 or 3 applications of the ointment daily, or at bedtime if drops have been used during the day.

Contra-indications, warnings, etc Sofradex is contra-indicated in: herpes simplex infections and other virus diseases of the cornea and conjunctiva; tuberculosis of the eye; fungal diseases of the eye; trachoma.

Purulent infections of the eye could be masked and indeed enhanced by the presence of the steroid, particularly when the infecting organism is not sensitive to the antibiotics contained in Sofradex.

Hypersensitivity to any of the active ingredients.

Preparations containing framycetin should not be used for treating otitis externa when the ear drum is perforated, because of the risk of ototoxicity.

Side effects:

1. Raised intra-ocular pressure may result from extended use of topical steroid therapy in some individuals.

2. In conditions causing thinning of the cornea, any topical steroid may cause perforation.

3. Cataract has been reported to have occurred after unduly prolonged treatment of eye conditions with topical corticosteroids.

Note:

In pregnant animals, administration of corticosteroids can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical corticosteroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

Although it is unlikely that infants will be treated long-term with Sofradex, it must be remembered that if steroids are applied to the skin of infants for continued periods of time, there is a risk of adrenal suppression occurring, even without occlusion.

Pharmaceutical precautions Store cool.

Legal category POM.

Package quantities *Sofradex Ear/Eye Drops:* Bottles of 8 ml.

Sofradex Ear/Eye Ointment: Tubes of 5 g (fitted with ophthalmic nozzle).

Further information Nil.

Product licence numbers

Sofradex Ear/Eye Drops 0109/0030

Sofradex Ear/Eye Ointment 0109/0031

SOFRAMYCIN* STERILE EYE DROPS/OINTMENT

Presentation Soframycin is available as a sterile eye ointment and as colourless, sterile eye drops.

Each gram of ointment contains Framycetin Sulphate BP (Soframycin) 5 mg in a sterile, non-irritating greasy base.

Each millilitre of drops contains Framycetin Sulphate BP (Soframycin) 5 mg in a sterile, buffered, isotonic, aqueous solution.

Uses Soframycin is used for the treatment of bacterial infections of the eye, notably conjunctivitis and blepharitis, for styes, corneal abrasions and burns, and prophylactically following the removal of foreign bodies. It is also indicated for corneal ulcers (alone or as a complement to the use of Soframycin by subconjunctival injection).

Dosage and administration *Soframycin Drops:* For rapid effect, preferably during the daytime, 1 or 2 drops every one or two hours should be instilled in acute conditions (generally for two or three days), reducing to 1 or 2 drops three or four times daily.

Soframycin Ointment: For continued effect, 2 or 3 applications of the ointment daily, or at bedtime if drops have been used during the day.

Contra-indications, warnings, etc Soframycin is contra-indicated when there is a known hypersensitivity to any ingredient of the preparation.

Pharmaceutical precautions Store cool.

Legal category POM.

Package quantities *Soframycin Eye Drops:* 8 ml in ophthalmic dispenser.

Soframycin Eye Ointment: Tubes of 5 g (fitted with ophthalmic nozzle).

Further information Nil.

Product licence numbers

Soframycin Eye Drops	0109/5040
Soframycin Eye Ointment	0109/5041

SOFRA-TULLE*

Presentation Sofra-Tulle is a sterile, lightweight, lanoparaffin gauze dressing impregnated with Framycetin Sulphate BP 1% (Soframycin).

Uses Sofra-Tulle has a wide range of antibacterial activity and is an ideal dressing for immediate use in a variety of infected lesions.

Thermal: Burns, scalds.

Traumatic: Lacerations, abrasions, bites, puncture wounds, crush injuries.

Ulcerative: Varicose, diabetic, decubitus and tropic ulcers.

Elective: Skin grafts (donor and receptor sites), avulsion of finger and/or toe nails, circumcision, suture lines.

Miscellaneous: Secondarily infected skin conditions (e.g. eczema, dermatitis, herpes zoster), colostomy ileostomies, tracheostomies, incised abscesses, incision perionychia.

Dosage and administration If necessary, the lesion should first be cleansed, then a single layer of Sofra-Tulle applied and covered with a suitable dressing. When dressing ulcers, the tulle should be shaped to fit the ulcer crater. If the lesion exudes profusely it is advisable to change the dressings at least once a day.

Contra-indications, warnings, etc Sofra-Tulle is contra-indicated where there is known allergy to lanolin or to Soframycin, or where organisms are known to be resistant to the latter.

Precautions: Cross-sensitisation to Soframycin may occur in patients known to be allergic to Streptomycin derived antibiotics (neomycin, paramomycin, kanamycin).

In most cases, absorption of the antibiotic is negligible. However, where large body areas are involved, e.g. 3rd or more body burn, the possibility of ototoxicity being produced by prolonged applications should be borne in mind.

Pharmaceutical precautions Store cool.

Legal category POM.

Package quantities Cartons of 10 and 50 units; each unit pack contains one sterile antibiotic gauze dressing 10 cm × 10 cm placed between two layers of parchment. Also available as a continuous gauze strip 30 cm × 10 cm packed in cartons of 10 units.

Further information Nil.

Product licence number 0109/5047.

*Trade Mark

A.M.*

BRONCHIAL ANTISPASMODIC SYRUP

Presentation Rybar C.A.M. is a pale-green coloured liquid. Each 5 ml contains:

Ephedrine Hydrochloride BP	4 mg
Butethamate citrate INN	4 mg

Uses C.A.M. is indicated in the symptomatic treatment of bronchospasm in children and adults with asthma or onchitis. C.A.M.'s antitussive action may also be useful in children with unproductive cough.

Dosage and administration *Age under 2 years:* half 5 ml spoonful three times daily.

2-4 years: One 5 ml spoonful three times daily.

Age over 4 years: Two 5 ml spoonful three times daily.

Adults: Four 5 ml spoonful, 3-4 times daily.

Contra-indications, warnings, etc C.A.M. is contra-indicated in children and adults with severe heart disease, hypertension and thyrotoxicosis.

Overdosage: Patients who have taken an overdosage of C.A.M. should have gastric lavage performed within four hours of the overdosage occurring. If overdosage is extreme, or there is delay in removing the drug from the stomach, symptomatic treatment of cardiac or respiratory embarrassment should be considered.

Side-effects: The synergistic action of butethamate citrate with ephedrine hydrochloride allows the dose of ephedrine to be kept low. This means that normal sympathomimetic side-effects, such as nausea, restlessness and sweating, due to overdosage of ephedrine are virtually absent.

Pharmaceutical precautions C.A.M. should not be exposed to bright sunlight, as this may cause the chemical degradation of ephedrine hydrochloride.

Legal category P.

Package quantities C.A.M. is available in bottles of 50 ml and 1 litre.

Further information Nil.

Product licence number 0237/5014.

FOLEX*-350 TABLETS

Presentation Each pink, sugar-coated Folex-350 tablet contains:

Ironous fumarate BP	308 mg (equivalent to 100 mg ferrous iron)
Folic Acid BP	350 mcg

Each pink tablet is overprinted with the word 'Folex-50'.

Uses The prevention and treatment of iron deficiency naemia of pregnancy; the prevention of megaloblastic naemia of pregnancy; nutritional anaemia.

Dosage and administration One tablet a day. In pregnancy it is recommended that Folex-350 should be started at the first ante-natal consultation and continued until 3 months after delivery.

Contra-indications, warnings, etc Folex-350 is contra-indicated in megaloblastic anaemia due to vitamin B₁₂ deficiency.

Overdosage: Patients who have taken an overdosage of Folex-350 should have gastric lavage performed, if possible within four hours of the overdosage occurring. In addition, patients should have such symptomatic treatment as appears necessary. In order to eliminate excess free iron, a chelating agent such as desferrioxamine may be administered.

Side-effects: Side-effects of iron and folic acid preparations which have been reported include nausea, vomiting, gastro-intestinal symptoms, constipation and diarrhoea.

Pharmaceutical precautions No special precautions are required.

Legal category POM.

Package quantities Folex-350 is supplied in containers of 30 (child-resistant), 100, 1000 and 5000 tablets.

Further information The high incidence of iron and folate deficiencies in pregnant women may result in possible obstetrical abnormalities. It is now considered advisable to administer daily iron and folic acid routinely, in one tablet, throughout pregnancy. Folex-350 is the recommended BNF 1978 formulation for combined iron and folic acid preparations used for the prevention of anaemia of pregnancy.

Product licence number 0237/5008.

RYBARVIN* INHALANT

Presentation Rybarvin Inhalant contains:

Atropine Methonitrate BP	0.1% w/v
Papaverine Hydrochloride BP	0.08% w/v
Adrenaline BP	0.4% w/v
Benzocaine BP	0.08% w/v
Saline base to 100%	

Uses Rybarvin is indicated for the symptomatic relief of asthma.

Dosage and administration *Adults:* Rybarvin should be inhaled deeply, using a Rybar Inhaler for one to two minutes three times daily. Further inhalations may be taken at other times to relieve acute asthmatic attack.

Children: The length of inhalation should be reduced to a half to one minute. Inhalations should be taken twice daily in the morning and evening.

In conditions in which there is inflammation of the

bronchial mucous membrane the full effect of Rybarvin may not be obtained, owing to poor absorption of the active ingredients.

Contra-indications, warnings, etc Rybarvin Inhalant is contra-indicated in patients with heart conditions or hypertension.

Pharmaceutical precautions The activity of Rybarvin Inhalant is destroyed by the action of light and metal. It is very important that the specially designed Rybar Inhaler is used by patients using Rybarvin.

Legal category P.

Package quantities Rybarvin is available in 28 ml bottles.

Further information Rybarvin has not been shown to be habit-forming.

The Rybar Inhaler is made of glass and fitted with a rubber bulb so that no metal parts come into contact with Rybarvin Inhalant.

The Rybar Inhaler provides a very fine mist of droplets which enables rapid absorption of the active ingredients from the lungs. Full instructions for the patient are given with each inhaler.

Product licence number 0237/5016.

**Trade Mark*

Sandoz Products Limited
Sandoz House
18 The Centre
Eltham, Middlesex TW13 4EP



ELLERGAL*
ELLERGAL* RETARD

Presentation *Bellergal*: Pinkish-brown, coated, round tablets, 5.9–6 mm diameter, weighing 100 mg, branded 'ANDOZ' on one side. Each tablet contains 100 mcg total alkaloids of belladonna, 300 mcg Ergotamine Tartrate PhEur and 20 mg Phenobarbitone PhEur.

ellergal Retard: Speckled yellow, deep pink and brown coated, round tablets, 8.5 mm diameter, convex, 3.7–9 mm thick, weighing 200 mg. Each tablet contains 100 mcg total alkaloids of belladonna, 600 mcg Ergotamine Tartrate PhEur and 40 mg Phenobarbitone PhEur.

Uses *Principal action*: Bellergal blocks excessive stimulation of the autonomic nervous system. The trochanteric action of ergotamine and the anticholinergic action of belladonna effectively suppress the peripheral effects of overstimulation of both sympathetic and parasympathetic divisions. At the same time central sedation with phenobarbitone renders the patient less reactive to mental and emotional stimuli.

Indications: Treatment of a wide range of functional symptoms due to autonomic imbalance, including: menstrual tension, menopausal syndrome and other gynaecological disorders. Some skin disorders, e.g. neurodermatitis. Gastro-intestinal dysfunction. Effort (de Costa's) syndrome (neurocirculatory asthenia). Migraine, interval treatment.

Dosage and administration *Bellergal*: 1 or 2 tablets three times a day.

ellergal Retard: 1 tablet night and morning.

The active principles in Bellergal Retard Tablets are contained in three different-coloured fractions from which they are gradually released at different rates in the gastro-intestinal tract. One tablet morning and evening ensures that an effective therapeutic level is maintained throughout the 24 hours.

Contra-indications, warnings, etc

Contra-indications: Although the quantities of ergotamine and belladonna in Bellergal are small, their presence should be taken into consideration in the treatment of patients suffering from narrow angle glaucoma, paralytic ileus, prostatic enlargement, coronary insufficiency, cardiac failure, obliterative vascular disease, impaired hepatic or renal function and porphyria. Bellergal is contra-indicated during pregnancy and breast feeding.

Precautions: Caution is advised in the presence of angina pectoris.

The possibility of impairment of patient reaction time should be noted and care advised when driving vehicles or operating machinery. Bellergal may potentiate the central effects of alcohol, sedatives, hypnotics, anticholinergics, psychotropic agents and narcotics.

Overdosage: Treatment should be directed to the elimination of the ingested material by emesis and gastric lavage. General supportive measures should be applied

with particular reference to the cardiovascular and respiratory systems. Large phenobarbitone overdoses are very unlikely with these preparations.

Side-effects: Side-effects are rare. They are predictably over-sedation with too high dosage for the individual and very rare instances of skin reactions due to individual idiosyncratic reactions to one or more of the ingredients; most commonly to the phenobarbitone.

Dryness of the mouth and disturbance of vision due to cholinergic blockade may occur.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities *Bellergal*: Containers of 100, 250 and 1,000.

Bellergal Retard: Containers of 100 and 250.

Further information Nil.

Product licence numbers

Bellergal 0101/5019

Bellergal Retard 0101/5020

BRINALDIX*

Presentation White, uncoated, bi-convex tablets, 8 mm diameter, 3.3 mm thick, 200 mg weight branded 'SANDOZ' on one side and with a single break line on the other. Each tablet contains furosemide 20 mg.

Uses *Principal actions*: Brinaldix is an efficient diuretic with a regular, easily controlled action. Pharmacological studies demonstrate that the maximum sodium-excreting effect of furosemide is 25–30% greater than that of chlorothiazide. In man, the maximum effective dose of furosemide has been shown to have a diuretic and sodium-excreting effect over 50% greater than with bendroflumethiazide and a diuretic effect 26% greater than chlorothiazide. The sodium excreting effect in the same trial was 60% higher than chlorothiazide.

The efficient but not precipitate diuresis produced by Brinaldix minimises the risk of severe dehydration and circulatory collapse. The diuretic effect of Brinaldix is predictable and readily controlled. The onset of diuresis is generally within two hours of administration; the maximum diuretic effect is attained in the first three to six hours and the major diuresis is over within 12–24 hours according to dosage.

The urinary excretion of sodium and chloride ions remains in the ratio of approximately 1:1 throughout the dosage range, thus minimising the risk of disturbance to acid/base balance.

The sodium/potassium excretion ratio of Brinaldix is high.

Indications: Oedema of cardiac, renal or hepatic origin. Hypertension.

Dosage and administration *Oedema*: Initial treatment: 2 or 3 tablets daily at breakfast time.

Maintenance: 1 or 2 tablets a day at breakfast time either on consecutive days or intermittently according to the patient's condition or response.

Hypertension: Treatment: 1–2 tablets daily at breakfast time.

Contra-indications, warnings, etc

Contra-indications: Acute glomerulonephritis; severe impairment of renal or hepatic function; hypersensitivity to sulphonamides.

Precautions: Brinaldix should be used with care in patients with diabetes and in patients receiving concurrent antihypertensive therapy. Hypokalaemia (indicated by weakness, muscle cramps, drowsiness, cardiac arrhythmias, gastro-intestinal distension or ileus) may develop in patients likely to be excreting large quantities of potassium in association with high dosage or prolonged continuous diuretic administration, hepatic cirrhosis, aldosteronism, during corticosteroid administration, or during a severely restricted salt intake (below 25 mmol Na⁺ daily). Potassium depletion may result in an increased sensitivity to digitalis, with signs of overdosage. It is recommended that patients be observed for early signs of fluid and electrolyte imbalance. Periodic examination of serum electrolyte levels may be indicated in certain circumstances. In the treatment of established hypokalaemia, the dose of potassium administered should be adjusted to the individual patient's requirements.

Overdosage: Symptoms of overdosage may include thirst, nausea, vomiting, polyuria, hypokalaemia, drowsiness, confusion, hypotension and convulsions. Treatment should be directed to the removal of ingested material by induced emesis or gastric lavage as appropriate. Fluid intake and output should be monitored and measures directed to the restoration of fluid and electrolyte balance. Measures to combat hypotension should be taken if required.

Side-effects: Brinaldix is well tolerated and side-effects are rare. In a small number of patients nausea and headache have been reported, and skin rash has occurred. There are no reports of blood dyscrasias associated with Brinaldix administration. As with thiazide diuretics, Brinaldix may cause a rise in serum uric acid levels. This is likely to be asymptomatic, but an attack of gout may be precipitated. Increase in blood urea, sugar and insulin concentrations have occasionally been reported. The dosage of antidiabetic drugs and/or diet may have to be adjusted in diabetic patients.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Containers of 100 tablets.

Further information Nil.

Product licence number 0101/5021.

BRINALDIX* K

Presentation Flat, round, white, effervescent tablets with a rough surface, of 22 mm diameter, 4.25 mm thick and 2.4 g weight. Each effervescent tablet contains 20 mg clopamide, 600 mg Potassium Chloride PhEur and 400 mg Potassium Bicarbonate BPC and provides 470 mg potassium (12 mmol: 12 mEq K⁺), 286 mg

chloride (8 mmol: 8 mEq Cl⁻) and 800 mg anhydro citric acid (787.4 mg citrate ion).

Uses Principal actions: Brinaldix K effervescent tablets provide a unique diuretic/potassium preparation. Brinaldix is an efficient diuretic with a regular, easy controlled action. Pharmacological studies demonstrate that the maximum sodium-excreting effect of clopamide is 25–30% greater than that of chlorothiazide. In man the maximum effective dose of clopamide has been shown to have a diuretic and sodium-excreting effect over 50% greater than with bendrofluzide and a diuretic effect 26% greater than chlorothiazide. The sodium-excreting effect in the same trial was 60% higher than chlorothiazide.

The efficient but not precipitate diuresis produced by Brinaldix minimises the risk of severe dehydration and circulatory collapse. The diuretic effect of Brinaldix is predictable and readily controlled. The onset of diuresis is generally within two hours of administration; the maximum diuretic effect is attained in the first three to six hours and the major diuresis is over within 12–24 hours according to dosage. The urinary excretion of sodium and chloride ions remains in the ratio of approximately 1 : 1 throughout the dosage range, thus minimising the risk of disturbance to acid/base balance. The sodium/potassium excretion ratio of Brinaldix is high.

Brinaldix K effervescent tablets are a unique diuretic/potassium formulation to be taken in water as a palatable drink.

Each effervescent tablet provides 12 mmol K⁺ and 8 mmol Cl⁻ thus reducing the risk of hypokalaemia, hypochloreaemic alkalosis. Enteric-coated diuretic/potassium tablets have been incriminated in the development of small-bowel ulceration and stenosis. The provision of potassium in solution obviates this risk.

Indications: Oedema of cardiac, renal or hepatic origin. Hypertension.

Brinaldix K is particularly suitable for long-term treatment.

Dosage and administration

Oedema: Initial treatment: 2 or 3 effervescent tablets daily dissolved in 60 ml ($\frac{1}{3}$ – $\frac{1}{2}$ a tumblerful) of water at breakfast time.

Maintenance: 1–3 effervescent tablets dissolved in 60 ml ($\frac{1}{3}$ – $\frac{1}{2}$ a tumblerful) of water at breakfast time either on consecutive days or intermittently according to the patient's condition or response.

Hypertension: Treatment: 1–2 effervescent tablets daily dissolved in 60 ml ($\frac{1}{3}$ – $\frac{1}{2}$ a tumblerful) of water at breakfast time.

Contra-indications, warnings, etc

Contra-indications: Acute glomerulonephritis; severe impairment of renal or hepatic function; hypersensitivity to sulphonamides.

Precautions: Brinaldix K should be used with care in patients with diabetes and in patients receiving concurrent antihypertensive therapy. Although the unique effervescent diuretic preparation Brinaldix K has been formulated to limit the occurrence of hypokalaemia (indicated by weakness, muscle cramps, drowsiness, cardiac arrhythmias, gastro-intestinal distension or ileus) the latter may develop in patients likely to be excreting large quantities of potassium in association with high dosage or prolonged continuous diuretic administration, hepatic cirrhosis, aldosteronism, during corticosteroid administration, or during a severely restricted salt intake.

below 25 mmol Na⁺ daily). Potassium depletion may result in an increased sensitivity to digitalis, with signs of overdosage. It is recommended that patients be observed for early signs of fluid and electrolyte imbalance. Periodic determination of serum electrolyte levels may be indicated in certain circumstances. In the treatment of established hypokalaemia, the dose of potassium administered should be adjusted to the individual patient's requirements.

verdosage: Symptoms of overdosage may include first, nausea, vomiting, polyuria, hypokalaemia, drowsiness, confusion, hypotension and convulsions. Treatment should be directed to the removal of ingested material by induced emesis or gastric lavage as appropriate. Fluid intake and output should be monitored and measures directed to the restoration of fluid and electrolyte balance. Measures to combat hypotension should be taken if required. However deliberate overdosage is unlikely with effervescent preparations.

side-effects: Brinaldix is well tolerated and side-effects are rare. In a small number of patients nausea and headache have been reported, and skin rash has occurred. There are no reports of blood dyscrasias associated with Brinaldix administration. As with thiazide diuretics, Brinaldix may cause a rise in serum urate levels. This is likely to be asymptomatic, but an attack of gout may be precipitated. Increase in blood urea, sugar and insulin concentrations have occasionally been reported. The dosage of antidiabetic drugs and/or diet may have to be adjusted in diabetic patients.

pharmaceutical precautions Brinaldix K Tablets are effervescent and should be dispensed in their original containers which carry a note to the patient requesting that the containers be kept tightly closed in a cool dry place.

pharmaceutical category POM.

package quantities Containers of 100 effervescent tablets (5 tubes of 20).

further information Brinaldix K Tablets each contain 37.5 mg sucrose and have an absolute calorific value of 4.5 kJ.

product licence number 0101/5022.

EDILANID*

resenation Cedilanid is available as tablets and injection.

tablets: White, uncoated tablets weighing 85 mg. Flat and of 6 mm diameter with a bevelled edge, coded GO and scored on one side with SANDOZ engraved on the other.

mpoules: 2 ml of Cedilanid Injection contains 400 mcg edlanoside BP.

ses *Principal action:* In common with all cardioactive glycosides of digitalis, Cedilanid improves cardiac function in the failing heart by increasing the force of myocardial contraction and by correcting disturbances of heart rhythm by a direct effect on the excitatory mechanism and the conduction system probably mediated by ion transport mechanisms. The onset of action of Cedilanid is very rapid by the intravenous route, the effect being apparent within 10 minutes and at maximum

in 1½–2 hours. When parenteral therapy is essential and the intravenous route impracticable, Cedilanid may be given intramuscularly. The Cedilanid Ampoule solution does not need dilution before use.

Indications: Acute heart failure. Routine digitalisation and maintenance of the patient in congestive heart failure.

Dosage and administration *Rapid digitalisation:* 800 mcg–1.6 mg intravenously or intramuscularly as a single dose or divided over 24 hours.

Slow digitalisation: Oral administration of 1.5–2 mg daily over a 3–5 day period.

Maintenance: 250 mcg–1.5 mg orally per day as indicated by the patient's requirements.

Children: The rapid digitalising dose is 20 to 40 mcg/kg body weight in a single dose or divided over 24 hours.

Oral maintenance doses are 10–30 mcg/kg body weight in 3 divided doses.

Lower doses should be given to elderly patients and dosage should be reduced in the presence of chronic cor pulmonale, coronary insufficiency, electrolyte disturbances and renal or hepatic insufficiency.

It is particularly important to warn patients stabilised on Cedilanid of the change in appearance of the tablet. Patients at risk i.e. the young, the elderly and those with previous history of a toxic reaction to digitalis glycosides, should be carefully monitored during the changeover period as there is evidence of greater bioavailability of the active ingredient with the new tablet.

Contra-indications, warnings, etc

Contra-indications: Complete AV block and 2nd degree AV block (especially 2 : 1), excessive sinus bradycardia (particularly when associated with Stokes-Adams seizures).

Precautions: Digitalised patients should not be given calcium by parenteral injection. The dose of Cedilanid administered should be adjusted to compensate for any other digitalis preparations administered in the recent past. High dose oral calcium supplements, psychotropic drugs (including lithium) and sympathomimetics should be given with caution to digitalised patients. Potassium depletion sensitises the heart to cardiac glycosides.

Overdosage: Fatalities from ingestion of massive oral doses of Cedilanid are rare because vomiting usually occurs. Common symptoms of overdosage include anorexia, nausea, vomiting, headache, visual disturbances and disorientation. Slow or irregular pulse, fall of blood pressure and a wide range of cardiac arrhythmias and conduction defects have been reported as a result of digitalis toxicity. Death is usually due to ventricular fibrillation and is sometimes preceded by delirium and convulsions. Chronic poisoning by cumulation produces gradual onset of these symptoms.

Treatment: Activated charcoal may reduce absorption. Emesis or gastric lavage within eight hours, to empty the stomach. Check and carefully monitor serum potassium. Correct hypo- or hyperkalaemia. Treat arrhythmias.

Atropine 0.3–0.6 mg will reverse profound bradycardia. A cardiac pacemaker may be required.

Side-effects: Toxic effects occur if the dose of Cedilanid has not been carefully tailored to the specific requirements and tolerance of each individual patient.

The most frequent side-effects noted are: *CNS and gastro-intestinal disturbances:* anorexia, nausea, vomiting; in rare instances (especially in elderly arterioscle-

rotics), confusion, disorientation, aphasia and visual disturbances including chromatopsia.

Cardiac: Disturbances of heart rate, conduction and rhythm (bigeminy), lowering of the S-T segment with preterminal T-wave inversion.

Allergic skin reactions: (Pruritus, urticaria, macular rashes) occur very occasionally.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities *Cedilanid Tablets:* Containers of 100 and 500.

Cedilanid Injection: Boxes of 5 × 2 ml ampoules.

Further information Nil.

Product licence numbers

Tablets 0101/5025

Ampoules 0101/5005

DIHYDERGOT*

Presentation *Tablets:* Off-white, uncoated, round tablets weighing 100 mg, 6 mm diameter, 2.5–3 mm thick, flat with bevelled edge. Single break line coded OL on one side, branded 'SANDOZ' the other. Each tablet contains 1 mg dihydroergotamine mesylate (equivalent to 860 mcg dihydroergotamine base).

Oral Solution: Clear, colourless solution. Each 1 ml contains 2 mg dihydroergotamine mesylate. The dropper bottle delivers 1 ml (2 mg) per 20 drops.

Ampoules: Clear, colourless solution. Each 1 ml contains 1 mg dihydroergotamine mesylate.

Uses The hydrogenation of ergotamine to dihydroergotamine reduces the uterotonic effect and the pressor effect is modified. Dihyergot contracts hypotonic vessels by stimulation of the alpha-adrenoceptors. It also possesses alpha-adrenergic properties (i.e. it is a partial agonist). Its tonic effect on capacitance vessels is more pronounced than its effect on resistance vessels. This activity results in increased venous tone and prevents excessive venous pooling.

During prolonged oral administration, Dihyergot induces a stabilization of the tone of extracranial vessels and therefore is of value for the prophylactic treatment of the migraine attack. It may be used orally or by injection as an alternative to ergotamine for the symptomatic relief of the migraine attack.

Dihyergot injection is effective in the prophylactic treatment of postoperative deep vein thrombosis. This activity is considerably enhanced by administration in combination with a low-dose heparin regimen. In this way impaired venous return and activation of clotting factors, two conditions contributing to the development of postoperative thrombosis, can be controlled.

Indications: Prophylactic treatment of migraine. May also be used for the symptomatic treatment of the migraine attack.

Prophylactic treatment of postoperative deep vein thrombosis using Dihyergot Injection in conjunction with a low dose heparin regimen.

Dosage and administration *Prevention of migraine:* 1–2 tablets or 10–20 drops of oral solution three times daily reduce the frequency and severity of attacks in most patients.

Treatment of migraine: 2–3 tablets or 20–30 dro repeated half-hourly if necessary, up to a total of tablets or 100 drops per day.

Intramuscular or subcutaneous injection of 1–2 r (1–2 ml) given as soon as the prodromal symptom appear usually aborts the attack within half an hour. the attack is not relieved by this time a further dose m be given.

Prevention of postoperative deep vein thrombosis Inje tion only: Individual injections of Dihyergot 500 m (0.5 ml) with heparin 5000 iu given subcutaneous every 8–12 hours. Treatment is started 1–2 hours bef surgery and continued not less than 6 hours pos operatively. Subsequent doses are given 8–12 hourly f at least 7–10 days depending on the risk of thrombosi

Contra-indications, warnings, etc *Contra-indic tions:* Parenteral administration of Dihyergot is contr indicated in patients suffering from uncontrolled cardi failure, coronary artery disease (see also precautions inadequately controlled hypertension and in pregnanc

Precautions: A small number of patients with corona insufficiency have been treated with twice daily injections of Dihyergot 500 mcg intramuscularly and resting conditions and only in severe coronary disabili were anginal attacks precipitated. However, due to th possibility of increased cardiac filling pressure, great ca should be exercised in treating such patients, and th dose of 500 mcg (0.5 ml) should not be exceeded.

Intra-arterial injection of Dihyergot must be avoide Should this occur by accident an alpha-blocker shou be administered. Caution is indicated where Dihyergo is being given on a long-term basis to patients wi severe renal disease unless they are receiving dialys and for patients with severe liver disease. In such cas the dosage should be reduced.

Concomitant use of the antibiotic triacetyloleandc mycin, which is not available in the UK, or erythromyci and Dihyergot by mouth should be avoided.

When using heparin in combination with Dihyergo Injection the general contra-indications and precautio implicit with the use of heparin should be observe Mean plasma heparin levels have been reported to b higher in patients receiving Dihyergot concurrently.

The tendency to haemorrhage and total intra-operativ and postoperative blood loss in patients on Dihyde got/heparin treatment has been found to be similar t that encountered with low-dose heparin therapy.

Subcutaneous administration may give rise to loca discomfort at the injection site.

Side-effects: Nausea and vomiting may occasionall occur. Following parenteral treatment, numbness an tingling of the fingers and toes as well as precordial pai have been reported in a few cases. With oral use however, such effects are extremely rare.

Pharmaceutical precautions Protect from light. D not dilute the Oral Solution.

Once Ampoule is opened contents should be use immediately. Dihyergot and heparin injections shou be administered individually.

Legal category POM.

Package quantities *Tablets:* Containers of 50.

Oral Solution: Dropper bottles of 15 ml.

Ampoules: Boxes of 5 × 1 ml.

Further information Snap ampoule: no file require

Product licence numbers

Tablets	0101/5027
Oral Solution	0101/5006
Suppositories	0101/5007

HYDERGINE®

Representation *1.5 mg Tablets:* Hydergine 1.5 mg is available as white, flat, bevel-edged tablets, scored on one side and coded 'ZM', with 'SANDOZ' engraved on the other, and of 240 mg weight, 9 mm diameter and 9 mm thickness. Each tablet contains 1.5 mg Co-Dergocrine Mesylate BP.

4.5 mg Tablets: Hydergine 4.5 mg is available as white, round biconvex tablets coded HYDERGINE in regular form on one side with 4.5 engraved on the other, and of 240 mg weight and 9 mm diameter. Each tablet contains 4.5 mg Co-Dergocrine mesylate BP.

Uses *Principal Actions:* Double-blind controlled clinical trials have demonstrated that Hydergine significantly improves symptoms associated with senile dementia presenting as mild to moderate impairment of mental function in the elderly.

Hydergine improves:

Mental performance—assessed in terms of alertness, recent memory, orientation, relief from confusion.

Motional state—assessed in terms of relief from anxiety, depression, emotional instability and lack of motivation/initiative.

Social behaviour—assessed in terms of improvement in self-care: i.e. decreased difficulty with eating, washing, dressing, walking.

Physical manifestations—assessed in terms of mobility, appetite, dizziness, fatigue.

Hydergine exerts a favourable metabolic effect on cerebral neurones indicated by changes which occur in the EEG in both test animals and patients and by the improvement in mental function after the treatment period.

Studies on brain tissue of hypoxic animals demonstrate that Hydergine conserves adenosine triphosphate, the main energy donor in the cell, by inhibiting the enzymes ATPase and adenylcyclase. It also inhibits phosphodiesterase, the enzyme which takes part in the breakdown of cyclic adenosine monophosphate thus conserving metabolic turnover.

Indications: Symptoms of senile dementia presenting as mild to moderate impairment of mental function in the elderly.

Dosage and administration 1.5 mg three times a day or once daily dosage of 4.5 mg.

The effect of Hydergine is not immediately manifest, improvement in clinical symptoms and EEG patterns not being evident for two to three weeks, continuous improvement being maintained thereafter for at least three months.

Contra-indications, warnings, etc *Contra-indications:* The pharmacological studies and clinical trials with Hydergine do not indicate any contra-indications.

Precautions: Caution should be exercised in the administration of Hydergine to patients with severe bradycardia.

Overdosage: In cases of overdosage, supportive measures are all that are likely to be required.

Side-effects: Side-effects are infrequent following ad-

ministration of Hydergine and even relatively large doses are well tolerated. Minor side-effects including gastrointestinal disturbance, flushes, rashes, nasal stuffiness, abdominal cramps and postural hypotension in hypertensive patients have on occasion been reported.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities *1.5 mg Tablets:* containers of 100.

4.5 mg Tablets: calendar pack of 28.

Further information A patient assessment chart and record cards are available on request to assist the physician in his patient selection for Hydergine.

Product licence numbers

1.5 mg Tablets	0101/0042
4.5 mg Tablets	0101/0117

MELLERIL®

Presentation *Suspension:* An opaque creamy/white semi-viscous fluid, available in two strengths:

25 mg in 5 ml (0.5%): Each 5 ml spoonful contains 25 mg thioridazine base equivalent to 27.5 mg of thioridazine hydrochloride.

100 mg in 5 ml (2%): Each 5 ml spoonful contains 100 mg thioridazine base equivalent to 110 mg of thioridazine hydrochloride.

Syrup: A clear, orange liquid. Each 5 ml spoonful contains 25 mg thioridazine base equivalent to 27.5 mg of thioridazine hydrochloride.

Concentrate for Syrup: A clear, orange liquid. Each 5 ml of Concentrate diluted to 150 ml with Syrup BP produces a Melleril syrup containing 25 mg of thioridazine base, equivalent to 27.5 mg of thioridazine hydrochloride, in 5 ml.

Tablets: White, coated tablets available in four strengths:

10 mg Thioridazine Tablets BP, 5.5 mm diameter, 3.5 mm thickness, weight 100 mg, branded MEL 10.

25 mg Thioridazine Tablets BP, 8.2–8.4 mm diameter 5.0–5.3 mm thickness, weight 260 mg, branded MELLERIL 25.

50 mg Thioridazine Tablets BP, 10.0–10.3 mm diameter, 5.5 mm thickness, weight 450 mg, branded MELLERIL 50.

100 mg Thioridazine Tablets BP, 11.1–11.5 mm diameter, 6.0–6.3 mm thickness, weight 600 mg, branded MELLERIL 100.

Uses *Principal action:* Melleril is a phenothiazine tranquilliser with specificity of psychotherapeutic action. The most striking aspect of Melleril therapy is the low incidence of side-effects throughout the full therapeutic range. Although the basic pharmacological actions of Melleril are similar to those of the phenothiazines generally, properties have been described which support the observation that the antipsychotic activity is more specific than that of other tranquillisers. Controlled clinical trials have established that Melleril is extremely effective and singularly free from the serious side-effects associated with the use of other phenothiazines—particularly extrapyramidal, allergic, hepatic and haemopoietic complications. Melleril is often well tolerated by patients experiencing untoward reactions with other tranquillisers.

† **Hospitals only.**

Indications: Melleril is indicated for the restoration of normal behaviour in a wide range of mental and emotional disturbances characterised by anxiety, tension and agitation. It is particularly effective in the management of acute and subacute schizophrenia and manic psychoses. Good results have been reported in the treatment of chronic psychoses, acute and chronic psychoneuroses, senile confusional states and behaviour disorders in children. Melleril controls the patient without excitation or undue drowsiness. It improves thought disorders and enables communication to be established. The patient is more alert, is more co-ordinated and is more able to co-operate in rehabilitation programmes.

Dosage and administration

	<i>Daily dose range in terms of hydrochloride</i>
Adults	
<i>Mental and emotional disturbance</i>	
Severe: acute schizophrenia, manic psychoses, etc.	150–600 mg
For acute schizophrenia, an initial loading dose of 200 mg may be given. In resistant patients, up to 800 mg daily may be administered for not more than four weeks.	
Moderate: psychomotor agitation in severe psychoneuroses, etc.	75–200 mg
Mild: anxiety, tension, apprehension, etc	30–100 mg
Children	
<i>Behaviour disorders</i>	
Under 5	1 mg (thioridazine hydrochloride) kg/body weight
Over 5	$\frac{1}{4}$ – $\frac{1}{2}$ adult dosage

Contra-indications, warnings, etc

Contra-indications: Severely depressed or comatose states.

Precautions: Cross-sensitivity to phenothiazines in general has been suggested whereby patients who have demonstrated a hypersensitivity reaction to one phenothiazine may be more prone to undergo a similar reaction to others. Phenothiazines are capable of potentiating central nervous system depressants (e.g. anaesthetics, analgesics, hypnotics, narcotics, antihistamines, alcohol, etc) as well as atropine and phosphorus insecticides. Melleril may potentiate the inhibitory effect of quinidine on cardiac contractility. Like other phenothiazines Melleril has an adrenolytic action and may therefore interfere with the pressor effects of adrenergic vasoconstrictors. Phenothiazines should be administered with caution to patients who participate in activities requiring complete mental alertness.

Regular blood counts are recommended during the first three to four months of treatment or if any clinical signs of blood dyscrasias appear.

In liver disease regular monitoring of liver function is necessary. During pregnancy and breast feeding, Melleril should only be administered under compelling circumstances.

Overdosage: Acute overdosage of Melleril usually gives rise to coma with shallow breathing, hypotension and absence of reflexes. Epileptiform convulsions, motor restlessness and hyperflexia may occur. Treatment should be directed to the elimination of the ingested material by emesis and gastric lavage. General supportive measures should be applied with particular reference to the cardiovascular and respiratory systems.

Side-effects: Melleril is extremely well tolerated, as world-wide clinical usage has underlined the low incidence of side-effects. Minor side-effects such as drowsiness, dizziness, faintness, disturbances of accommodation, urinary incontinence, dryness of the mouth and nasal stuffiness may occur initially with high dosage but are usually transient. The incidence of extrapyramidal side-effects is low: moreover patients disabled by Parkinsonism with other phenothiazines may have troublesome symptoms on therapeutically equivalent larger doses of Melleril. Tardive dyskinesias have been reported after prolonged treatment with high doses, but very infrequently. Amenorrhoea, galactorrhoea and impairment of male sexual function may occur, but respond to a reduction in dosage. Oedema and weight gain have occurred. Transient leucopenia and other blood dyscrasias have been reported, but agranulocytosis has not occurred in a few isolated cases. Altered seizure control is very rare during Melleril treatment, as are photoallergic and phototoxic reactions. ECG changes associated with the administration of phenothiazines have been reported but these are not regarded as evidence of cardiotoxicity. The changes reported include prolongation of the Q-T interval, a lowering and inversion of the T-wave, an appearance of a wave tentatively identified as a bifid or a U-wave. These changes are due to altered myocardial repolarisation and are not related to myocardial damage. They are more likely to occur in the presence of low potassium blood levels and are reversible. There is no clear evidence that they are precursors of the arrhythmias which occur very rarely. Pigmentary retinopathy with disturbance of visual function has been reported as a toxic reaction to excessive doses given long term in very small number of patients. Treatment with Melleril in doses in excess of 1,000 mg per day over long period is not recommended. There may be instances when it is considered necessary to exceed the recommended maximum daily dose of 600 mg, but clinical experience suggests that Melleril is unlikely to be suitable for the patient who does not respond to doses up to 800 mg per day.

Pharmaceutical precautions Melleril Concentrate should be diluted with preservative-free Syrup BP.

For the diabetic patient, Melleril Concentrate may be diluted with Sorbitol Solution BPC.

Melleril Suspension should not be diluted with any of the usual diluents, but the two strengths may be admixed to give a dosage range of between 25 mg and 100 mg per 5 ml spoonful. If an electric stirrer is used, care should be taken to avoid the incorporation of air. Melleril Concentrate, Syrup and Suspension should be protected from light.

Legal category POM.

Package quantities *Melleril Suspension:* 25 mg in 5 ml: Bottles of 1 litre.

100 mg in 5 ml: Bottles of 1 litre.

Melleril Syrup: Bottles of 100 ml, 500 ml, 1 litre and 2 litres.

Melleril Concentrate: Bottles of 500 ml.

Melleril Tablets: 10 mg: Containers of 100 tablets.

25 mg and 50 mg: Containers of 100, 1,000 and 5,000 tablets.

100 mg: Containers of 100 (2 × 50) 1,000 and 5,000 tablets.

Further information Both strengths of Melleril Suspension contain 3.16 g of sucrose per 5 ml spoonful and have an absolute calorific value of 14 kJ.

Melleril Syrup contains 2.25 g of sucrose per 5 ml of syrup and has an absolute calorific value of 1.36 kcal per dose.

Product licence numbers

Suspension 25 mg/5 ml	0101/0052
Suspension 100 mg/5 ml	0101/0053
Syrup	0101/5034
Concentrate	0101/5035
Tablets 10 mg	0101/5033
Tablets 25 mg	0101/5053
Tablets 50 mg	0101/5054
Tablets 100 mg	0101/5055

PARAGESIC*

Presentation Paragesic are yellow, uncoated, round, 10 tablets with a rough surface, 25.4 mm diameter, 4.7–5.1 mm thick, weighing 3.5 g. Each effervescent tablet contains:

Paracetamol PhEur	500 mg
Pseudoephedrine Hydrochloride BP	20 mg
Caffeine PhEur	10 mg

Uses Paragesic is a decongestant analgesic preparation containing pseudoephedrine, paracetamol and caffeine. Rapid solution in water gives a pleasant drink which provides the active ingredients in a form immediately available for gastro-intestinal absorption.

Indications: Paragesic is indicated for the relief of conditions where upper respiratory congestion is associated with pain, as in coryza, naso-pharyngitis and influenza; also as an adjunct for the relief of symptoms associated with sinusitis or hay fever.

Dosage and administration One to two tablets dissolved in $\frac{1}{2}$ – $\frac{3}{4}$ a tumblerful of either warm or cold water very four hours. Not more than 8 tablets should be taken in a 24-hour period.

Contra-indications, warnings, etc As pseudoephedrine is a sympathomimetic amine, Paragesic should be administered with caution to hypertensive patients, patients suffering from heart failure or to patients with incipient or established urinary retention and should not be given to patients being treated with monoamine oxidase inhibitors or antihypertensives. Caution is necessary in patients receiving beta-blockers. Paragesic is not suitable for patients on a restricted sodium intake.

Overdosage: Only one case of overdosage has been reported to the Company. Large overdoses are unlikely with effervescent preparations but if more than ten tablets are taken, paracetamol levels should be checked and the antidotes, methionine or N-acetyl cysteine should be given if indicated by ingested dose, plasma level and time since ingestion to prevent liver damage.

Pharmaceutical precautions Store in a cool dry place.

Legal category P.

Package quantities Boxes of 100 effervescent tablets (5 tubes of 20).

Further information Paragesic Tablets each contain 17.7 mg sucrose and have an absolute calorific value of 1.76 kcal.

Dessicant capsule contains 1.2 g silica gel with 6 mg talc and is harmless.

Product licence number 0101/5037.

PARLODEL*

Presentation 2.5 mg Tablets: White, round, flat, bevel-edged tablets, 7 mm in diameter, scored and coded 'XC' on one side and marked 'SANDOZ' on the other side, weight 140 mg. Each tablet contains 2.87 mg bromocriptine mesylate equivalent to 2.5 mg bromocriptine base.

10 mg Capsules: Opaque, white, hard gelatin capsules, size 1 each containing 11.47 mg bromocriptine mesylate equivalent to 10 mg bromocriptine base.

Uses *Principal action:* Parlodel is a dopaminergic-receptor stimulant or dopamine agonist. This pharmacological action is manifest in normal individuals and those with hyperprolactinaemic states by an inhibition of the secretion of prolactin by the pituitary; in many acromegalic patients a lowering of elevated circulating growth hormone levels results.

In patients with prolactin secreting adenomas there is radiological evidence to indicate tumour regression in some cases. Improvement in visual field defects and in general anterior pituitary function may also occur.

Because of its dopaminergic activity Parlodel is also effective in idiopathic Parkinson's disease, which is characterised by a specific nigro-striatal dopamine deficiency.

Indications: The inhibition or suppression of puerperal lactation.

The treatment of hyperprolactinaemia in men and women with hypogonadism and/or galactorrhoea.

The treatment of hyperprolactinaemic infertility.

Parlodel has been used successfully in the treatment of a number of infertile women who do not have demonstrable hyperprolactinaemia.

In a number of specialised units, patients who have been shown to have prolactin secreting adenomas have been treated successfully with Parlodel.

In particular Parlodel can be considered as a first choice of treatment in patients with macroadenomas and as an alternative to the surgical procedure, transphenoidal hypophysectomy, in patients with microadenomas.

The treatment of cyclical benign breast disease/cyclical pronounced mastalgia.

Cyclical menstrual disorders have also responded to Parlodel, particularly breast symptomatology but, in the premenstrual syndrome, there is also some evidence that other symptoms, such as headache, mood changes and bloatedness, may be alleviated.

Parlodel has also been used in a number of specialised units, as an adjunct to surgery and/or radiotherapy, to reduce circulating growth hormone levels in the management of acromegalic patients.

In the treatment of idiopathic Parkinson's disease, Parlodel has been used both alone and in combination with levodopa in the management of previously untreated patients and those disabled by 'on-off' phenomena. Parlodel has been used with occasional benefit in patients who do not respond to or are unable to tolerate levodopa and those whose response to levodopa is declining.

Dosage and administration Parlodel should always be taken during a meal.

A number of disparate conditions are amenable to treatment with Parlodel and, for this reason, the recommended dosage regimens are variable. In most indications, irrespective of the final dosage, the optimum response with the minimum of side-effects is best

achieved by gradual introduction of Parlodel. The following scheme is suggested:

Initially, $\frac{1}{2}$ a tablet (1.25 mg) at bedtime, increasing after two to three days to 1 tablet (2.5 mg) at bedtime. Dosage may then be increased by $\frac{1}{2}$ to 1 tablet at two to 3 day intervals until a dosage of 2.5 mg twice daily is achieved. Further dosage increments, if necessary, should be added in a similar manner.

Prevention of lactation: 2.5 mg on the day of delivery followed by 2.5 mg twice daily for 14 days. Gradual introduction of Parlodel is not necessary in this indication.

Suppression of lactation: 2.5 mg on the first day, increasing after two to three days to 2.5 mg twice daily for 14 days. Gradual introduction of Parlodel is not necessary in this indication.

Hypogonadism/galactorrhoea syndromes/infertility: Introduce Parlodel gradually according to the suggested scheme. Most patients with hyperprolactinaemia have responded to 7.5 mg daily, in divided doses, but doses of up to 30 mg daily have been used. In infertile patients, without demonstrably elevated serum prolactin levels, the usual dosage is 2.5 mg twice daily.

Prolactinomas: Introduce Parlodel gradually according to the suggested scheme. Dosage may then be increased by 1 tablet daily at 2–3 day intervals as follows: 2.5 mg eight hourly, 2.5 mg six hourly, 5 mg six hourly. Patients have responded to doses of up to 30 mg using 2.5 mg tablets or 10 mg capsules as appropriate.

Cyclical benign breast disease/cyclical pronounced mastalgia/cyclical menstrual disorders.

Introduce Parlodel gradually, according to the suggested scheme, until the recommended dosage of 2.5 mg twice daily is reached.

Acromegaly: Introduce Parlodel gradually, according to the suggested scheme. Dosage may then be increased by 1 tablet daily at two to three-day intervals as follows: 2.5 mg eight hourly, 2.5 mg six hourly, 5 mg six hourly.

Patients have responded to doses of between 20 mg and 60 mg daily using 2.5 mg tablets or 10 mg capsules as appropriate.

Parkinson's Disease: Introduce Parlodel gradually as follows: Week 1, 1.25 mg at bedtime, Week 2, 2.5 mg at bedtime, Week 3, 2.5 mg twice daily. Thereafter, take 3 times a day increasing by 2.5 mg every 3 to 14 days depending on the patient's response. Continue until the optimum dose is reached. This will usually be between 10 and 80 mg daily. In patients already receiving levodopa the dosage of this drug may be gradually decreased whilst the dosage of Parlodel is increased until the optimum balance is determined.

Contra-indications, warnings, etc *Contra-indications:* No absolute contra-indications to treatment with Parlodel are known. For procedure during pregnancy see Precautions and Further Information.

Precautions: Hyperprolactinaemia may be idiopathic, drug-induced, or due to hypothalamic or pituitary disease. The possibility that hyperprolactinaemic patients may have a pituitary tumour should be recognised and complete investigation at specialised units to identify such patients is advisable. Parlodel will effectively lower prolactin levels in patients with pituitary tumours but does not obviate the necessity for radiotherapy or surgical intervention where appropriate in acromegaly. Rare reports have been made of rapid expansion of pre-existing pituitary tumours during pregnancy and this may also occur in patients who have been able to conceive

as a result of Parlodel therapy. As a precautionary measure, in cases of established pregnancy, visual field should be monitored to detect untoward effects; pituitary enlargement so that Parlodel may be reintroduced or other appropriate treatment instituted.

If pregnancy occurs it is advisable to withdraw Parlodel after the first missed menstrual period for most patients. However, with increasing evidence of lack of teratogenic and embryopathic effect in the human subject, consideration should be given to maintaining treatment in those cases where there is evidence of a large tumour or expansion.

Treatment of women suffering from hyperprolactinaemic amenorrhoea with Parlodel results in ovulation. Patients in whom pregnancy is undesirable, or unwanted should be advised to take contraceptive measures other than an oral contraceptive. When women of child-bearing age are treated with Parlodel for conditions not associated with hyperprolactinaemia the lowest effective dose should be used. This is in order to avoid suppression of prolactin to below normal levels, with consequent impairment of luteal function.

Gynaecological assessment, preferably including cervical and endometrial cytology, is recommended for women receiving Parlodel for extensive periods. Six monthly assessment is suggested for post-menopausal women and annual assessment for women with regular menstruation.

Hypotensive reactions may be disturbing in some patients during the first few days of treatment; an particular care should be exercised when driving vehicle or operating machinery. Tolerance to Parlodel may be reduced by alcohol.

Parlodel has been administered to patients concurrently with phenothiazines, effectively lowering raised prolactin levels but without apparently interfering with the psychotropic effects of these drugs. Adverse reactions between psychotropic agents and Parlodel have not been reported to the company.

In acromegalic patients, whilst Parlodel may effectively lower growth hormone levels, treatment to limit expansion of the tumour is also indicated. An acromegalic patient should be carefully assessed for peptic ulceration prior to treatment with Parlodel and advised to report gastrointestinal side-effects promptly, as gastro-intestinal bleeding has been reported, though the connection with treatment is not proven.

Caution is required where Parlodel is being given in high doses to patients with a history of psychotic disorders or severe cardiovascular disease.

Among Parkinsonian patients on long-term, high-dose Parlodel treatment, pleural effusions have been observed in some cases. While a causal relationship between Parlodel and these findings is uncertain, patients presenting with unexplained pleuro-pulmonary signs or symptoms should be examined thoroughly and discontinuation of Parlodel therapy should be contemplated.

Overdosage: Overdosage with Parlodel is likely to result in vomiting and other symptoms which could be due to over-stimulation of the dopaminergic receptors, and might include confusion, hallucinations and hypotension. General supportive measures should be undertaken to remove any unabsorbed material and maintain the blood pressure if necessary.

Side-effects: Nausea is the most commonly occurring side-effect. Postural hypotension, dizziness, headache, vomiting, and mild constipation have also occasionally been reported. The occurrence of side-effects is mini-

ised by taking Parlodel during a meal and by gradual introduction of the dose. If side-effects do occur a reduction of dosage, followed in a few days by a more gradual increase, will ameliorate the symptoms.

In acromegalic and Parkinsonian patients receiving high doses of Parlodel, digital vasospasm induced by cold has occasionally occurred. Drowsiness and, less frequently, confusion, psychomotor excitation, hallucinations, dyskinesia, dry mouth and leg cramps have been reported during high-dose treatment of Parkinson's disease with Parlodel. All these side-effects are dose-dependent and can usually be controlled by a reduction of dosage and a more gradual implementation of dosage increments.

Pharmaceutical precautions

Tablets: Protect from heat and damp.

Capsules: Protect from heat and damp.

Legal category POM.

Package quantities 2.5 mg Tablets: Containers of 30 and 500.

0 mg Capsules: Containers of 100.

Further information Based on the outcome of over 400 completed pregnancies in mothers who were given Parlodel at some stage in the early weeks of pregnancy, it may be concluded that the use of Parlodel to restore fertility is not associated with an increased risk of abortion, premature delivery, multiple pregnancy or occurrence of malformation in infants.

Product licence numbers

2.5 mg Tablets 0101/0061

0 mg Capsules 0101/0108

'PHOSPHATE-SANDOZ'

Presentation Flat, round, white, effervescent tablets with a rough surface, weight 3.7 g, 25.4 mm diameter and 4.5 mm thick. Citrus flavoured. Each effervescent tablet contains 1.936 g anhydrous sodium acid phosphate, 350 mg Sodium Bicarbonate PhEur and 315 mg Potassium Bicarbonate BPC. This provides the equivalent of 500 mg elemental phosphorus, 468.8 mg sodium (20.4 mmol: 20.4 mEqNa⁺), 123 mg potassium (3.1 mmol: 3.1 mEq K⁺), also 800 mg anhydrous citric acid (787.4 mg citrate ion).

Uses *Principal action:* High-dose phosphate supplement.

Oral administration of inorganic phosphates produces a fall in serum calcium in patients with hypercalcaemia. Phosphate-Sandoz Effervescent Tablets also contain sodium ions which aid the correction of the dehydration and sodium depletion seen in hypercalcaemia.

Indications: Hypercalcaemia associated with such conditions as hyperparathyroidism, multiple myelomatosis and metastatic bone disease.

Dosage and administration Phosphate-Sandoz Effervescent Tablets should be dissolved in $\frac{1}{3}$ – $\frac{1}{2}$ a tumblerful of water.

Dosage should be adjusted to suit the requirements of individual patients. Excessive dosage has been reported to produce hypocalcaemia in isolated cases.

Adults: Hypercalcaemia: Up to 6 tablets daily (adjustment being made accordingly to requirements).

Vitamin D resistant rickets: 4–6 tablets daily.

Children under five years: half the adult dose should be given.

Contra-indications, warnings, etc *Precautions:* Consideration should be given to the sodium and potassium content of Phosphate-Sandoz Effervescent Tablets before administration to patients suffering from conditions associated with significant electrolyte imbalance, impaired renal function or where limitation in sodium intake is indicated, e.g. in the treatment of congestive cardiac failure, hypertension, pre-eclampsic toxemia, etc.

Soft-tissue calcification and nephrocalcinosis have been reported in isolated cases following intravenous therapy with phosphate. This is thought to be a function of dosage and rapidity of phosphate administration. While such effects appear less likely to occur following treatment with oral phosphates, careful surveillance of patients is recommended, especially if on long-term therapy.

Side-effects: Apart from diarrhoea, very few side-effects have been reported.

Overdosage: Excessive dosage has been reported to produce hypocalcaemia in isolated cases. This has proved reversible when dosage has been adjusted. However, deliberate overdosage is unlikely with effervescent preparations.

Pharmaceutical precautions Phosphate-Sandoz Tablets must be stored in a cool dry place, and since they are hygroscopic they should be dispensed in their original containers.

Legal category P.

Package quantities Boxes of 100 (5 tubes of 20 effervescent tablets).

Further information Phosphate-Sandoz Tablets each contain 136 mg sucrose and have an absolute calorific value of 2.5 kcal.

Product licence number 0101/5038.

SANCOS®

Presentation A clear, colourless liquid with a citrus flavour. Each 5 ml spoonful contains 5 mg Pholcodine PhEur, 750 mg Glycerol PhEur and 5.25 g Syrup BP.

Uses *Principal action:* Cough sedative.

Pholcodine has a specific depressant effect on the cough centre in the medulla. The central antitussive action of pholcodine is at least three times as powerful as that of codeine. Pholcodine is many times less toxic than codeine and is employed in much smaller doses. It causes less respiratory depression than morphine and is not implicated in gastro-intestinal side-effects such as constipation, anorexia, vomiting, etc.

Indications: Unproductive cough.

Dosage and administration **Adults:** Two 5 ml spoonfuls every three to four hours as required.

Children: Half to one 5 ml spoonful according to age and weight, every three to four hours as required.

Contra-indications, warnings, etc

Contra-indications and precautions: There are no known contra-indications to Sancos apart from use in patients where suppression of cough reflex is inadvisable.

Side-effects: Side-effects from Sancos are rare, however pholcodine may occasionally cause nausea and drowsiness.

Overdosage: Treatment should be directed to the elimination of the ingested material by gastric lavage. General supportive measures are of importance.

Pholcodine may cause respiratory depression and there may be pin-point pupils. This can be reversed by naloxone given 0.4 to 1.2 mg i.v. for adults and 0.01–0.1 mg/kg body weight for children. The dose may be repeated if initial response is not maintained.

Pharmaceutical precautions Sancos may be diluted with Syrup BP. The diluted syrup should be used within 14 days.

Legal category P.

Package quantities Bottles of 100 ml and 2 litres.

Further information Sucrose content of 3.5 g per 5 ml. Absolute calorific value 15 kJ per 5 ml.

Product licence number 0101/5041.

SANCOS* CO

Presentation Clear, colourless syrup with a citrus flavour. Each 5 ml spoonful contains 5 mg Pholcodine PhEur, 20 mg Pseudoephedrine Hydrochloride BP, 2 mg Chlorpheniramine Maleate BP, 600 mg Glycerol PhEur and 5.25 g Syrup BP.

Uses *Principal action:* Sancos Compound Linctus is a cough suppressant and decongestant. Of the active ingredients, pholcodine has a specific depressant effect on the cough centre in the medulla, has a more potent action than codeine and causes less respiratory depression than morphine. It is not implicated in gastrointestinal side-effects such as constipation, anorexia or vomiting and it also has the advantage of being well tolerated by children. Pseudoephedrine hydrochloride is an effective nasal and bronchial decongestant. Chlorpheniramine maleate is a well-tried antihistamine beneficial in the management of nasal irritation and in associated allergic symptoms.

Indications: The relief of cough, particularly when associated with congestion of nasal and bronchial mucous membranes.

Dosage and administration *Adults:* two to three 5 ml spoonfuls every six hours as required.

Children: 6 to 12 years: one to two 5 ml spoonfuls every six hours as required.

2 to 6 years: half to one 5 ml spoonful every six hours as required.

Do not exceed 3 doses (adults or children) in 24 hours.

Contra-indications, warnings, etc *Precautions.* As pseudoephedrine is a sympathomimetic amine, Sancos Compound Linctus should be given with caution to hypertensive patients, patients suffering from heart failure or to patients with incipient or established urinary retention, and should not be given to those being treated with monoamine oxidase inhibitors or antihypertensives. Caution is necessary in patients receiving beta-blockers.

Antihistamines may cause drowsiness and dulling of mental alertness. Patients undergoing treatment with Sancos Compound Linctus are advised not to take charge of vehicles, or other means of transport or machinery where loss of attention may lead to accidents.

Care should be exercised when administering an antihistamine to patients with epilepsy as convulsions may be precipitated, especially in children.

Side-effects: The side-effects are those attributed to antihistamines generally and the commonest include drowsiness, nausea, vomiting, headache, blurred vision, anorexia and dryness of the mouth.

Overdosage: Treatment should be directed to the elimination of the ingested material by gastric lavage. General supportive measures are of importance.

Pholcodine may cause respiratory depression and there may be pin-point pupils. This can be reversed by naloxone given 0.4 to 1.2 mg i.v. for adults and 0.01–0.1 mg/kg body weight for children. The dose may be repeated if the initial response is not maintained.

Pharmaceutical precautions Sancos Compound Linctus may be diluted with Syrup BP. The diluted syrup should be used within 14 days.

Legal category P.

Package quantities Bottles of 100 ml and 2 litres.

Further information Sucrose content 3.5 g per 5 ml dose. Absolute calorific value 15 kJ per 5 ml.

Product licence number 0101/5042.

SANDOCAL* CALCIUM-SANDOZ*

Presentation *Sandocal:* Orange, slightly speckled, flat-faced, round, effervescent tablets with a rough surface, weighing 6.3 g, 33 mm diameter and 5.6 mm thick. Orange-flavoured. Each effervescent tablet contains 3.08 g calcium lactate gluconate, equivalent to 4.5 g calcium gluconate and provides 400 mg calcium (10 mmol: 20 mEq Ca⁺⁺), 137 mg sodium (6 mmol: 6 mEq Na⁺), 176 mg potassium (4.5 mmol: 4.5 mEq K⁺) and 1.1 g anhydrous citric acid (1.08 g citrate ion).

Calcium-Sandoz Syrup: Colourless to pale straw coloured, fruit-flavoured syrup. Each 15 ml contains 3.27 g calcium gluconate and 2.17 g calcium galactogluconate. Three 5 ml spoonfuls provide 3.25 mg calcium (8.1 mmol: 16.2 mEq Ca⁺⁺).

Calcium-Sandoz Ampoules 10%: Clear, colourless solution. Each 10 ml contains 1.375 g calcium gluconate, equivalent to 10% calcium gluconate (93 mg calcium–2.32 mmol: 4.64 mEq Ca⁺⁺).

Uses *Principal action:* Calcium in convenient dosage forms to correct deficiency states.

Indications: High-dose oral calcium in the form of Sandocal Effervescent Tablets and Calcium-Sandoz Syrup is indicated in the treatment of pregnancy cramp and neonatal tetany, and as a therapeutic supplement in osteoporosis, post-gastrectomy malabsorption, osteomalacia, rickets, pregnancy, lactation.

Parenteral administration is indicated when the pharmacological action of a high calcium ion concentration is required.

Dosage and administration *Oral:* See table.

Parenteral: 5–10 ml of Calcium-Sandoz 10% i.v. or i.m. daily or every other day.

Children require about half the adult dosage.

Intramuscular injections should be given deep in the gluteus medius muscle using a long needle; this route is not recommended for children.

<i>Indication</i>	<i>Daily dosage Effervescent Tablets (The tablets must be dissolved in $\frac{3}{4}$–$\frac{1}{2}$ tumblerful of water)</i>	<i>Syrup (ml)</i>
osteoporosis		
post-gastrectomy		
malabsorption	3–5 tablets	60–100
osteomalacia and rickets		
osteostation		
pregnancy supplement	1–3 tablets	20–60
pregnancy cramps		
neonatal tetany		5 ml four-hourly, mixed with milk feed

Intravenous injections should be given very slowly (three minutes for 10 ml).

Calcium-Sandoz should not be injected subcutaneously.

Contra-indications, warnings, etc

Contra-indications: Severe hypercalcaemia and hypercalciuria (e.g. in hyperparathyroidism, vitamin D over-dosage, decalcifying tumours such as plasmacytoma and skeletal metastases, in severe renal failure and in osteoporosis due to immobilisation). Parenteral calcium therapy is strictly contra-indicated in patients receiving cardiac glycosides.

Precautions: Consideration should be given to the sodium and potassium content of Sandocal Effervescent tablets (see under 'Presentation') before administration to patients suffering from conditions associated with significant electrolyte imbalance, impaired renal function or where limitation in sodium intake is indicated e.g. in the treatment of congestive cardiac failure, hypertension, re-eclamptic toxemia, etc. In these cases Calcium-Sandoz Syrup, which contains neither sodium nor potassium, may be substituted for the tablet. Careful monitoring of blood levels and urinary calcium excretion is especially necessary when high-dose parenteral calcium therapy is administered, particularly in children. Treatment should be suspended immediately if blood calcium exceeds 105–110 mg/litre or if the 24-hour urinary calcium excretion exceeds 5 mg/kg when it is also necessary to be alert to the possibility of cardiac dysrhythmias.

Overdosage: No cases of intoxication with calcium due to deliberate or accidental overdosage have been reported to the Company. Deliberate overdose is unlikely with effervescent preparations.

Side-effects: Diarrhoea has occurred in a very small number of patients receiving Sandocal. If intravenous injection is administered too rapidly, nausea, vomiting, hot flushes, sweating, hypotension and even vaso motor collapse may ensue.

Pharmaceutical precautions Sandocal Tablets must be stored in a cool dry place.

Calcium-Sandoz Syrup may be diluted with Syrup BP; the diluted syrup should be used within 14 days.

Legal category Sandocal P.
Calcium-Sandoz Syrup P.
Calcium-Sandoz Injection POM.

Package quantities Sandocal Effervescent Tablets: boxes of 100 (5 tubes of 20).

Calcium-Sandoz Syrup: Bottles of 500 ml.
Calcium-Sandoz Ampoules: Boxes 5 × 10 ml.

Further information Sandocal Tablets contain 935.5 mg sucrose per tablet and have an absolute calorific value of 18.33 kcals.

Calcium-Sandoz Syrup contains 4.536 g sucrose per 15 ml dose. Absolute calorific value 54 kcals per 15 ml dose.

Product licence numbers

Effervescent Tablets 0101/5043
Syrup 0101/5024
Ampoules 0101/5003

SANDO-K*

Presentation Flat, round, white, effervescent tablets with a slightly rough surface, weighing 2.4 g and of 22 mm diameter and 4.25 mm thickness. Salty taste. Each tablet contains 600 mg Potassium Chloride PhEur, 400 mg Potassium Bicarbonate BPC and 800 mg of anhydrous citric acid. This provides the equivalent of 470 mg potassium (12 mmol: 12 mEq K⁺) and 285 mg chloride (8 mmol: 8 mEq Cl⁻); also 2.1 mg sodium content.

Uses *Principal action:* Sando-K Effervescent Tablets provide a high-dose, palatable potassium supplement in solution.

Enteric-coated and matrix-type solid-dose forms of potassium have been incriminated in the development of small-bowel ulceration, obstruction, perforation, stenosis and haemorrhage, probably produced by high local potassium concentration. Sando-K Effervescent Tablets when dissolved in water prevent such local concentration, thus minimising gastro-intestinal irritation. Sando-K Effervescent Tablets contain 8 mmol of chloride ion, now believed to be of significance in limiting hypokalaemic, hypochloralaemic alkalosis.

Indications: Prevention and treatment of hypokalaemic states such as those associated with: administration of diuretics of the sulphamoyl group (includes thiazides, etc.); ulcerative colitis; renal tubular acidosis; Cushing's syndrome.

Dosage and administration Sando-K Effervescent Tablets must be dissolved in $\frac{3}{4}$ – $\frac{1}{2}$ a tumblerful of water and may be taken with food if preferred.

Dosage will depend upon the clinical conditions and diet of the patient and will vary widely, but 2–4 tablets daily (24 to 48 mmol K⁺) are likely to provide an adequate prophylactic or therapeutic dose in most patients. Large doses may be indicated in more severe hypokalaemic conditions when the dose should be regulated by the patient's response as determined by serum electrolyte levels.

Contra-indications, warnings, etc

Contra-indications and precautions: Care should be taken to avoid dosage in excess of requirements for patients with impaired renal function.

Side-effects: Side-effects are rare with Sando-K. If there are any signs of gastric irritancy, Sando-K, in common with all other potassium salts, should be given with or after food.

Overdosage: Hyperkalaemia. Deliberate overdosage is unlikely with effervescent preparations. Poisoning is usually minimal below 6.5 mmol: mEq/L. moderate between 6.5 and 8 mmol: mEq/L and severe above that

level. The absolute toxicity is governed by both pH and associated sodium levels. Hyperkalaemic symptoms, and particularly the ECG effects, may be transiently controlled by calcium gluconate, administration of glucose or glucose and insulin, sodium bicarbonate or hypertonic sodium infusions, cation exchange resins or by haemodialysis and peritoneal dialysis. Caution should be exercised in patients who are digitalised and who may experience acute digitalis intoxication in the course of potassium removal.

Pharmaceutical precautions Store in a cool dry place. Sando-K Effervescent Tablets are hygroscopic and wherever possible should be dispensed in their original containers which carry a note to the patient requesting that the containers be kept tightly closed in a cool dry place.

Legal category P.

Package quantities Boxes of 100 (5 × 20 effervescent tablets).

Further information Sando-K Tablets each contain 557.5 mg sucrose and have an absolute calorific value of 4.5 kJ.

Product licence number 0101/5044.

SYNTOCINON* NASAL SPRAY

Presentation Syntocinon Spray is available as a solution containing 40 units of synthetic oxytocin in 1 ml for intranasal administration.

Uses *Principal action:* Syntocinon is synthetic oxytocin, identical to the polypeptide hormone released by the posterior lobe of the pituitary gland. It has been demonstrated that oxytocin has a physiological function in the neurohumoral reflex which makes milk available to the suckling infant.

The bulk of the milk secreted is held in the alveoli and small ductules of the breast by capillary attraction. The negative pressure induced by suckling only suffices to withdraw the small amount of milk in the larger ducts and cisterns. When a mother takes a baby to the breast, the stimulation of the nipple by suckling causes a nervous impulse to pass by an unknown afferent pathway to the hypothalamus and thence by the hypothalamo-hypophyseal tract to the posterior lobe of the pituitary which releases oxytocin into the bloodstream.

The hormone is carried by the blood, the efferent pathway, to the breast where it causes contraction of the myoepithelial cells surrounding the alveoli and small ductules forcing their milk content into the larger ducts converging on the nipple. This reflex which makes milk available to the baby is known as the milk let-down or milk ejection reflex. This reflex may be inhibited in conditions of stress and it is possible to counteract the inhibitory processes by administering oxytocin. By allowing a free flow of milk, breast feeding is facilitated, resulting in an easier, more rapid and more complete emptying of the breast. The possibility of damage to the nipple is reduced as is milk engorgement and breast abscess formation. There is evidence to suggest that when the milk let-down reflex is established by the routine administration of oxytocin there is an increase in milk production.

The role of oxytocin in establishing the milk let down reflex has not been fully exploited in clinical medicine, since parenteral injection was considered necessary for

satisfactory absorption. Development work has been directed to the formulation of a spray solution and to the production of a container which enables a reasonably accurate dose of Syntocinon to be administered intranasally in the form of a fine spray. In this form, oxytocin has been shown to be sufficiently well absorbed from the nasal mucosa to elicit the milk let-down response.

Indications: To facilitate the establishment of breast feeding by eliciting the milk let-down reflex and allowing a free flow of milk. Thereby a) permitting a satisfactory feed; b) reducing damage to the nipples; c) preventing or relieving milk engorgement of the breasts; d) preventing breast abscess formation.

Dosage and administration The patient should be advised to hold the spray upright, insert the nozzle in the nostril and give the container one firm squeeze (approx. 2 oxytocic units) into one or both nostrils as directed by the doctor.

The spray should be used two to five minutes before the baby is put to the breast.

Contra-indications, warnings, etc

Contra-indications: Pregnancy; hypersensitivity.

Overdosage: It is considered that intoxication resulting from judicious usage is unlikely to occur with oxytocin administered by this route as it is rapidly inactivated by proteolytic enzymes in the alimentary tract.

Pharmaceutical precautions Store at temperature below 5°C, but do NOT freeze. Use within one month of opening.

Legal category POM.

Package quantities Spray bottles of 5 ml.

Further information Nil.

Product licence number 0101/5011.

SYNTOCINON* PARENTERAL SOLUTION

Presentation Syntocinon is available as Oxytocin Injection BP containing 2 units in 2 ml, 5 units in 5 ml or 10 units in 10 ml or 50 units in 50 ml.

Uses *Principal action:* Syntocinon is synthetic oxytocin which is identical with the polypeptide hormone released by the posterior lobe of the pituitary gland. Unlike oxytocin from natural sources, Syntocinon is completely free from vasopressin and extraneous animal protein.

At normal therapeutic doses, Syntocinon selectively stimulates the contraction of uterine smooth muscle.

Indications: Syntocinon Parenteral Solution may be used for: Induction of labour. Stimulation of labour in hypotonic uterine inertia. Management of missed and incomplete abortion. Postpartum haemorrhage in the occasional patient who does not respond to ergometrine.

Dosage and administration By intravenous drip infusion: 1 IU of oxytocin in 1 litre 5% dextrose solution delivers approximately 1 mU/min when infused at a rate of 15 drops per minute.

For induction or stimulation of labour:

1. Physiological oxytocin infusion. The range of dosage is between 2 mU and 5 mU/min.

2. Pharmacological oxytocin infusion. Initially 1½–2 mU/min adjusted gradually until contractions occur every two to five minutes, rate of infusion not exceeding 12 mU/min.

3. Oxytocin titration: Initially 1 mU/min, then double the rate of flow every 10 minutes until contractions commence. Thereafter double the rate of flow every 20 minutes until contractions lasting 40–50 seconds occur at intervals of two to three minutes. Doses of oxytocin up to 128 mU/min have been used.

Issued abortion: 10–20 units per 500 ml of 5% dextrose solution increasing by 10–20 units per 500 ml every hour to a maximum of 100 units per 500 ml if necessary. The rate of infusion recommended is 10–30 drops per minute.

Contra-indications, warnings, etc

Contra-indications: The use of Syntocinon is contraindicated in hypertonic uterine inertia, mechanical obstruction to delivery, failed trial labour, severe toxæmia, predisposition to amniotic fluid embolism, foetal distress and placenta prævia.

Precautions: Considerable caution should be exercised in abnormal presentation, multiple pregnancy, excessive irritability and previous caesarian section. High doses of oxytocin should only be used in fully equipped centres where patients can be kept under constant observation. In patients with cardiovascular disorders the infusion volume should be low.

Overdosage: The fatal dose of Syntocinon has not been established. Syntocinon is subject to inactivation by proteolytic enzymes of the alimentary tract. Hence it is not absorbed from the intestine and is not likely to have toxic effects when ingested.

Where high doses of Syntocinon are given with large volumes of electrolyte-free fluid, the following symptoms of water intoxication may occur:

1. Headache, anorexia, nausea, vomiting and abdominal pain.
2. Lethargy, drowsiness, unconsciousness and grand mal type seizures.
3. The electrolyte concentration in blood is low.

Treatment: All fluid intake should be restricted. Diuresis should be promoted as soon as possible and the electrolyte imbalance should be corrected. Convulsions may be controlled by judicious use of diazepam. In the case of coma, a free airway should be maintained with the routine measures normally employed in the nursing of the unconscious patient.

Side-effects: As there is a wide variation in uterine sensitivity, uterine spasm may be caused in some instances by what are normally considered to be low doses.

Very high doses may cause violent uterine contractions leading to uterine rupture, tissue damage and asphyxia of the foetus.

Pharmaceutical precautions Protect from light. Store between 4° and 22°C.

Syntocinon should not be infused via the same apparatus as blood or plasma, because the peptide packages are rapidly inactivated by oxytocinase. Syntocinon is incompatible with solutions containing sodium metabisulphite as a stabiliser.

Syntocinon is compatible with the following commonly used infusion fluids, but due attention should be paid to the advisability of using electrolyte fluids in individual patients. Dextrose 5%. Sodium/potassium chloride 103 mmol Na⁺ and 51 mmol K⁺. Laevulose 20%. Macrodex 6%. Sodium bicarbonate 1.39%. Sodium chloride 0.9%. Sodium lactate 1.72%. Rheomacrodex 0%. Ringer's solution.

Legal category POM.

Package quantities 50IU/5 ml: Boxes of 5.

10IU/1 ml: Boxes of 10.

5IU/1 ml: Boxes of 10.

2IU/2 ml: Boxes of 10.

Further information Nil.

Product licence numbers

50 IU 0101/0071

10 IU 0101/0070

5 IU 0101/0069

2 IU 0101/0068

SYNTOMETRINE*

Presentation Syntometrine is available as a parenteral solution containing Ergometrine Maleate PhEur 500 mcg and 5 units of oxytocin in 1 ml.

Uses *Principal action:* Designed for intramuscular injection. Syntometrine combines the known sustained oxytocic action of ergometrine with the more rapid action of oxytocin on the uterus. The latent period following an intramuscular injection of Syntometrine is considerably shorter than with any other ergot preparation.

Indications: Syntometrine is indicated in the active management of the third stage of labour or, routinely following the birth of the placenta, to prevent or treat postpartum haemorrhage.

Dosage and administration Intramuscular injection of 1 ml. May also be administered by intravenous injection in a dose of $\frac{1}{2}$ –1 ml.

Contra-indications, warnings, etc

Contra-indications: Severe disorders of liver or kidney function.

Precautions: When the intravenous route is employed, care should be exercised in patients of doubtful cardiac status.

Caution should be exercised in the presence of hypertension, sepsis, obliterative vascular disorders and liver or kidney failure.

Side-effects: Occasional reports of nausea, vomiting and abdominal pain.

Overdosage: No case of maternal intoxication with Syntometrine has been reported to the Company. Inadvertent administration to the newborn infant has proved fatal. In reported accidental neonatal overdosage cases, respiratory and cardiovascular support have been required.

Pharmaceutical precautions Protect from light. Store between 4° and 22°C.

Legal category POM.

Package quantities Boxes of 10 × 1 ml.

Further information Snap ampoules: no file required.

Product licence number 0101/5046.

SYNTOPRESSIN* NASAL SPRAY

Presentation Syntopressin is available as a solution containing lypressin 50 units per ml for use as a nasal spray.

Uses *Principal action:* Syntopressin is synthetic 8-lysine-vasopressin (lypressin). It is completely free of

oxytocin and extraneous animal protein. Syntopressin has a direct antidiuretic action. It is used for the control of polyuria in diabetes insipidus.

Indications: Diabetes insipidus, spontaneous or induced.

Dosage and administration One or two applications of the spray (2.5–5.0 i.u.) to one or both nostrils, repeated three to seven times a day according to the response of the patient.

The patient should be advised to hold the bottle upright and to spray the inside of one or both nostrils by squeezing the bottle firmly then removing from the nostril to release the pressure, one or more times at intervals as required to produce the desired dose.

Contra-indications, warnings, etc Coronary heart disease, anaesthesia with halothane or cyclopropane.

Precautions: As with other forms of vasopressin, caution is advised in the administration of this drug to patients suffering from advanced arteriosclerosis, peripheral vascular disease, hypertension, epilepsy and during pregnancy, particularly toxæmic.

Overdosage: No reports of overdosage have been reported to the Company.

Side-effects: Nausea, abdominal pain or urge to defæcate may follow injudicious use. On rare occasions nasal congestion with ulceration of the nasal mucosa has been reported.

Pharmaceutical precautions Store in a cool place, but do NOT freeze.

Legal category POM.

Package quantities Spray bottles of 5 ml.

Further information Nil.

Product licence number 0101/5047.

TORECAN®

Presentation *Tablets:* White, bi-convex, sugar-coated tablets of 7 mm diameter, weighing 180 mg and printed 'SANDOZ' on one face. Each tablet contains thiethylperazine maleate equivalent to 6.33 mg base (10 mg salt).

Ampoules: Clear, colourless-to-yellow-tinge parenteral solution. Each 1 ml ampoule contains thiethylperazine maleate equivalent to 6.5 mg base (10.86 mg salt).

Suppositories: White to pale-yellow suppositories weighing 1.93 g. Each suppository contains thiethylperazine maleate equivalent to 6.5 mg base (10.28 mg salt).

Uses *Principal actions:* Torecan is an anti-emetic and antinauseant. It controls vomiting, nausea and vertigo.

Torecan is a phenothiazine derivative which, unlike many other compounds in this group, exhibits specific anti-emetic and antivertiginous properties with little or no tranquillising, sedative or other effects.

The present concept of the vomiting mechanism is that emesis may be induced by direct action on the vomiting centre in the medulla or by lowering its threshold to stimulation. Excitation of the vomiting centre may result from direct visceral impulses or be secondary to stimulation of the chemoreceptor trigger zone. Pharmacological studies have shown that Torecan in similar doses will control vomiting induced by stimulation of both the chemoreceptor trigger zone and

the vomiting centre. This suggests that Torecan may possess a more effective action than other anti-emetic agents.

Indications: Torecan is indicated for the relief of vertigo and the control of nausea and vomiting associated with various causes, notably:

1. Labyrinthine disturbances – Ménière's disease, labyrinthitis, surgery, motion sickness, cerebral irritability and damage or disease of the inner ear.
2. Miscellaneous conditions – uraemia, drug idiosyncrasy, hepatic disorders, biliary diseases, migraine, alcoholism and malignant disease.
3. Gastro-intestinal disturbances – gastroenteritis.
4. Radiotherapy and treatment with cytostatic agents.
5. Post-operative nausea, vomiting and vertigo.

Dosage and administration *Tablets: Adults:* 1 tablet two or three times daily.

Children: Not recommended for children under 15 years.

Ampoules: Adults: 1 ml by intramuscular injection. Effective in 30–60 minutes.

Children: Not recommended for children under 15 years.

Suppositories: Adults: 1 suppository night and morning.

Children: Not recommended for children under 15 years.

Contra-indications, warnings, etc

Contra-indications: Severely depressed or comatose states. Hypersensitivity to phenothiazines.

Precautions: No cases of bone-marrow depression or renal toxicity have been reported. As with many synthetic drugs, the physician should nevertheless be alert to the possibility in susceptible individuals. On a very few occasions, jaundice has occurred following administration of Torecan, but a drug-effect relationship has not been established. Like most phenothiazines, Torecan may occasionally provoke extrapyramidal side-effects: females under 30 and particularly children appear more susceptible. Consequently, Torecan is not recommended for children under 15 years. These symptoms respond to withdrawal of the drug, or to treatment with sedative and anti-parkinsonian agents.

Torecan may impair reaction time and can potentiate the effects of sedatives and alcohol. Torecan should be given in pregnancy and during breast feeding only if strictly indicated.

Side-effects: Drowsiness, dryness of the mouth and occasional postural hypotension may occur, particularly if the maximum recommended dosage of 30 mg daily is exceeded.

Extra-pyramidal side effects – see 'Precautions'.

Overdosage: The symptoms of Torecan overdosage are similar to those of other phenothiazines with the exception that there is less CNS depression with Torecan. There is no specific antidote for acute phenothiazine poisoning therefore treatment is directed at minimising the amount of the drug absorbed, eliminating the absorbed drug from the body and combating the toxic effects of the overdose by gastric lavage, maintenance of adequate pulmonary ventilation and general supportive measures. Emetics are obviously of less value. If emetics are given and do not work, then do not exceed the normal dose. Peritoneal dialysis and haemodialysis are ineffective in treatment of phenothiazine poisoning. Symptoms of hypotension should be corrected.

Severe extrapyramidal reactions usually respond to

intravenous administration of anti-parkinsonian agents, e.g. Benztropine 2 mg i.v. or i.m.

Prophylactic antibiotic therapy is generally favoured. Hypothermia; body temperature should be allowed to recover naturally unless it falls below 30°C.

Pharmaceutical precautions Suppositories should be stored in a cool place.

Ampoules should be protected from light.

Legal category POM.

Package quantities *Tablets:* Containers of 50.

Ampoules: Boxes of 5 × 1 ml.

Suppositories: Boxes of 6.

Further information Nil.

Product licence numbers

Tablets 0101/5048

Ampoules 0101/5012

Suppositories 0101/5013

/ISKALDIX*

Presentation White, uncoated, round, flat, bevelled tablets of 7 mm diameter and weighing 120 mg. Coded 7D with a single breakline on one side. Each tablet contains 10 mg pindolol and 5 mg clopamide.

Uses *Principal action:* Viskaldix is a combination of the beta-adrenoceptor blocking agent pindolol and the diuretic clopamide; each component lowers blood pressure through a different mechanism of action. Clinical studies have shown that the combination is an effective and well-tolerated antihypertensive agent, that both components contribute to this effect, and that the combination is more effective than pindolol alone.

Pindolol is a specific beta-adrenoceptor blocking agent with some intrinsic sympathomimetic activity which minimises myocardial depression and other undesirable effects of beta-blockade, including bradycardia and bronchoconstriction. Clopamide, in the dosage present in Viskaldix, contributes to a lowering of blood pressure without marked diuresis. The hypotensive effect of the combination is often seen after five to seven days but the maximum effect may not be achieved for two to three weeks.

Indications: Mild to moderate hypertension.

Dosage and administration 1 tablet daily in the morning. If blood pressure is not satisfactorily lowered after two to three weeks, two tablets may be taken as a single dose in the morning. A maximum dose of three tablets daily may be taken if necessary.

Contra-indications, warnings, etc

Contra-indications: Cardiac failure unless satisfactorily controlled by digitalis (see also precautions). Atrioventricular block, pronounced bradycardia, obstructive pulmonary disease, cor pulmonale, severe renal or hepatic failure, metabolic acidosis, prolonged fasting, hypokalaemia, pregnancy.

Viskaldix should not be taken in conjunction with agents which inhibit calcium transport, e.g. verapamil, during concomitant administration of lithium, or by patients with known hypersensitivity to sulphonamides.

Precautions: Patients with a poor cardiac reserve should be stabilised with digitalis before treatment with Viskaldix to prevent impairment of myocardial contractility. Viskaldix should be used with caution in patients with a

history of bronchial asthma or recent myocardial infarction and also in patients with spontaneous hypoglycaemia and diabetics under treatment with insulin or oral hypoglycaemic agents. Viskaldix should be administered during breast feeding only in compelling circumstances.

During treatment with Viskaldix, patients should not undergo anaesthesia with agents causing myocardial depression (e.g. halothane, cyclopropane, trichlorethylene, ether, chloroform). Viskaldix should be gradually withdrawn before elective surgery. In emergency surgery or cases where withdrawal of Viskaldix would cause deterioration in cardiac condition, atropine sulphate 1–2 mg intravenously should be given to prevent severe bradycardia.

If a beta-blocker is indicated in a patient with a pheochromocytoma it must always be given in conjunction with an alpha-blocker. Pre-existing peripheral vascular disorders may be aggravated by beta-blockers.

In severe renal failure a further impairment of renal function following beta-blockade has been reported in a few cases. Potassium levels should be checked in patients with kidney or liver failure, and urate levels in patients suffering from gout.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenoceptor blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuance of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-blocker should be gradual.

Overdosage: Overdosage may cause alterations in heart rate, nausea, vomiting, orthostatic disturbances, collapse, hypokalaemia and its accompanying disorders.

Treat by elimination of any unabsorbed drug and general supportive measures. Plasma electrolytes should be closely monitored. Marked bradycardia, as a result of overdosage or idiosyncrasy, should be treated with atropine sulphate 1–2 mg intravenously. If necessary, isoprenaline hydrochloride can be administered by slow intravenous injection, and under constant supervision, beginning with 25 mcg (5 mcg/min) until the desired effect is achieved. A cardiac pacemaker may be required.

Intravenous glucagon (5–10 mg) has been reported to overcome some of the features of serious overdosage with beta-blockers and may be useful.

Side-effects: Few serious side-effects have been reported. Depression, diarrhoea, insomnia, headaches, sleep disturbance, epigastric pain, fatigue, dizziness, hypotension have occurred but are usually transient and disappear if dosage is reduced.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Calendar pack of 28.

Product licence number 0101/0113.

VISKEN*

Presentation *5 mg Tablets:* Visken 5 mg is available as white, round, flat, bevel-edged tablets of 7 mm diameter, and weighing 120 mg. Branded 'SANDOZ' on one side, and coded 'LB' with a single break line on the reverse. Each tablet contains 5 mg of pindolol base.

15 mg Tablets: Visken 15 mg is available as white, round, flat, bevel-edged tablets of 9 mm diameter and weighing 200 mg. Branded SANDOZ on one side, and coded JU

with a single break line on the reverse. Each tablet contains 15 mg of pindolol base.

Uses *Principal action:* Visken is a specific beta-adrenoreceptor blocking agent with low cardiodepressant activity at therapeutic dose. Its beta-blocking activity prevents excessive sympathetic drive to the heart, resulting in a fall in heart rate, and a decrease in cardiac work and myocardial oxygen consumption. Visken possesses some intrinsic sympathomimetic activity even at low dosage which may prevent reduction of resting sympathetic tone to an undesirably low level and minimise myocardial depression.

Indications: **Hypertension:** For reduction of blood pressure in essential hypertension. Onset of action of Visken is usually rapid, most patients showing a response within the first one to two weeks of treatment.

However, maximum response may take several weeks to develop.

Angina pectoris: Prophylactic treatment with Visken reduces the frequency and severity of anginal attacks and increases work capacity.

Dosage and administration *Hypertension:* Initially one 15 mg tablet daily, with breakfast or 5 mg two or three times daily. Most patients respond to a once-daily dose of from 15 mg to 30 mg.

If necessary, dosage may be increased at weekly intervals up to a maximum of 45 mg daily in single or divided doses. Patients not responding after three to four weeks at this dosage level rarely benefit from further elevations in dosage. Addition of Visken to existing diuretic therapy increases the hypotensive effect and combination with other anti-hypertensives enables reduction in dosage of these agents.

Angina pectoris: Usually half to one 5 mg tablet up to three times a day according to response.

Contra-indications, warnings, etc

Contra-indications: Cardiac failure unless satisfactorily controlled by digitalis (see also 'Precautions').

Atrio-ventricular block pronounced bradycardia, obstructive pulmonary disease cor pulmonale, metabolic acidosis, prolonged fasting, severe renal failure, pregnancy.

Visken should not be taken in conjunction with agents which inhibit calcium transport, e.g. verapamil.

Precautions: Patients with a poor cardiac reserve should be stabilised with digitalis before treatment with Visken to prevent impairment of myocardial contractility.

As with all beta-blockers, Visken should be used with caution in patients with a history of bronchial asthma or recent myocardial infarction and in the treatment of patients with spontaneous hypoglycaemia and diabetics under treatment with insulin or oral hypoglycaemic agents. Visken should be administered during breast feeding only in compelling circumstances.

During treatment with Visken patients should not undergo anaesthesia with agents causing myocardial

depression (e.g. halothane, cyclopropane, trichlorethylene, ether, chloroform). Visken should be gradually withdrawn before elective surgery. In emergency surgery or cases where withdrawal of Visken would cause deterioration in cardiac condition, atropine sulphate 1-2 mg intravenously should be given to prevent severe bradycardia.

If a beta-blocker is indicated in a patient with a pheochromocytoma it must always be given in conjunction with an alpha-blocker. Pre-existing peripheral vascular disorders may be aggravated by beta-blockers.

In severe renal failure a further impairment of renal function following beta blockade has been reported in a few cases.

There have reports of skin rashes and/or dry eyes associated with the use of beta-adrenoreceptor blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuance of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-blocker should be gradual.

Overdosage: Treat by elimination of any unabsorbed drug and general supportive measures. Marked bradycardia as a result of overdosage or idiosyncrasy should be treated with atropine sulphate 1-2 mg intravenously. If necessary, isoprenaline hydrochloride can be administered by a slow intravenous injection and under constant supervision beginning with 25 mcg (5 mcg/min) until the desired effect is achieved. A cardiac pacemaker may be required; i.v. glucagon (5-10 mg) has been reported to overcome some of the features of serious overdosage and may be useful.

Side-effects: Few serious side-effects have been reported. Depression, diarrhoea, insomnia, headaches, sleep disturbance, epigastric pain, fatigue, dizziness, hypotension have occurred but are usually transient and disappear if the dosage is reduced. Allergic skin reactions have occasionally been reported.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities 5 mg tablets: Containers of 100.
15 mg tablets: Containers of 30.

Further information Since Visken is a specific adrenergic beta-receptor blocking agent, effective control of the blood pressure can be achieved without inducing the problems often associated with other antihypertensive therapy, e.g. postural and effort hypotension, impotence and sedation. Many patients treated with Visken have reported an increased sense of well-being.

Product licence numbers

Tablets 5 mg 0101/0065
Tablets 15 mg 0101/0110

**Trade Mark*

Sanol Schwarz Pharmaceuticals Ltd

The Limes, 130 High Street
Chesham
Bucks HP5 1EF



ELANTAN® 20 ▼

Presentation White tablets with break score, containing 20 mg Isosorbide mononitrate.

Uses Prophylaxis of angina pectoris.

Dosage and administration Long term treatment, 1 tablet three times a day after meals taken unchewed with a little fluid. The dosage can be increased to two tablets three times a day.

Contra-indications, warnings, etc Elantan should not be used in cases of: acute myocardial infarction with low filling pressures; acute circulatory failure; very low blood pressure. The drug should not be used during the first three months of pregnancy except under the direction of a doctor. Symptoms of circulatory collapse may arise after the first dose in patients with labile circulation; nitrate headache may also occur. Both symptoms can be largely avoided if the treatment is started with half a tablet of Elantan morning and evening.

Reaction capacity may be reduced if alcohol is consumed during treatment.

Pharmaceutical precautions No special storage conditions are necessary.

Legal category POM.

Package quantities Elantan is blister-packed in cartons of 50 and 100 tablets.

Further information Isosorbide mononitrate is the British approved name for isosorbide-5-mononitrate.

Product licence number 4438/0005.

ISOKET® I.V.

Presentation Isoket IV is supplied as ampoules containing Isosorbide dinitrate in 10 ml colourless, sterile, isotonic saline and in bottles containing 100 mg Isosorbide dinitrate in 100 ml colourless, sterile, isotonic saline. The solutions contain no alcohol.

Uses Isoket is indicated in the treatment of unresponsive left ventricular failure secondary to acute myocardial infarction, unresponsive left ventricular failure of various aetiology and severe or unstable angina pectoris.

Isosorbide dinitrate has a relaxant action on the smooth musculature, especially in the blood vessels. The major site of action comprises the peripheral capacitance veins, the dilation of which leads to a reduced return of blood to the heart. This applies to both the systemic and pulmonary circulations. At the same time, the resistance arterial vessels also become dilated, though to a lesser degree. As a result of these actions there is a favourable effect on all conditions associated with elevated ventricular pressure and a consequent reduction in the workload of the heart, with a reduction in myocardial oxygen consumption.

Therapeutic doses of Isoket produce a reduction in left ventricular end diastolic pressure and left ventricular end diastolic volume. By reduction of the previously elevated ventricular wall tension, the intramural coronary vessels, even in the post-stenotic area, can fill better during diastole. The endocardial region, which is particularly endangered by ischaemia then receives an improved blood supply. The myocardium, previously overstressed by the elevated preload, then resumes its normal action, either wholly or partly, depending of course on the severity and extent of the anatomical injury.

Isosorbide dinitrate has been shown to improve the effective renal plasma flow index and to increase urine flow in patients with congestive heart failure, possibly due to a normalization of blood flow distribution in the kidney. The dilation of the coronary vessels following Isoket administration is of clinical relevance in cases of angina pectoris due to coronary artery spasm.

Dosage and administration *Dosage:* The dose employed must be adjusted according to the patient's response. In general, a dose of between 2 and 7 mg per hour is suitable, although doses as high as 10 mg per hour may be necessary.

Children: The safety and efficacy of Isoket has not yet been established in children.

Administration: Isoket is a concentrated solution and should never be injected directly as a bolus. It should always be administered as an intravenous admixture with a suitable vehicle such as Sodium Chloride Injection B.P. or Dextrose Injection B.P. Prepared Isoket admixtures are always given by intravenous infusion or with the aid of an infusion pump. During administration, there should be close monitoring of the patient's blood pressure and pulse. Admixtures are prepared by exchanging the required volume of Isoket with an equal volume of the infusion vehicle. For example, if a dose of 6 mg per hour is required, 50 ml of Isoket (equivalent to 5×10 ml ampoules) should be added to 450 ml of the infusion vehicle to give a final volume of 500 ml. This admixture now contains 1 mg in 10 ml and the required dosage can be obtained by giving 60 ml per hour which is equivalent to a drip rate of 60 paediatric microdrops per minute or 20 standard drops per minute. This drip rate provides enough solution for an infusion time of 8 hours and 20 minutes.

When it is necessary to further reduce the fluid intake, a more concentrated solution may be obtained by using one bottle (100 mg Isosorbide dinitrate) of Isoket IV made up to 500 ml. This gives a final concentration of 200 mg/ml. The Isoket IV should be added to the infusion solution immediately after opening the admixture should be made up under aseptic conditions.

Contra-indications, warnings

Contra-indications: Isoket should not be used in the treatment of cardiogenic shock unless some means of

maintaining an adequate diastolic aortic pressure are undertaken. Isoket is contra-indicated in circulatory collapse and severe hypotension.

Precautions: Close attention to pulse and blood pressure is necessary during the administration of Isoket infusions.

Adverse Effects: Whilst sharp falls in systemic arterial pressure can give rise to symptoms of cerebral flow deficiency and decreased coronary perfusion, clinical experience with Isoket has shown that this is not normally a problem. This is consistent with the known vasodilatory effects of Isosorbide dinitrate which occur predominantly on the venous rather than the arterial side of the circulation. In common with other nitrates, headache and nausea may occur during administration.

Pharmaceutical precautions

Compatibility: Isoket contains Isosorbide dinitrate in isotonic saline and is compatible with commonly employed infusion solutions. No incompatibilities have so far been demonstrated.

Isoket is compatible with glass infusion bottles and infusion packs made of polyethylene, e.g. Polyfusor* (Boots), or Bottle-paks* and Flat-Paks* distributed by Dylade of Runcorn, Cheshire.

Isoket may be infused slowly using a syringe pump with a glass or rigid plastic syringe (Gillette Sabre syringe or Brunswick Disposable Plastipak* syringes). Isoket is incompatible with infusion bags and administration sets made from PVC and a loss of activity of up to 40% is possible on prolonged contact, e.g. 8 hours. Loss after 1 hour is approximately 30%. The use of PVC containers should therefore be avoided, e.g. Vialflex* (Travenol) or Steriflex* (Boots).

Legal category POM.

Package quantities Each pack contains 10 × 10 ml ampoules.

Bottles: Each pack contains 4 × 100 ml bottles.

Further information Nil.

Product licence number 4438/0001

ISOKET RETARD*

Presentation Circular yellow tablets, scored on one side, and containing 20 mg Isosorbide dinitrate in a sustained release formulation.

Uses For the prevention of anginal attacks.

Dosage and administration The tablets are for oral administration. The deep score-line permits easy division of the tablets when low dosages are prescribed.

The usual dose for long-term treatment is one tablet every 12 hours; the tablets should be swallowed without chewing. Up to four tablets daily may be taken if necessary.

For controlling an anginal attack, half a tablet should be chewed and left to dissolve in the mouth.

Contra-indications, warnings, etc

Contra-indications: A history of sensitivity to the drug. Very low blood pressure.

Warnings: Headaches may develop in sensitive persons and these may be minimized by commencing with low gradually increasing doses. Cutaneous vasodilatation postural hypotension and dry rashes may occasionally occur.

Precautions: Alcohol intake may enhance the effect of the drug and induce hypotension. During the first three months of pregnancy drugs should only be used if absolutely essential.

Pharmaceutical precautions Store in a cool, dry place.

Legal category P.

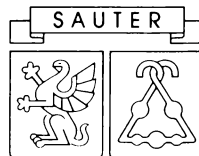
Package quantities The tablets are supplied in blister-packs of 50 tablets.

Further information Isosorbide dinitrate is a long acting substance and the special sustained release formulation of Isoket Retard tablets permits onset of action within 20 minutes and a duration of up to 12 hours.

Product licence number 4438/0004

*Trade Mark

Sauter Laboratories
 Division of Roche Products Limited
 PO Box 8
 Welwyn Garden City
 Hertfordshire AL7 3AY



LIBRAXIN*

Presentation Round, yellow-green, film-coated tablets with 'LIBRAXIN' imprinted on one face, containing 5 mg chlordiazepoxide and 2.5 mg clidinium bromide.

Uses Properties: Libraxin combines the anti-anxiety properties of Librium* and the antispasmodic and antisecretory properties of clidinium bromide. Accepted concepts of gastro-intestinal physiology and physiology recognise two important components in gastro-intestinal dysfunction: the emotional factor and the somatic factor. Librium is an effective and well-tolerated drug for the treatment of patients in whom anxiety and tension are contributory or causative factors in a psychosomatic illness. Clidinium bromide is a synthetic anticholinergic agent which has been shown in experimental and clinical studies to have a pronounced antispasmodic and antisecretory effect on the gastro-intestinal tract. Its anticholinergic action appears to be approximately equal to that of atropine but its side-effects are milder and less frequent.

Indications: For the control of hypersecretion, hypermotility and emotional factors associated with gastro-intestinal disorders, such as nervous dyspepsia, peptic ulcer, cardiospasm, pylorospasm, irritable bowel syndrome.

Dosage and administration Adults: 1 or 2 tablets three or four times daily – before meals and at bedtime. The majority of patients, 1 tablet three times daily gives excellent results. In elderly patients it is recommended that the initial dose be 1 tablet twice daily.

Children: No dosage recommendations are made for the administration of Libraxin to children. Libraxin Tablets are for oral administration.

Contra-indications, warnings, etc

Contra-indications: Because of its anticholinergic effects, Libraxin should not be given to patients suffering from glaucoma or prostatic enlargement.

Precautions: With Libraxin, as with other drugs acting on the central nervous system, patients should be cautioned to avoid alcohol while under treatment, since the individual response cannot be foreseen. Like all sedatives of this type, Libraxin may modify patients' reactions (driving ability, operation of machinery, etc) to a varying extent, depending on dosage and individual susceptibility.

The established medical principle of prescribing sedatives in early pregnancy only when absolutely indicated should be observed.

Side-effects: Libraxin is very well tolerated. Minor side-effects are infrequent and are controlled by reduction of dosage. They include drowsiness, muscle weakness, dryness of the mouth, blurring of vision, constipation and hesitancy of micturition.

While blood dyscrasias and jaundice have been reported to have occurred during Librium therapy, evidence is inconclusive that these were related to the administration of Librium.

Effects of overdosage and their treatment: Primary signs and symptoms of overdosage may include drowsiness, confusion, dry mouth, urinary retention, dilated pupils and coma.

Gastric lavage should be performed within a few hours of ingestion, and symptoms treated as they arise. Pilocarpine is an antidote to clidinium overdosage. Noradrenaline may be given to correct hypotension, if it develops, and Valium* Roche or pentobarbitone sodium for severe excitement states.

Pharmaceutical precautions *Storage:* Libraxin Tablets should be stored in well-closed containers. The recommended maximum storage temperature for Libraxin Tablets is 30°C.

Legal category POM.

Package quantities Libraxin Tablets in packings of 100 and 500.

Further information Nil.

Product licence number 0031/5024.

LIBRIUM*

Presentation Capsules with opaque green cap and opaque yellow body marked 'LIBRIUM', containing 5 mg chlordiazepoxide hydrochloride.

Capsules with black cap and opaque green body marked 'LIBRIUM', containing 10 mg chlordiazepoxide hydrochloride.

Round, yellowish-green, film-coated tablets marked 'LIBRIUM', containing 5 mg chlordiazepoxide.

Round, pale green, film-coated tablets marked 'LIBRIUM', containing 10 mg chlordiazepoxide.

Round, deep green, film-coated tablets marked 'LIBRIUM', containing 25 mg chlordiazepoxide.

Ampoules containing 100 mg chlordiazepoxide (in the form of 112 mg chlordiazepoxide hydrochloride) accompanied by ampoules of 2 ml of solvent.

Uses Properties: Librium has tranquillising properties with a specific anxiolytic action. It also possesses muscle-relaxant and anticonvulsant properties.

Indications: Acute and chronic anxiety states and agitation; obsessive-compulsive neuroses and panic states; psychosomatic and organic illness with associated anxiety, e.g. angina pectoris, peptic ulcer, skin disorders; alcoholic psychoses (including delirium tremens); tension headaches; insomnia; nocturnal enuresis; behaviour disorders; musculoskeletal disorders;

spastic conditions; epilepsy (as adjuvant to treatment); premedication.

Dosage and administration *Capsules and Tablets* – *Adults*: Mild anxiety neuroses; anxiety associated with organic disease; neuromuscular spasm – 30 mg daily in divided doses.

Severe anxiety neuroses; phobias; acute agitation; obsessive-compulsive syndrome – 40–100 mg daily in divided doses.

Elderly and debilitated patients – 10 mg daily initially.

Children: 5–20 mg daily in divided doses.

Librium Capsules and Tablets are for oral administration.

Ampoules – *Adults*: Symptomatic relief of acute episodes in the chronic alcoholic (delirium tremens) – 50–100 mg by intramuscular injection, repeated if necessary in two to four hours.

Rapid relief of acute anxiety, phobia or panic reactions – 50–100 mg by intramuscular injection, followed by 25–100 mg three or four times daily if necessary.

Intramuscular injection: Add 2 ml of the special solvent to the contents of one 5 ml dry-filled amber ampoule of Librium hydrochloride sterile powder. Avoid excessive pressure in injecting the solvent into the ampoule containing the Librium as this may cause bubbles to form on the surface of the solution. Agitate gently until completely dissolved. The solution should be prepared immediately before administration and should be colourless to pale yellow when reconstituted. Administer slowly by deep intramuscular injection.

Caution: Librium preparations made with the special solvent should **not** be given intravenously. Do not use the solvent if opalescent or hazy.

Librium ampoules made with the special solvent should not be diluted.

Contra-indications, warnings, etc *Precautions*: Potentiation of alcohol by Librium has not been demonstrated, but with Librium, as with other drugs acting on the central nervous system, patients should be instructed to avoid alcohol while under treatment, since the individual response cannot be foreseen. Like all medicaments of this type, Librium may modify patients reactions (driving ability, operation of machinery, etc) to a varying extent, depending on dosage, administration and individual susceptibility.

The use of high doses of benzodiazepines, especially over prolonged periods, may sometimes lead to dependence, particularly in patients with a history of alcoholism or drug abuse. Treatment in these cases should be withdrawn gradually.

Results obtained in trials with several generations of mice, rats, rabbits and dogs indicate that no danger of teratogenic effects need be expected from therapeutic doses of Librium. Nevertheless, the established medical principle of prescribing medicaments in early pregnancy only when absolutely indicated should be observed.

Side effects: Librium is very well tolerated. Minor side-effects such as ataxia and drowsiness have been reported during early treatment and occur most commonly in elderly or debilitated patients. These can be controlled by reduction of dosage.

While blood dyscrasias and jaundice have been reported to have occurred during Librium therapy, evidence is inconclusive that these were related to the administration of Librium.

Effects of overdosage and their treatment: Reported experience of inadvertent or deliberate overdosage indicates that these present virtually no problem. Dose of up to approximately 2.5 g have produced no long term ill-effects. Drowsiness, ataxia and dysarthria may occur, with coma in severe cases.

Treatment is symptomatic, but gastric lavage may be useful if performed soon after ingestion.

Pharmaceutical precautions *Storage*: Librium Capsules and Tablets should be stored in well-closed containers and protected from light. The recommended maximum storage temperature for Librium Capsules is 30°C and for Librium Tablets is 25°C.

Librium Ampoules should be kept in a refrigerator.

Legal category POM.

Package quantities Librium Tablets 5 mg, 10 mg and 25 mg in packings of 100 and 500.

Librium Capsules 5 mg and 10 mg in packings of 10 and 500.

Librium Ampoules 100 mg accompanied by ampoule with 2 ml solvent in boxes of 10.

Further information Nil.

Product licence numbers

Dry Ampoules 100 mg	0031/5078
Solvent Ampoules	0031/5030
Capsules 5 mg	0031/5025
Capsules 10 mg	0031/5026
Tablets 5 mg	0031/5027
Tablets 10 mg	0031/5028
Tablets 25 mg	0031/5029

LIMBITROL*

Presentation Limbitrol 5 Capsules with opaque green cap and opaque pink body marked 'LIMBITROL' containing 5 mg chlordiazepoxide and 14.15 mg amitriptyline hydrochloride (equivalent to 12.5 mg amitriptyline base).

Limbitrol 10 Capsules with opaque, dark green cap and opaque pink body marked 'LIMBITROL', containing 10 mg chlordiazepoxide and 28.3 mg amitriptyline hydrochloride (equivalent to 25 mg amitriptyline base).

Uses *Properties*: Limbitrol combines the anxiolytic effect of chlordiazepoxide with the antidepressant action of amitriptyline.

Indications: The treatment of the symptoms of depressive illness with associated anxiety.

Dosage and administration *Adults*: It is recommended that patients should be started on one capsule Limbitrol 5 three times daily. If the response is inadequate the dose should be increased to one capsule Limbitrol 10 three times daily.

In more severe cases it may be necessary to initiate treatment with one capsule Limbitrol 10 three times daily. If necessary, dosage may be increased to two capsules three times daily.

Elderly patients: Limbitrol is not for geriatric use.

Children: Limbitrol is not for paediatric use.

Limbitrol Capsules are for oral administration.

Contra-indications, warnings, etc

Contra-indications: Patients with known sensitivity to benzodiazepines; acute pulmonary insufficiency.

Recent myocardial infarction; heart block of any degree; cardiac arrhythmias. Patients with mania, whose condition may be exacerbated by tricyclic antidepressants.

Precautions: In patients with chronic pulmonary insufficiency, and patients with chronic renal or hepatic disease, dosage may need to be modified.

The use of Limbitrol during pregnancy, especially in the first trimester, should be avoided.

The administration of high doses or prolonged administration of low doses of benzodiazepines in the last trimester of pregnancy and during labour has been reported to produce irregularities in the foetal heart, and hypotonia, poor sucking and hypothermia in the neonate.

Tricyclic antidepressants, when administered during the last trimester of pregnancy, have also been associated with adverse effects such as withdrawal symptoms, respiratory depression and agitation in the foetus.

Chlordiazepoxide and amitriptyline may appear in breast milk. Limbitrol should therefore be avoided during lactation.

Because of its anticholinergic effects Limbitrol should not be given to patients suffering from narrow angle glaucoma or symptoms suggestive of prostatic hypertrophy.

Limbitrol should be avoided in patients with a history of epilepsy.

If Limbitrol is combined with centrally-acting drugs such as neuroleptics, tranquillizers, antidepressants, hypnotics, analgesics and anaesthetics, the sedative effects may be intensified.

Patients should be advised that, like all medicaments of this type, Limbitrol may modify patients' performance of skilled tasks (driving, operating machinery, etc.) to a varying degree depending on dosage, administration and individual susceptibility. Patients should further be advised that alcohol may intensify any impairment and should therefore be avoided during treatment.

Anaesthesia given during tricyclic antidepressant therapy may increase the risk of arrhythmias and hypotension. If anaesthesia is necessary, the anaesthetist should be informed that the patient is being treated with imbitrol.

Limbitrol should not be taken with monoamine oxidase inhibitors, or within two weeks of cessation of therapy with monoamine oxidase inhibitors.

Amitriptyline may decrease the antihypertensive effect of adrenergic neurone-blocking drugs such as guanethidine, bethanidine or debrisoquine (Declinax[®]), and possibly also clonidine. It is advisable to review all antihypertensive therapy during treatment with imbitrol.

Limbitrol should not be given with sympathomimetic agents such as adrenaline, ephedrine, isoprenaline, oradrenaline, phenylephrine and phenylpropanolamine.

Barbiturates may decrease and methylphenidate may increase the antidepressant action of amitriptyline.

The possibility of suicide in depressed patients should be borne in mind, and patients should be carefully supervised, especially during the early stages of treatment.

Withdrawal symptoms are known to occur on abrupt cessation of benzodiazepine drugs and amitriptyline when given alone. However, withdrawal symptoms have not been reported after termination of Limbitrol treatment. Nevertheless, following prolonged use, particularly at high dosage, Limbitrol should be withdrawn gradually.

The efficacy and safety of Limbitrol in elderly patients has not been demonstrated.

The fixed dosage of chlordiazepoxide and amitriptyline provided in Limbitrol may not be appropriate for some patients, for whom the alternative of prescribing the two active ingredients separately in the necessary amounts should be considered.

Side-effects: The most common side-effects are drowsiness, dry mouth and dizziness during the first few days of treatment, and anticholinergic effects such as constipation, disturbances of accommodation, tachycardia and hesitancy of micturition, which also usually lessen or disappear with time.

Other adverse effects are rare and include headache, hypotension, gastro-intestinal upsets, skin rashes, tremor, interference with sexual function, and urinary retention. Isolated cases of blood dyscrasias, jaundice, hypomania, convulsions, and peripheral neuropathy have also been reported.

Cardiac arrhythmias and severe hypotension are likely to occur with high dosage and in deliberate overdosage of amitriptyline. They may also occur with normal dosage in patients with pre-existing heart disease.

Psychotic manifestations, including mania and paranoid delusions, may be exacerbated during treatment with tricyclic antidepressants.

Treatment of overdosage: Deaths by deliberate or accidental overdosage of amitriptyline have occurred. Symptoms of amitriptyline overdosage may include drowsiness, stupor and coma; tachycardia and other cardiac arrhythmias including ventricular fibrillation; severe hypotension and congestive cardiac failure; agitation, hyper-reflexia and convulsions; hyperpyrexia, dilated pupils and paralytic ileus.

Symptoms of chlordiazepoxide overdosage may include drowsiness, ataxia and dysarthria, with coma in severe cases.

Treatment is symptomatic and supportive. Gastric lavage should be performed as quickly as possible and followed by the use of activated charcoal. Maintain an open airway and adequate fluid intake. Continuous ECG monitoring is essential; serious cardiac arrhythmias may be treated with neostigmine (Prostigmin[®]), pyridostigmine (Mestinon[®]) or propranolol. Intravenous fluids may be required to maintain the blood pressure. Body temperature should be regulated. Intravenous diazepam (Valium Roche[®]) is recommended for the control of convulsions.

There is no specific antidote to amitriptyline and chlordiazepoxide overdosage but the intravenous administration of physostigmine (1 to 3 mg) has been reported to reverse the symptoms. This dose should be repeated as indicated.

When taken with centrally-depressant drugs, especially alcohol, the effects of overdosage are likely to be more severe.

Pharmaceutical precautions *Storage:* Recommended maximum storage temperature 30°C.

Legal category POM.

Package quantities Limbitrol 5 Capsules in packings of 100 and 500.

Limbitrol 10 Capsules in packings of 100 and 500.

Further information Nil.

Product licence numbers

Limbitrol 5 Capsules 0031/5066R

Limbitrol 10 Capsules 0031/5067R

RIVOTRIL*

Presentation Round, pale orange tablets with 'RIVOTRIL' imprinted on one face and two break bars on the other, containing 0.5 mg clonazepam.

Round, white tablets with 'RIVOTRIL' imprinted on one face and two break bars on the other, containing 2 mg clonazepam.

Ampoules containing 1 mg clonazepam in 1 ml solvent, each accompanied by an ampoule containing 1 ml Water for Injection USP as a diluent. The ampoule solution is colourless.

Uses *Properties:* Rivotril is a benzodiazepine derivative exhibiting marked anticonvulsant properties. These have been demonstrated in the many tests in animals which are employed to establish the anti-epileptic properties of a drug. Animal experiments and electroencephalographic studies in man have shown that Rivotril prevents generalisation of convulsive activity and raises the seizure threshold. In many cases, abnormal electroencephalograms become normal. Rivotril improves both focal seizures and primarily generalised attacks. Administered intravenously, Rivotril quickly controls status epilepticus.

Indications: All clinical forms of epileptic disease and seizures in infants, children or adults, especially: typical or atypical petit mal; generalised primary or secondary tonic-clonic seizures including grand mal; status epilepticus in all clinical forms; focal seizures with elementary or complex symptomatology, various forms of myoclonus and associated abnormal movements.

Dosage and administration *Tablets:* Treatment should be started with low doses. These should not exceed 1 mg/day for adults, 0.5 mg/day for children and 0.25 mg/day for infants and small children. If desired, the total dose may be given at night for the first four days of treatment. The dose may be increased progressively until the maintenance dose suited to the individual patient has been found.

The dosage of Rivotril must be adjusted to the needs of each individual and depends on the age of the patient and the individual response to therapy. The maintenance dosage must be determined according to clinical response and tolerance.

The normal daily dosage for various age groups falls in the following ranges:

Adults	4–8 mg
School children (5–12 years)	3–6 mg
Small children (1–5 years)	1–3 mg
Infants (0–1 year)	0.5–1 mg

These are total daily dosages which should be divided into three or four doses taken at intervals throughout the day. If necessary, larger doses may be given at the discretion of the physician. The maintenance dose should be attained after two to four weeks of treatment.

In some forms of childhood epilepsy, certain patients may cease to be adequately controlled by Rivotril. Control may be re-established by increasing the dose, or interrupting treatment with Rivotril for two to three weeks. During the interruption in therapy careful observation and other drugs may be needed.

Simultaneous administration of more than one anti-epileptic drug is a common practice in the treatment of epilepsy and may be undertaken with Rivotril. The dosage of each drug may be required to be adjusted to obtain the optimum effect. If status epilepticus occurs in

a patient receiving oral R still control the status.

Rivotril Tablets are for

Ampoules: for the treatment dose and rate of administration response of the patient.

Adults: 1 mg (1 ampoule 1 ampoule of diluent) by
Infants and children: 0.5 active substance mixed slow intravenous injection

This dose should be given by slow intravenous

Intravenous injection in vein of the antecubital given slowly – in adult: seconds. This will result hypotension or apnoea or for resuscitation should.

The contents of the Water for Injection USP of the other ampoule, in 1 ml, IMMEDIATELY

Rivotril Ampoule solution in intravenous infusions: customary in the treatment up to 3 mg (3 ampoule solutions is permissible: Dextrose Injection BP 1 and Dextrose Injection 1 2.5% dextrose). This infusion freshly and used within

Rivotril Ampoules are

Maintenance of stable Rivotril Ampoule solution

Contra-indications.

Since alcohol can provoke of therapy, patients should avoid alcohol while under Rivotril, alcohol may not compromise the success: unpredictable side-effects

As a general rule, epileptic drive. Even when adequate should be remembered alteration in timings of reactions, depending on patient is allowed to operate be warned of these possibilities

When Rivotril is used with epileptic drugs, side-effects evident, particularly with combinations include care in adjusting dosage

As with all other anti-epileptic drugs Rivotril must not be abruptly withdrawn by gradual reduction must also be taken while the patient is still on

Although results obtained from studies of rats and rabbits indicate no teratogenic effects need doses of Rivotril, the phases and disadvantages of pregnancy.

Side-effects: The side-effects: drowsiness, somnolence, occu

co-ordination disturbances. Such effects are usually transitory and disappear spontaneously as treatment continues or with dosage reduction. They tend to occur early in treatment and can be greatly reduced, if not avoided, by commencing with low dosages followed by progressive increases.

In infants and small children, and particularly those with a degree of mental impairment. Rivotril may give rise to salivary or bronchial hypersecretion with drooling. Supervision of the airway may be required.

Extensive clinical and laboratory investigations have revealed no significant changes in the blood picture or renal or hepatic function following treatment with Rivotril.

Rivotril may affect the behaviour of epileptic patients. Paradoxical effects such as aggressiveness, irritability or agitation have been reported as well as grand mal or stimulation of a new type of seizure. Conversely, improvement in behaviour may be observed in some patients suffering from certain behavioural forms of epilepsy.

Effects of overdosage and their treatment: As with other benzodiazepine drugs, overdosage should not present undue problems of management or threat to life. Patients have recovered from overdoses in excess of 60 mg without special treatment. Severe somnolence with muscle hypotonia will be present. Treatment is symptomatic and may include the need to maintain an airway. Gastric lavage may be useful if performed soon after ingestion.

harmaceutical precautions *Storage:* Rivotril Tablets should be stored in well-closed containers, in a cool place. Rivotril Tablets and Ampoules should be protected from light.

Legal category POM.

Package quantities Rivotril Tablets 0.5 mg in packages of 100 and 500.

Rivotril Tablets 2 mg in packages of 100 and 500.

Rivotril Ampoules 1 mg in packages of 10, accompanied by 1 ml ampoules Water for Injection USP as solvent.

Further information Nil.

Product licence numbers

Tablets 0.5 mg 0031/0076

Tablets 2 mg 0031/0077

Ampoules 1 mg 0031/0078

OHYPNOL* ▼

Presentation A purple film-coated, bi-convex diamond-shaped tablet with a single break bar on one side and 'ROHYPNOL' on the other side, containing 1 mg of nitrazepam.

Uses *Properties:* Rohypnol is a benzodiazepine compound with hypnotic properties.

Indications: The short-term treatment of sleep disturbances, particularly in patients who have difficulty in falling asleep.

The induction of sleep at unusual times on a short-term or irregular basis.

Dosage and administration *Adults:* 0.5–1 mg before retiring.

Adults with severe sleep disturbances: 1–2 mg.

Elderly or debilitated patients: It is recommended that the initial dose to be taken before retiring should not exceed 0.5 mg; tolerability at this dosage level is excellent. In exceptional cases, where the hypnotic effect is less than adequate but tolerability is satisfactory, the dose may be increased to 1 mg.

Rohypnol tablets are not for paediatric use.

Rohypnol tablets are for oral administration.

Contra-indications, warnings, etc

Contra-indications: Patients with known sensitivity to benzodiazepines; acute pulmonary insufficiency; respiratory depression.

Precautions: In patients with chronic pulmonary insufficiency, and in patients with chronic renal or hepatic disease, dosage may need to be reduced.

The use of Rohypnol during pregnancy should be avoided.

The administration of high doses or prolonged administration of low doses of benzodiazepines in the last trimester of pregnancy or during labour has been reported to produce irregularities in the foetal heart, and hypotonia, poor sucking and hypothermia in the neonate.

Rohypnol has been detected in breast milk. If possible, the use of Rohypnol should be avoided during lactation.

If Rohypnol is combined with centrally-acting drugs such as neuroleptics, tranquilizers, antidepressants, hypnotics, analgesics and anaesthetics, the sedative effects may be intensified.

Patients should be advised that, like all medicaments of this type, Rohypnol may modify patients' performance at skilled tasks (driving, operating machinery, etc.) to a varying degree depending upon dosage and individual susceptibility. Patients should further be advised that alcohol may intensify any impairment and should, therefore, be avoided during treatment.

The dependence potential of the benzodiazepines is low but this increases when high doses are used, especially when given over long periods. This is particularly so in patients with a history of alcoholism or drug abuse or in patients with marked personality disorders. Regular monitoring in such patients is essential; routine repeat prescriptions should be avoided and treatment should be withdrawn gradually. Symptoms such as depression, nervousness, rebound insomnia, irritability, sweating, and diarrhoea have been reported following abrupt cessation of treatment with normal therapeutic doses.

In rare instances, withdrawal following excessive dosages may produce confusional states, psychotic manifestations and convulsions.

Abnormal psychological reactions to benzodiazepines have been reported. Rare behavioural effects include paradoxical aggressive outbursts, excitement, confusion and the uncovering of depression with suicidal tendencies.

Side-effects: Adverse effects include drowsiness, unsteadiness and ataxia; these are dose-related and are likely to be uncommon with the recommended dosage. The elderly are particularly sensitive to the effects of central depressant drugs and may experience confusion. If organic brain changes are present, the dosage of Rohypnol should not exceed 0.5 mg in these patients.

Other adverse effects are less common and include headache, vertigo, hypotension, gastro-intestinal upsets, skin rashes, visual disturbances, changes in libido, and urinary retention. Isolated cases of blood dyscrasias and jaundice have also been reported.

Treatment of overdosage: When taken alone in overdosage Rohypnol presents few problems in management. Signs may include drowsiness, ataxia, and dysarthria, with coma in severe cases. Treatment is symptomatic. Gastric lavage is useful only if performed soon after ingestion. There is no specific antidote to Rohypnol.

When taken with centrally acting drugs, especially alcohol, the effects of overdosage are likely to be more severe and, in the absence of supportive measures, may prove fatal.

Pharmaceutical precautions *Storage:* Rohypnol tablets should be stored in a dry place.

Legal category POM.

Package quantities Rohypnol tablets 1 mg are blister-packed in packings of 100.

Further information The distribution half-life of flunitrazepam is about three hours; the elimination half-life is, on average, 22 hours.

The onset of effect is rapid and the duration of effect is dose-dependent.

Treatment should be kept to a minimum and given only under close medical supervision. Little is known regarding the efficacy or safety of benzodiazepines in long-term use.

Product licence number 0031/0104.

ROSCORBIC*

Presentation Round, white tablets with $\frac{C}{25}$ imprinted on one face, containing 25 mg ascorbic acid.

Round, white tablets with $\frac{C}{50}$ imprinted on one face, containing 50 mg ascorbic acid.

Round, white tablets with $\frac{C}{200}$ imprinted on one face, containing 200 mg ascorbic acid.

Round, white tablets with $\frac{C}{500}$ imprinted on one face, containing 500 mg ascorbic acid.

Round, white, effervescent tablets, diameter 25 mm with no superficial markings, containing 1 g ascorbic acid.

Uses *Properties:* Roscorbic is a synthetic vitamin C preparation. The most clearly established function of vitamin C in the body is the control of the formation of colloidal intercellular substances.

Deficiency of vitamin C leads to scurvy. In the absence of the vitamin a typical nutritional anaemia develops; the vitamin acts directly on the blood-forming centres and is essential for the maturation of the red blood cells.

Indications: Vitamin C is specific in the treatment of scurvy.

It has been proved useful as an adjunct to the treatment of: wounds and fractures; corneal ulcers; infectious rheumatic conditions; anaemia.

Dosage and administration

Adults:

Scurvy	0.5 to 1 g two or three times daily
Infections, rheumatic conditions, wound healing, fractures	1 g two or three times daily after meals
All other indications	200 to 500 mg daily

Children:

Over 12 years	three-quarters adult dose
4 to 12 years	half adult dose
Under 4 years	one-quarter adult dose

Roscorbic effervescent 1 g tablets are particularly suitable for the administration of large doses. They should be dissolved in a tumbler of water immediately before use.

Roscorbic tablets are for oral administration.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions *Storage:* The recommended maximum storage temperature for Roscorbic 25 mg, 50 mg, 200 mg and 500 mg is 25°C; the tablets should be protected from moisture and light. The recommended maximum storage temperature for Roscorbic effervescent 1 g tablets is 30°C; the effervescent tablets should be protected from moisture.

Legal category P.

Package quantities

Roscorbic 25 mg tablets in packings of 200.
 Roscorbic 50 mg tablets in packings of 100 and 500.
 Roscorbic 200 mg tablets in packings of 100.
 Roscorbic 500 mg tablets in packings of 50.
 Roscorbic effervescent tablets 1 g in packings of 10.

Further information Nil.

Product licence numbers

Tablets 25 mg	0031/5088
Tablets 50 mg	0031/5089
Tablets 200 mg	0031/5090
Tablets 500 mg	0031/5091
Effervescent tablets 1 g	0031/0067

* *Trade Mark*

Schering Pharmaceuticals

Division of Schering Chemicals Limited
The Brow, Burgess Hill
West Sussex RH15 9NE



MINOVLAR* 21 MINOVLAR* 21 MINOVLAR* MINOVLAR* ED

Representation *Anovlar 21*: Each green, sugar-coated tablet bears a printed white A in a white regular hexagon on both sides, and contains 4 mg norethisterone acetate and 0.05 mg ethinyloestradiol.

Minovlar 21: Each pink, sugar-coated tablet contains 4 mg norethisterone acetate and 0.05 mg ethinyloestradiol.

Minovlar: Each ochre, sugar-coated tablet bears a printed black A in a black regular hexagon on both sides, and contains 1 mg norethisterone acetate and 0.05 mg ethinyloestradiol.

Minovlar ED: 21 Minovlar tablets plus 7 inactive bridging tablets.

Uses Oral contraception and the recognised gynaecological indications for such oestrogen-progestogen combinations. The mode of action includes the inhibition of ovulation by suppression of the mid-cycle surge of oestrogen hormone, the inspissation of cervical mucus so as to constitute a barrier to sperm, and the rendering of the endometrium unreceptive to implantation.

Dosage and administration *Anovlar 21*, *Gynovlar 21* and *Minovlar*.

First treatment cycle: 1 tablet daily for 21 days, starting on the fifth day of the menstrual cycle (the first day of menstruation counting as day 1). In the first cycle only, an additional form of contraception (except the rhythm, temperature or cervical-mucus methods) must be used for the first 14 days of tablet-taking.

Subsequent cycles: Each subsequent course is started after seven tablet-free days have followed the preceding course.

Minovlar ED: **First treatment cycle**: 1 tablet daily for 28 days, starting in the red sector on the first day of bleeding, the starting tablet being the one marked with the appropriate day of the week.

Subsequent cycles: Each subsequent course is started on the red sector on the day after the previous one has been finished. Pack, therefore, follows pack without interval. In the first cycle only, an additional form of contraception (except the rhythm, temperature or cervical-mucus methods) must be used for the first 14 days of tablet-taking.

Changing from high-dosed to low-dosed preparations: Additional (non-hormonal) precautions, other than the rhythm, temperature or cervical-mucus methods, should also be used for the first 14 days when changing product.

Post-partum and post-abortion use: After pregnancy oral contraception is usually started as soon as spontaneous menstruation has been resumed. However, oral

contraception can be started within 7–12 days of a vaginal delivery, provided that the patient is fully ambulant and there are no puerperal complications. Starting within 12 days of delivery obviates additional contraceptive precautions. After a first-trimester abortion, oral contraception may be started immediately.

Special circumstances requiring additional contraception: Incorrect administration: If a tablet is delayed, it should be taken as soon as possible, and if it is taken within 12 hours of the correct time additional contraception is not needed. Further tablets should then be taken at the usual time. However, if the delay exceeds 12 hours, ovulation may occur. In those circumstances, any tablet or tablets delayed more than 12 hours should be omitted, the remaining tablets should be taken on the correct days at the usual time, and extra precautions (except the rhythm, temperature and cervical-mucus methods) should be used until the next withdrawal bleed.

Gastro-intestinal upset: Vomiting or diarrhoea may reduce the effectiveness of the tablets by preventing them from being fully absorbed. Therefore, it is advisable that an additional method of contraception be used throughout the remainder of the course concerned. Mild laxatives do not impair contraceptive action.

Interaction with other drugs: Some drugs accelerate the metabolism of oral contraceptives taken concurrently. Drugs suspected of having the capacity to reduce the efficacy of oral contraceptives include barbiturates, phenylbutazone, phenytoin, rifampicin, ampicillin and other antibiotics. It is, therefore, advisable to use non-hormonal methods of contraception (except the rhythm, temperature or cervical-mucus methods) in addition to the oral contraceptive as long as an extremely high degree of protection must be provided during treatment with such drugs.

Contra-indications, warnings, etc

Contra-indications: Pregnancy. Thrombotic disorders and a history of these conditions, sickle-cell anaemia, disorders of lipid metabolism and other conditions in which, in individual cases, there is known or suspected to be a much increased risk of thrombosis. Acute or severe chronic liver diseases. Dubin-Johnson syndrome. Rotor syndrome. History, during pregnancy, of idiopathic jaundice or severe pruritus. History of herpes gestationis. Mammary or endometrial carcinoma, or a history of these conditions. Abnormal vaginal bleeding of unknown cause. Deterioration of otosclerosis during pregnancy.

Warnings: There is a general opinion, based on statistical evidence, that users of combined oral contraceptives experience, more often than non-users, venous thromboembolism, arterial thrombosis, including cerebral and myocardial infarction, and subarachnoid haemorrhage. Full recovery from such disorders does not always occur, and it should be realised that in a few cases they are fatal. How often these disorders occur in users of the modern low-dose pills is not known, but there are

reasons for suggesting that they may occur less often than with older pills.

Certain factors may entail some risk of thrombosis, e.g. smoking, obesity, varicose veins, cardiovascular diseases, diabetes and migraine. The suitability of a combined oral contraceptive should be judged according to the severity of such conditions in the individual case, and should be discussed with the patient before she decides to take it. The risk of arterial thrombosis associated with oral contraceptives increases with age, and this risk is aggravated by cigarette-smoking. The use of combined oral contraceptives by women in the older age-group, especially those who are cigarette-smokers should therefore be discouraged, and alternative methods advised.

The possibility cannot be ruled out that certain chronic diseases may occasionally deteriorate during the use of combined oral contraceptives (see 'Precautions'). Hepatic tumours have been reported very rarely in women taking combined oral contraceptives, generally for a protracted period of time. A hepatic tumour should be considered in the differential diagnosis when upper abdominal pain, enlarged liver or signs of intra-abdominal haemorrhage occur.

Reasons for stopping oral contraception immediately: Occurrence of migraine in patients who have never previously suffered from it. Exacerbation of pre-existing migraine. Any unusually frequent or unusually severe headaches. Any kind of acute disturbance of vision. Suspicion of thrombosis or infarction. Six weeks before elective operations and during immobilisation, e.g. after accidents, etc. Significant rise in blood-pressure. Jaundice. Clear exacerbation of conditions known to be capable of deteriorating during oral contraception or pregnancy. Pregnancy is a reason for stopping immediately because it has been suggested by some investigations that oral contraceptives taken in early pregnancy may slightly increase the risk of foetal malformations. Other investigations have failed to support these findings. The possibility therefore cannot be excluded, but it is certain that if a risk exists at all, it is very small.

Precautions: Examination of the pelvic organs, breasts and blood-pressure should precede the prescribing of any combined oral contraceptive, and should be repeated regularly. Before starting treatment, pregnancy must be excluded.

The following conditions required careful consideration: a history of severe depressive states, varicose veins, diabetes, hypertension, epilepsy, otosclerosis, multiple sclerosis, porphyria, tetany, disturbed liver function, gallstones, cardiovascular diseases, renal diseases, chloasma, uterine fibroids, asthma, the wearing of contact lenses, or any disease that is prone to worsen during pregnancy. The first appearance or deterioration of any of these conditions may indicate that the oral contraceptive should be stopped.

The risk of the deterioration of chloasma, which is often not fully reversible, is reduced by the avoidance of excessive exposure to sunlight.

Side-effects: Occasional side-effects may include nausea, vomiting, headaches, breast tension, changed body weight or libido, depressive moods and chloasma.

Menstrual changes:

1. **Reduction of menstrual flow:** This is not abnormal and it is to be expected in some patients. Indeed, it may be beneficial where heavy periods were previously experienced.

2. **Missed menstruation:** Occasionally, withdrawal bleeding may not occur at all. If the tablets have been taken correctly, pregnancy is very unlikely, but should be ruled out before a new course of tablets is started.

Intermenstrual bleeding: Very light 'spotting' or heavy 'breakthrough bleeding' may occur during tablet-taking, especially in the first few cycles. It appears to be generally of no significance, except where it indicates errors of tablet-taking, or where the possibility of interaction with other drugs exists (q.v.). However, if irregular bleeding is persistent, an organic cause should be considered.

Effect on adrenal and thyroid glands: Oral contraceptives have no significant influence on adrenocortical function. The ACTH function test for the adrenal cortex remains unchanged. The reduction in corticosteroid excretion and the elevation of plasma corticosteroids are due to a increased cortisol-binding capacity of the plasma proteins.

The response to metyrapone is less pronounced than in untreated women and is thus similar to that during pregnancy.

The radio-iodine uptake shows that thyroid function is unchanged. There is a rise in serum protein-bound iodine, similar to that in pregnancy and during the administration of oestrogens. This is due to the increased capacity of the plasma proteins for binding thyroid hormones, rather than to any change in glandular function. In women taking oral contraceptives, the content of protein-bound iodine in blood serum should therefore, not be used for evaluation of thyroid function.

Effect on blood chemistry: Oral contraceptives may accelerate erythrocyte sedimentation in the absence of any disease. This effect is due to a change in the proportion of the plasma protein fractions. Increases in plasma copper, iron and alkaline phosphatase have also been recorded.

Overdosage: There have been no reports of serious ill effects from overdosage, even when a considerable number of tablets have been taken by a small child. In general, it is, therefore, unnecessary to treat overdosage. However, if overdosage is discovered within two or three hours and is so large that treatment seems desirable, gastric lavage can be safely used.

There are no specific antidotes and further treatment should be symptomatic.

Pharmaceutical precautions Store in cool, dry conditions: shelf-life five years.

Legal category POM.

Package quantities All Schering combined oral contraceptives are available in packs containing on months' supply.

Further information Nil.

Product licence numbers

Anovlar 21	0053/5019
Gynovlar 21	0053/5000
Minovlar	0053/5010
Minovlar ED	0053/5016

BILIGRAM®

Presentation *Biligram* is a 35% w/v aqueous solution of ioglycamide (meglumine ioglycamate), with an iodine content of 176 mg/ml.

Biligram for infusion is a 17% aqueous solution of

glycamide (meglumine ioglycamate), with an iodine content of 85 mg/ml.

uses Cholegraphy, infusion cholegraphy.

Intravenous cholegraphy should be performed as the first examination only when there is strong evidence of disease involving the biliary tract. In all other cases for diagnosis—especially in obscure upper abdominal complaints—oral cholegraphy (Biloptin, Solu-Biloptin) is to be preferred.

usage and administration The infusion should always be started at a low rate and then increased to the usual higher rate after three to five minutes. This technique induces heterotopic excretion and improves the clearance.

dosage

Adults: *Injection* 30 ml Biligram ensures optimum contrast for normal to overweight adults. Injection time not less than 5 minutes.

Infusion: One 100 ml bottle. Infusion time not less than 30 min.

Children aged 12 years and over:

Injection: 0.4 ml/kg body weight. Injection time not less than 10 minutes.

Infusion: 0.8–1.0 ml/kg body weight. Infusion time one or two every two seconds.

Children aged under 12 years:

Injection: (2 months–1 yr) 0.8 ml/kg body weight. (1–5 yrs) 0.6 ml/kg body weight. (6–11 yrs) 0.45 ml/kg body weight. Injection time: not less than 10 minutes.

contra-indications, warnings, etc

contra-indications: Severe cardiovascular insufficiency, particularly right ventricular failure. Proven or suspected hypersensitivity to iodine-containing contrast media. Manifest thyrotoxicosis. Severe functional disturbance of the liver or kidneys. Monoclonal IgM gammopathy (e.g. macroglobulinaemia (Waldenström's disease)).

warnings/side-effects: In patients with multiple myeloma, other severe diseases, poor general health or thyroid hyperfunction, the need for examination merits particularly careful consideration. This applies to patients with a history of allergy (e.g. bronchial asthma, endogenous eczema), since experience has shown that they may exhibit hypersensitivity to drugs. Pre-testing does not give a reliable warning of allergic reactions to iodine-containing contrast media. Some radiologists give an antihistamine or a corticoid prophylactically to patients with a history of allergy. Because of the possibility of precipitation, contrast medium and prophylactic agents must not be administered mixed together.

Since radiation should, if possible, be avoided during pregnancy, and moreover it has not yet been demonstrated whether it is safe to use Biligram in pregnant patients, Biligram should be administered during pregnancy only if the doctor regards the examination as essential.

Thyroid hyperfunction can increase for some time after administration of biliary contrast media.

If iodine isotopes are to be administered for diagnosing thyroid disease, it should be borne in mind that the capacity of the thyroid tissue to take up iodine will be reduced for eight to ten weeks or more by iodinated biliary contrast media.

Some investigators have reported temporary and reversible changes in liver-function tests after Biligram. These changes are not thought to reflect liver damage.

The opinion has been expressed that intravenous

cholegraphy should not be performed immediately after negative oral cholegraphy. A large number of radiologists do not share this view – provided that the patient is adequately hydrated and renal function is not impaired.

The patient should be recumbent during the administration of Biligram. Thereafter, the patient must be kept under close observation for at least 15 minutes, since about 90% of all severe incidents occur within that time, and must not be left unsupervised until the end of the examination. If the administration does not take place on the X-ray table, any patient with a labile circulation should be brought to the X-ray machine sitting or lying down. Inadvertent paravenous administration of Biligram can cause pain, but experience has shown that it is very rarely followed by serious tissue reactions. A local anaesthetic helps to relieve the pain. With more extensive paravenous infiltration, it is recommended that a hyaluronidase preparation be injected into the affected area to hasten absorption.

The greater the rate of administration of Biligram, the higher the incidence of common side-effects, such as an unpleasant taste, nausea, vomiting or a sensation of heat. These side-effects are rare if the recommended rate of administration is adhered to. Too rapid an administration may put the patient's life at risk – particularly if he has cardiovascular damage, whether manifest or not, or if his general condition is poor. Each bottle of Biligram for infusion should be used for one investigation only, and any remaining medium should be discarded.

Particular caution should be exercised in allergic patients who have previously tolerated injectable iodine-containing contrast media without any complication, since they may have become sensitised to these substances. As with any contrast medium, the possibility of hypersensitivity must always be considered. If marked side-effects or suspected allergic reactions occur during infusion or injection and persist or even worsen when the administration is interrupted, it is probable that the patient has such a hypersensitivity. Therefore, the investigation must be abandoned. The needle or cannula should be left in the vein for some time in order to maintain access for intravenous therapy. Even relatively minor symptoms, such as itching of the skin, sneezing, violent yawns, tickling in the throat, hoarseness or attacks or coughing may be early signs of a severe reaction and, therefore, merit careful attention.

Very rarely, severe or even life-threatening incidents, such as severe hypotension and collapse, circulatory failure, ventricular fibrillation, cardiac arrest, pulmonary oedema, anaphylactic shock or other allergic manifestations, convulsions or other cerebral symptoms may occur.

At present there is no clinical test that is suitable for predicting an incident. It must be emphasised that every use of a contrast medium therefore entails a certain risk and requires appropriate precautions. Ready availability of all drugs and equipment for emergency treatment and familiarity with the various procedures are prerequisites for the effective management of contrast-medium incidents.

Some guidance in the treatment of such incidents is contained in the leaflet supplied with the pack.

Pharmaceutical precautions Storage: Protect from light and heat. Shelf-life five years.

Legal category POM.

Package quantities

<i>Biligram</i>	Packs of 5 × 30 ml ampoules
<i>Biligram for infusion</i>	Packs of 5 × 100 ml vials

Pharmaceutical precautions

Storage: Protect from light and heat.

Shelf-life: Five years.

Legal category POM.

Package quantities *Biliscopin*: Packs of 10 × 30 ml ampoules. *Biliscopin for infusion*: Packs of 10 × 100 ml infusion bottles.

Further information Nil.

Product licence numbers

iliscopin 0053/0109

iliscopin for infusion 0053/0110

ILOPTIN* AND SOLU-BILOPTIN*

Presentation *Biloptin*: Capsules of sodium iopodate. *Biloptin* capsules, containing a total 1.84 g iodine in g of sodium iopodate.

Solu-Biloptin: Sachets, each containing 1.85 g iodine in g of calcium iopodate.

Uses Oral contrast media for cholecystography andolangiography.

Dosage and administration See table below.

Routine cholecystography

<i>Solu-Biloptin</i>	<i>Biloptin</i>
Other media should be taken after the last meal on the evening before the examination.	
Adults	
The contents of 1 sachet.	6 capsules
Children:	
Under 4 yrs or under 20 kg	<i>Solu-Biloptin</i> is
body weight 0.30 g of	recommended.
powder/kg body	
weight.	
Over 4 yrs or over 20 kg	
body weight 0.15 g of	
powder/kg body	
weight.	
 neonates and infants:	
Ilgam is recommended but a trial by the oral route, may be undertaken using 0.45 g of <i>Solu-Biloptin</i> powder/kg body weight.	
The results are improved if an enema is given on the evening preceding and another immediately before the examination.	

Other examination techniques in adults only

<i>iloptin</i>	<i>Solu-Biloptin</i>
rapid cholecystography	
capsules or double dose of 12 capsules.	The contents of 1 sachet or double dose of 2 sachets.
olangiography	
2 capsules	The contents of 2 sachets.
ractionated oral cholecystography	
capsules 10–12 hrs before the examination and another 6 capsules 3 hrs before the examination.	The contents of 1 sachet 10–12 hrs before the examination and another 1 sachet 3 hrs before the examination.

Contra-indications, warnings, etc

Contra-indications: Proven or suspected hypersensitivity to iodine-containing contrast media. Thyrotoxicosis. Severe impairment of hepatic or renal function.

Warnings/side-effects: *Biloptin* and *Solu-Biloptin* are well tolerated and side-effects, even of a trivial nature, are extraordinarily rare. Sensitive patients may occasionally complain of mild sensations of pressure in the stomach or nausea. Attacks of diarrhoea and vomiting are exceptional. Very few cases of urticaria have been observed.

If iodine isotopes are to be administered for diagnosing thyroid disease, it should be borne in mind that the capacity of the thyroid tissue to take up iodine will be reduced for 8–10 weeks or more by iodinated biliary X-ray contrast media.

Apart from the fact that X-ray examinations should if possible, be avoided during pregnancy, it must be pointed out that it has not yet been proved beyond question that *Biloptin* may be used without hesitation in pregnant patients. Therefore, such an examination with a contrast medium during pregnancy should be carried out only if considered absolutely necessary by the physician.

Pharmaceutical precautions **Storage:** cool, dry conditions. Shelf-life five years.

Legal category P.

Package quantities

Biloptin capsules. 0.5 g 20 × 6

Solu-Biloptin sachets. 3 g × 20

Further information Nil.

Product licence numbers

Biloptin 0053/5048

Solu-Biloptin 0053/5049

CONTROVLAR*

Presentation Each pink, sugar-coated tablet contains 3 mg norethisterone acetate and 0.05 mg ethinyl-oestradiol.

Uses *Controvlar* inhibits ovulation, which is of value in the treatment of dysmenorrhoea, since anovulatory cycles are almost always painless. Mittelschmerz is also prevented by the suppression of ovulation. *Controvlar* prevents the oestrogenic overstimulation that is responsible for menorrhagia, metropathia haemorrhagica and the symptoms of endometriosis. It imposes a regular cycle of bleeding and is, therefore, suitable for the treatment of menstrual irregularities, i.e. polymenorrhoea and oligomenorrhoea.

Dosage and administration **First treatment cycle:** One tablet daily for 21 days, starting on the fifth day of the menstrual cycle (the first day of menstruation counting as day 1).

Subsequent cycles: Each subsequent course is started after seven tablet-free days have followed the preceding course, irrespective of the menstrual pattern, with the proviso that, if no bleeding occurs at all, pregnancy should be excluded before treatment is resumed.

Contra-indications, warnings, etc

Contra-indications: Pregnancy. Thrombotic disorders and a history of these conditions, sickle-cell anaemia, disorders of lipid metabolism and other conditions in which, in individual cases, there is known or suspected

to be a much increased risk of thrombosis. Acute or severe chronic liver disease. Dubin-Johnson syndrome. Rotor syndrome. History, during pregnancy of idiopathic jaundice or severe pruritus. History of herpes gestationis. Mammary or endometrial carcinoma, or a history of these conditions. Deterioration of otosclerosis during pregnancy.

Warnings: There is a general opinion, based on statistical evidence, that users of this type of oestrogen-progestogen combination experience, more often than non-users, venous thromboembolism, arterial thrombosis, including cerebral and myocardial infarction, and subarachnoid haemorrhage. Full recovery from such disorders does not always occur, and it should be realised that in a few cases they are fatal.

Certain conditions may entail some risk of thrombosis, e.g. smoking, obesity, varicose veins, cardiovascular diseases, diabetes and migraine. The advisability of prescribing Controvar should be judged according to the severity of such conditions in the individual case and should be discussed with the patient.

The possibility cannot be ruled out that certain chronic diseases may occasionally deteriorate during the use of Controvar (see 'Precautions').

Hepatic tumours have been reported very rarely in women taking oestrogen-progestogen combinations of this type, generally for a protracted period of time. A hepatic tumour should be considered in the differential diagnosis when upper abdominal pain, enlarged liver or signs of intra-abdominal haemorrhage occur.

Reasons for stopping Controvar immediately: Occurrence of migraine in patients who have never previously suffered from it. Exacerbation of pre-existing migraine. Any unusually frequent or unusually severe headaches. Any kind of acute disturbance of vision. Suspicion of thrombosis or infarction. Six weeks before elective operations and during immobilisation, e.g. after accidents, etc. Significant rise in blood pressure. Jaundice. Clear exacerbation of conditions known to be capable of deteriorating during oral contraception or pregnancy. Pregnancy is a reason for stopping Controvar immediately because it has been suggested by some investigations that oestrogen-progestogen combinations taken in early pregnancy may slightly increase the risk of foetal malformations. Other investigations have failed to support these findings. The possibility therefore cannot be excluded, but it is certain that, if a risk exists at all, it is very small.

Precautions: Examination of the pelvic organs, breasts and blood-pressure should precede the prescribing of Controvar, and should be repeated regularly. Before starting treatment, pregnancy must be excluded.

The following conditions require careful consideration: a history of severe depressive states, varicose veins, diabetes, hypertension, epilepsy, otosclerosis, multiple sclerosis, porphyria, tetany, disturbed liver function, gallstones, cardiovascular diseases, renal diseases, chloasma, uterine fibroids, asthma, the wearing of contact lenses, or any disease that is prone to worsen during pregnancy. The first appearance or deterioration of any of these conditions may indicate that Controvar should be stopped. The risk of the deterioration of chloasma, which is often not fully reversible, is reduced by the avoidance of excessive exposure to sunlight.

Side-effects: Occasional side-effects may include: nausea, vomiting, headaches, breast tension, changed body weight or libido, depressive moods and chloasma.

Effect on adrenal and thyroid glands: Controvar has no significant influence on adrenocortical function. The ACTH function test for the adrenal cortex remain unchanged. The reduction in corticosteroid excretion and the elevation of plasma corticosteroids are due to an increased cortisol-binding capacity of the plasma proteins.

The response to metyrapone is less pronounced than in untreated women and is thus similar to that during pregnancy.

The radio-iodine uptake shows that thyroid function is unchanged. There is a rise in serum protein-bound iodine, similar to that in pregnancy and during the administration of oestrogens. This is due to the increased capacity of the plasma proteins for binding thyroid hormones, rather than to any change in glandular function. In women taking Controvar, the content of protein-bound iodine in blood serum should, therefore not be used for the evaluation of thyroid function.

Effect on blood chemistry: Controvar may accelerate erythrocyte sedimentation in the absence of any disease. This effect is due to a change in the proportion of the plasma protein fractions. Increases in plasma copper and alkaline phosphatase have also been recorded.

Overdosage: There have been no reports of serious ill effects from overdosage, even when a considerable number of tablets have been taken by a small child. In general, it is, therefore, unnecessary to treat overdosage. However, if overdosage is discovered within two or three hours and is so large that treatment seems desirable, gastric lavage can be safely used. There are no specific antidotes and further treatment should be symptomatic.

Pharmaceutical precautions Store in cool, dry conditions; shelf-life five years.

Legal category POM.

Package quantities 21 tablets.

Further information Nil.

Product licence number 0053/5014.

CYCLO-PROGYNOVA* 1 mg CYCLO-PROGYNOVA* 2 mg

Presentation *Cyclo-Progynova 1 mg:* The circular memo-pack holds 11 beige tablets, each containing 1 mg oestradiol valerate, and 10 light-brown tablets each containing 1 mg oestradiol valerate and 0.25 mg levonorgestrel. All tablets have a lustrous, sugar coating and bear a black B in a black regular hexagon printed on both sides.

Cyclo-Progynova 2 mg: The circular memo-pack holds 11 white tablets, each containing 2 mg oestradiol valerate, and 10 pale brown tablets, each containing 2 mg oestradiol valerate and 0.5 mg norgestrel. All tablets have a lustrous, sugar coating and bear a red B in a red regular hexagon printed on both sides.

Uses The treatment of the climacteric syndrome. The prophylaxis and treatment of the postmenopausal sequelae of oestrogen withdrawal, e.g. osteoporosis and senile vaginitis.

Cyclo-Progynova 1 mg and Cyclo-Progynova 2 mg are designed to provide hormone replacement therapy during and after the climacteric. The addition of progestogen in the second half of each course helps provide good control of the irregular cycles that a

characteristic of the premenopausal phase and opposes the production of endometrial hyperplasia. Whilst natural hormone production is little affected, Cyclo-Progynova 1 mg and Cyclo-Progynova 2 mg abolish or improve the characteristic symptoms of the climacteric such as hot flashes, sweating attacks and sleep disorders. Cyclo-Progynova 1 mg and Cyclo-Progynova 2 mg do not consistently inhibit ovulation and are therefore suitable for contraception.

Dosage and administration If the patient is still menstruating freely, treatment should begin on the 5th day of menstruation. Patients whose periods are very frequent or who are postmenopausal may start at any time, provided pregnancy has been excluded (see precautions and special information). Initial treatment should be with Cyclo-Progynova 1 mg. One beige tablet is taken daily for 11 days, followed by one light-brown tablet daily for 10 days. An interval of seven days follows, during which bleeding will normally occur. Cyclo-Progynova 2 mg should be substituted if the control of climacteric symptoms or dysfunctional bleeding is not fully achieved at the lower dosage. One white tablet is taken daily for 11 days, followed by one pale brown tablet for 10 days. An interval of seven days again follows, during which bleeding is to be expected.

When symptoms have been controlled, Cyclo-Progynova 1 mg will usually suffice for maintenance, but it could be borne in mind that the appropriate dosage will be determined by the rate of metabolism of Cyclo-Progynova, rather than by the initial severity of the symptoms.

Contra-indications, warnings, etc

Contra-indications: Pregnancy, (see Precautions and special information) severe disturbances of liver function, jaundice or general pruritus during a previous pregnancy, rubin-Johnson syndrome, Rotor syndrome, existing or previous thromboembolic processes, sickle-cell anaemia, suspected or existing hormone-dependent disorders, tumours of the uterus and breast, congenital disturbances of lipid metabolism, a history of herpes gestationis, sclerosis with deterioration in previous pregnancies.

Warnings/side-effects: Hormonal contraception should be stopped when Cyclo-Progynova is started and the patient should be advised to take non-hormonal contraceptive precautions. The following symptoms have been reported during treatment: anxiety, increased appetite, bloating, breast symptoms, cardiac symptoms, depression, dizziness, dyspepsia, leg pains and swelling, altered libido, nausea, rashes, vomiting and altered weight.

Some women are predisposed to cholestasis during steroid therapy.

Diseases that are known to be subject to deterioration during pregnancy (e.g. multiple sclerosis, epilepsy, diabetes, hypertension, porphyria, tetany and osteoporosis) should be carefully observed during treatment.

Precautions and special information: Before starting treatment, pregnancy must be excluded. If withdrawal bleeding fails to occur at about 28-day intervals, treatment should be stopped until pregnancy has been ruled out.

Treatment should be stopped at once if migrainous or frequent and unusually severe headaches occur for the first time, or if there are other symptoms that are possible prodromata of vascular occlusion.

Treatment should also be stopped if trauma, illness or

impending surgery is considered to entail a risk of thrombosis.

Treatment should be stopped at once if jaundice or pregnancy occurs, or if there is a significant rise in blood-pressure.

In patients with mild chronic liver disease, liver function should be checked every 8–12 weeks.

Examination of the pelvic organs, endometrium, breasts and blood-pressure is advised before and periodically during treatment with Cyclo-Progynova.

Irregular bleeding during tablet-taking should be investigated.

Prolonged exposure to unopposed oestrogens may increase the risk of development of endometrial carcinoma. The general consensus of opinion is that the addition of 10 days progestogen towards the end of the cycle, as in Cyclo-Progynova, diminishes the possibility of such a risk, and some investigators consider that it might be protective.

Overdosage: There have been no reports of ill-effects from overdosage which it is, therefore, generally unnecessary to treat. If overdosage is discovered within two or three hours and is so large that treatment seems desirable, gastric lavage can safely be used. There are no specific antidotes, and further treatment should be symptomatic.

Pharmaceutical precautions Store in cool, dry conditions. Shelf-life five years.

Legal category POM.

Package quantities Each outer carton contains a memo-pack containing 21 tablets.

Further information Nil.

Product licence numbers

Cyclo-Progynova 1 mg 0053/0108

Cyclo-Progynova 2 mg 0053/0053

CYPROSTAT* ▼

Presentation Each round white, 9 mm tablet is embossed on one side with 'BV' in a regular hexagon, and is scored on the other. It contains 50 mg cyproterone acetate (6-chloro-17 α -hydroxy-1 α , 2 α -methylene-pregna-4, 6-diene-3, 20-dione acetate).

Uses Palliative treatment of prostatic carcinoma. Prostatic carcinoma and its metastases are in general androgen-dependent. Cyprostat exerts a direct antiandrogenic action on the tumour and its metastases, and in addition it exerts a negative feedback effect on the hypothalamic receptors, so leading to a reduction in gonadotrophin release, and hence to diminished production of testicular androgens. Cyprostat may be used alone or in conjunction with surgery.

Dosage and administration The usual daily dose is 300 mg (6 tablets) orally, divided into 2–3 doses and taken after meals. Cyprostat therapy should not be discontinued when remission or improvement occurs. The dose may be reduced if side-effects are troublesome, but should be kept within the range of 200–300 mg daily.

Contra-indications, warnings, etc

Contra-indications: None.

Warnings, Side-effects: **Liver:** Cyproterone acetate has been found to cause liver abnormalities in animals, including the development of tumours. Cyprostat treat-

ment has shown good liver tolerance in man. Nevertheless, liver-function tests should be performed regularly during treatment.

Inhibition of spermatogenesis: The sperm count and the volume of ejaculate are reduced. Infertility is usual, and there may be azoospermia after 8 weeks. There is usually slight atrophy of seminiferous tubules. Follow-up examinations have shown these changes to be reversible, spermatogenesis usually reverting to its previous state about 3–5 months after stopping Cyprostat, or in some users, up to 20 months. That spermatogenesis can recover even after very long treatment is not yet known. There is evidence that abnormal sperms which might give rise to malformed embryos are produced during treatment with Cyprostat.

Thromboembolism: Patients with a history of thrombosis may be at risk of recurrence of the disease during Cyprostat therapy.

Chronic depression: It has been found that some patients with severe chronic depression deteriorate whilst taking Cyprostat therapy.

Tiredness: Fatigue and lassitude are common in the first few weeks of therapy but usually become much less from the third month. The marked lassitude and asthenia necessitate especial care when driving or operating machinery.

Gynaecomastia: Transient, and perhaps in some cases permanent, enlargement of the mammary glands has been reported. In rare cases, galactorrhoea and tender benign nodules have been reported. Symptoms generally subside after discontinuation of treatment or on reduction of dosage, but this should be weighed against the risk to the tumour of using inadequate doses.

Body weight: During long-term treatment, changes in body weight have been reported. Both increases and decreases have been seen.

Other changes that have been reported include reduction of sebum production leading to dryness of the skin, and transient patchy loss of body hair.

Adrenocortical function: During treatment adrenocortical function should be supervised, since suppression has been observed.

Diabetes: Cyprostat can influence carbohydrate metabolism. Parameters of carbohydrate metabolism should be examined carefully in all diabetics before and regularly during treatment.

Chronic alcohol: Chronic alcohol appears to reduce the effect of cyproterone acetate in male hypersexuality, but the relevance of this to the treatment of prostatic carcinoma is not known.

Haemoglobin: Hypochromic anaemia has been found rarely during long-term treatment, and blood-counts before and at regular intervals during treatment are advisable.

Nitrogen balance: A negative balance is usual at the start of treatment, but does not persist.

Overdosage: There have been no reports of ill-effects of overdosage, which it is, therefore, generally unnecessary to treat. If overdosage is discovered within two or three hours and is so large that treatment seems desirable, gastric lavage can safely be used. There are no specific antidotes, and further treatment should be symptomatic.

Pharmaceutical precautions Store in cool, dry conditions away from strong sunlight. **Shelf-life:** five years.

Package quantities: Containers of 200 tablets.

Legal category: POM.

Further information: Nil.

Product licence number 0053/0133.

DEPOSTAT*

Presentation Gestronol hexanoate in oily solution for intramuscular administration. Ampoules contain 200 mg in 2 ml.

Uses Endometrial carcinoma. Benign prostatic hyperplasia. Depostat is a depot progestogen, in a concentrated injectable non-aqueous solution, and is 25 times more potent than its parent substance progesterone. In the female, the action of Depostat is concentrated on the endometrium. This action is direct and does not involve suppression via the pituitary. Except in some high anaplastic tumours, Depostat has a strong antimitotic effect, with regression or arrest of primary endometrial carcinoma and of soft-tissue metastases.

In the male, Depostat has been shown to reduce prostatic weight significantly. It may effect an objective improvement in peak urine flow rates and residual urine and in subjective symptoms such as nocturia.

Dosage and administration Endometrial carcinoma: before hysterectomy and for advanced disease. A well tolerated adjunct to other therapy. To inhibit metastatic spread before and after operation, 200–400 mg intramuscularly every 5–7 days, starting immediately following diagnosis and continuing for a minimum of 12 weeks.

For treating existing metastases: 200–400 mg intramuscularly every 5–7 days. If the metastases are hormone-responsive, improvement will be observed within 8–12 weeks of therapy. Treatment should then be continued as long as it appears beneficial.

Benign prostatic hyperplasia where a) the patient is at operation risk; b) symptoms are mild; c) there is a waiting list for operation: standard dosage is 200 mg weekly by intramuscular injection, but in view of Depostat's good tolerance, this dosage can confidently be increased. In trials, 300 mg and 400 mg weekly have been used. The full benefit of treatment is unlikely to be established in a shorter period than three months, and trial results suggest that improvement can continue during substantially longer periods.

Contra-indications, warnings, etc

Contra-indications: Pregnancy. History of herpes gestationis.

Warning/side-effects: Rarely, local reactions may occur at the site of injection. Exacerbation of bronchial asthma, epilepsy and migraine may sometimes occur.

Side-effects are infrequent. In males, a reversible depression of libido and mammary discomfort have been reported by a few patients. Spermatogenesis is temporarily inhibited. In rare cases coughing, dyspnoea and circulatory irregularities may develop during or immediately after the injection.

Tolerance: In patients with chronic liver damage it is advisable to check liver function at intervals during long term treatment or repeated courses of Depostat. Transient moderate rises in bromsulphthalein retention and serum transaminases have occasionally been observed but have always proved harmless.

Pharmaceutical precautions Store in cool dry conditions away from strong sunlight: shelf-life five years.

Legal category POM.

Package quantities 5 ampoules of 2 ml.

Further information Nil.

Product licence number 0053/0018.

UGYNON* 30 UGYNON* 50 MICROGYNON* 30

Presentation *Eugynon 30*: Each white, sugar-coated tablet bears a printed black C in a regular hexagon on both sides and contains 0.25 mg levonorgestrel (formerly known as D-norgestrel) and 0.03 mg ethinylestradiol.

Ugynon 50: Each white, sugar-coated tablet contains 0.25 mg levonorgestrel (formerly known as D-norgestrel) in 0.5 mg norgestrel, and 0.05 mg ethinylestradiol.

Microgynon 30: Each beige, sugar-coated tablet bears a black A in a black hexagon printed on both sides and contains 0.15 mg levonorgestrel (formerly known as D-norgestrel) and 0.03 mg ethinylestradiol.

Uses Oral contraception and the recognised gynaecological indications for such oestrogen-progestogen combinations. The mode of action includes the inhibition of ovulation by suppression of the mid-cycle surge of uterine hormone, the inspissation of cervical mucus so as to constitute a barrier to sperm, and the rendering of the endometrium unresponsive to implantation.

Dosage and administration *First treatment cycle*: 1 tablet daily for 21 days, starting on the fifth day of the menstrual cycle (the first day of menstruation counting as day 1). In the first cycle only, an additional form of contraception (except the rhythm, temperature or cervical-mucus methods) must be used for the first 14 days of tablet-taking.

Subsequent cycles: Each subsequent course is started after seven tablet-free days have followed the preceding course.

Changing from high-dosed to low-dosed preparations: Additional (non-hormonal) precautions, other than the rhythm, temperature or cervical-mucus methods, should also be used for the first 14 days when changing products.

Post-partum and post-abortion use: After pregnancy oral contraception is usually started as soon as spontaneous menstruation has been resumed. However, oral contraception can be started within 7–12 days of a vaginal delivery, provided that the patient is fully ambulant and there are no puerperal complications. Starting within 12 days of delivery obviates additional contraceptive precautions. After a first-trimester abortion, oral contraception may be started immediately.

Special circumstances requiring additional contraception: Incorrect administration: If a tablet is delayed, it should be taken as soon as possible, and if it is taken within 12 hours of the correct time additional contraception is not needed. Further tablets should then be taken at the usual time. However, if the delay exceeds 12 hours, ovulation may occur. In those circumstances, any tablet or tablets delayed more than 12 hours should be

omitted, the remaining tablets should be taken on the correct days at the usual time, and extra precautions (except the rhythm, temperature and cervical-mucus methods) should be used until the next withdrawal bleed.

Gastro-intestinal upset: Vomiting or diarrhoea may reduce the effectiveness of the tablets by preventing them from being fully absorbed. Therefore, it is advisable that an additional method of contraception be used throughout the remainder of the course concerned. Mild laxatives do not impair contraceptive action.

Interaction with other drugs: Some drugs accelerate the metabolism of oral contraceptives taken concurrently. Drugs suspected of having the capacity to reduce the efficacy of oral contraceptives include barbiturates, phenylbutazone, phenytoin, rifampicin, ampicillin and other antibiotics. It is, therefore, advisable to use non-hormonal methods of contraception (except the rhythm, temperature or cervical-mucus methods) in addition to the oral contraceptive as long as an extremely high degree of protection must be provided during treatment with such drugs.

Contra-indications, warnings, etc

Contra-indications: Pregnancy. Thrombotic disorders and a history of these conditions, sickle-cell anaemia, disorders of lipid metabolism and other conditions in which, in individual cases, there is known or suspected to be a much increased risk of thrombosis. Acute or severe chronic liver diseases. Dubin-Johnson syndrome. Rotor syndrome. History, during pregnancy, of idiopathic jaundice or severe pruritus. History of herpes gestationis. Mammary or endometrial carcinoma, or a history of these conditions. Abnormal vaginal bleeding of unknown cause. Deterioration of otosclerosis during pregnancy.

Warnings: There is a general opinion, based on statistical evidence, that users of combined oral contraceptives experience, more often than non-users, venous thromboembolism, arterial thrombosis, including cerebral and myocardial infarction, and subarachnoid haemorrhage. Full recovery from such disorders does not always occur, and it should be realised that in a few cases they are fatal. How often these disorders occur in users of the modern low-dose pills is not known, but there are reasons for suggesting that they may occur less often than with older pills.

Certain factors may entail some risk of thrombosis, e.g. smoking, obesity, varicose veins, cardiovascular diseases, diabetes and migraine. The suitability of a combined oral contraceptive should be judged according to the severity of such conditions in the individual case, and should be discussed with the patient before she decides to take it. The risk of arterial thrombosis associated with oral contraceptives increases with age, and this risk is aggravated by cigarette-smoking. The use of combined oral contraceptives by women in the older age-group, especially those who are cigarette-smokers should therefore be discouraged, and alternative methods advised.

The possibility cannot be ruled out that certain chronic diseases may occasionally deteriorate during the use of combined oral contraceptives (see 'Precautions'). Hepatic tumours have been reported very rarely in women taking combined oral contraceptives, generally for a protracted period of time. A hepatic tumour should be considered in the differential diagnosis when upper abdominal pain, enlarged liver or signs of intra-abdominal haemorrhage occur.

Reasons for stopping oral contraception immediately:

Occurrence of migraine in patients who have never previously suffered from it. Exacerbation of pre-existing migraine. Any unusually frequent or unusually severe headaches. Any kind of acute disturbance of vision. Suspicion of thrombosis or infarction. Six weeks before elective operations and during immobilisation, e.g. after accidents, etc. Significant rise in blood-pressure. Jaundice. Clear exacerbation of conditions known to be capable of deteriorating during oral contraception or pregnancy. Pregnancy is a reason for stopping immediately because it has been suggested by some investigations that oral contraceptives taken in early pregnancy may slightly increase the risk of foetal malformations. Other investigations have failed to support these findings. The possibility therefore cannot be excluded, but it is certain that if a risk exists at all, it is very small.

Precautions: Examination of the pelvic organs, breasts and blood-pressure should precede the prescribing of any combined oral contraceptive, and should be repeated regularly. Before starting treatment, pregnancy must be excluded.

The following conditions required careful consideration: a history of severe depressive states, varicose veins, diabetes, hypertension, epilepsy, otosclerosis, multiple sclerosis, porphyria, tetany, disturbed liver function, gallstones, cardiovascular diseases, renal diseases, chloasma, uterine fibroids, asthma, the wearing of contact lenses, or any disease that is prone to worsen during pregnancy. The first appearance or deterioration of any of these conditions may indicate that the oral contraceptive should be stopped.

The risk of the deterioration of chloasma, which is often not fully reversible, is reduced by the avoidance of excessive exposure to sunlight.

Side-effects: Occasional side-effects may include nausea, vomiting, headaches, breast tension, changed body weight or libido, depressive moods and chloasma.

Menstrual changes:

1. **Reduction of menstrual flow:** This is not abnormal and it is to be expected in some patients. Indeed, it may be beneficial where heavy periods were previously experienced.

2. **Missed menstruation:** Occasionally, withdrawal bleeding may not occur at all. If the tablets have been taken correctly, pregnancy is very unlikely, but should be ruled out before a new course of tablets is started.

Intermenstrual bleeding: Very light 'spotting' or heavier 'breakthrough bleeding' may occur during tablet-taking, especially in the first few cycles. It appears to be generally of no significance, except where it indicates errors of tablet-taking, or where the possibility of interaction with other drugs exists (q.v.). However, if irregular bleeding is persistent, an organic cause should be considered.

Effect on adrenal and thyroid glands: Oral contraceptives have no significant influence on adrenocortical function. The ACTH function test for the adrenal cortex remains unchanged. The reduction in corticosteroid excretion and the elevation of plasma corticosteroids are due to an increased cortisol-binding capacity of the plasma proteins.

The response to metyrapone is less pronounced than in untreated women and is thus similar to that during pregnancy.

The radio-iodine uptake shows that thyroid function is unchanged. There is a rise in serum protein-bound iodine, similar to that in pregnancy and during the

administration of oestrogens. This is due to the increase capacity of the plasma proteins for binding thyroid hormones, rather than to any change in glandular function. In women taking oral contraceptives, the content of protein-bound iodine in blood serum should therefore, not be used for evaluation of thyroid function.

Effect on blood chemistry: Oral contraceptives may accelerate erythrocyte sedimentation in the absence of any disease. This effect is due to a change in the proportion of the plasma protein fractions. Increases in plasma copper, iron and alkaline phosphatase have also been recorded.

Overdosage: There have been no reports of serious ill effects from overdosage, even when a considerable number of tablets have been taken by a small child. In general, it is, therefore, unnecessary to treat overdosage. However, if overdosage is discovered within two or three hours and is so large that treatment seems desirable gastric lavage can be safely used.

There are no specific antidotes and further treatment should be symptomatic.

Pharmaceutical precautions Store in cool, dry conditions.

Shelf-life:

Eugynon 30 and Microgynon 30 – 5 years.

Eugynon 50 – 7 years.

Legal category POM.

Package quantities All Schering combined oral contraceptives are available in packs containing one month's supply.

Further information Nil.

Product licence numbers

Eugynon 30 0053/0049

Eugynon 50 0053/0061

Microgynon 30 0053/0064

GASTROGRAFIN®

Presentation Gastrografin contains 10% sodium diatrizoate and 66% meglumine diatrizoate in aqueous solution, with added flavouring and wetting agents. The iodine content is 370 mg/ml.

Uses Gastrografin is designed for investigation of the gastro-intestinal tract. It can be used either orally or as an enema. Follow-through examinations with barium can often be improved by combining it with Gastrografin. Gastrografin is of considerable value in the following instances.

1. Suspected partial or complete stenosis.
2. Acute haemorrhage.
3. Threatening perforation (peptic ulcer, diverticulum).
4. Megacolon.
5. Foreign bodies or tumours.
6. Gastro-colic fistula.
7. Before endoscopy.

Gastrografin is also recommended for the treatment of uncomplicated meconium ileus.

Dosage and administration Oral – Adults and children of 10 years of age or over: 60 ml Gastrografin

re sufficient for the visualisation of the stomach. Up to 100 ml may be needed for a follow-through examination of the gastro-intestinal tract.

For elderly or cachectic patients: Dilution with an equal volume of water is recommended.

Children up to 10 years of age: 15–30 ml are usually sufficient. This dose may be diluted with an equal volume of water.

For infants and debilitated small children: It is recommended that the contrast medium be diluted with twice its volume of water.

Rectal – Adults: The contrast medium should be diluted with three to four times its volume of water. Not more than 500 ml of Gastrografin solution should normally be required.

Children: The contrast medium should be diluted with four to five times its volume of water; up to five years of age the weaker dilution should be used.

Gastrografin and Barium Sulphate: Oral and rectal administration.

Adults: 30 ml Gastrografin plus the usual dose of barium should be adequate.

Children: 10 ml Gastrografin may be added to the barium.

For children up to five years of age: from 2–5 ml Gastrografin to 100 ml barium may be preferable. Further dilution which does not affect the contrast may be used if necessary in cases of pylorospasm or pyloric stenosis.

For the early diagnosis of a perforation or anastomosis in the oesophagus or gastro-intestinal tract, the patient should drink 100 ml Gastrografin. After 30–60 minutes later, if the defect is suspected of being in the distal gut, a urine specimen should be taken and 5 ml mixed with 5 drops of concentrated hydrochloric acid. The contrast medium which has undergone renal excretion will appear immediately or within two hours as a typical crystal formation in the precipitate.

Technique for the treatment of uncomplicated meconium ileus: Gastrografin can be given by enema to infants for non-operative treatment of uncomplicated meconium ileus, i.e. in the absence of volvulus, gangrene, perforation, peritonitis or atresia, all of which require immediate operation.

A large syringe and soft rubber catheter, No. 8 French, are recommended. The buttocks can be taped tightly together to minimise leakage but a Foley catheter should not be used. The procedure must be carried out slowly and only under fluoroscopic control. Injection should stop as soon as Gastrografin is seen to enter the ileum. Owing to its high osmolality, Gastrografin may cause the loss of a large amount of fluid into the intestines. An intravenous drip must therefore be set up before the enema is given and plasma should be infused as required. If the Gastrografin is not expelled during the first hour after removal of the rectal catheter, an X-ray should be taken to ensure that over-distension of the bowel as a result of the high osmolality of Gastrografin has not occurred.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to iodine-containing contrast media.

Because of its high osmotic pressure and minimal absorption, Gastrografin should not be administered to infants in higher doses than those recommended above. Gastrografin must not be given to a dehydrated infant

unless appropriate measures for correcting electrolyte and water balance have been taken before investigation.

Warnings/side-effects: Caution should be observed in patients with thyroid disease. Patients with enteritis or colitis may experience a transitory worsening of their symptoms. Caution is required in cases of oesophago-tracheal fistulae to avoid passage of the medium into the lungs, with consequent exudation of liquid. Systemic effects are rare, since Gastrografin is only minimally absorbed from the alimentary tract.

Owing to its hypertonicity, Gastrografin in full dosage may occasionally cause diarrhoea.

Pharmaceutical precautions *Storage:* Protect from light and heat. Shelf-life five years.

Legal category P.

Package quantities Bottles 5 × 100 ml.

Further information Nil.

Product licence number 0053/5023.

GONDAFON®

Presentation Each white, half-scored, torpedo-shaped tablet contains 500 mg of glymidine (the sodium salt of 2-benzene-sulphonamido-5-methoxyethoxy-pyrimidine).

Uses Maturity-onset diabetes, not adequately controlled by diet alone.

Dosage and administration Generally, initial dosage of 2–3 tablets daily with breakfast, or rarely 2 with breakfast and 1 in the late afternoon. After stabilisation, 1 or 2 tablets with breakfast often suffices.

The maximum permissible dosage of 4 tablets daily should be taken as 3 tablets with breakfast and 1 in the late afternoon.

Contra-indications, warnings, etc

Contra-indications: Pregnancy; diabetic coma and pre-coma; acetonaemia, all forms of metabolic decompensation during infection, operations and severe stress conditions. Severe hepatic and renal disease.

As with all benzenesulphonamides, treatment should be stopped immediately if allergies or blood dyscrasias occur. Similarly, any patient likely to undergo a major operation should probably be transferred temporarily to insulin therapy.

Although Gondaфон has a short biological half-life, care should be taken to avoid insidious hypoglycaemia in the elderly patient. This can be mistaken for a stroke.

There is no known cross-allergy between Gondaфон and other sulphonylureas or sulphonamides. However, caution is recommended in giving Gondaфон to a person with a history of allergy to either of these classes of compound.

Gondaфон reduces the tolerance of ethyl alcohol.

Hypoglycaemia: Mild symptoms of hypoglycaemia should be treated with a sandwich. Severe hypoglycaemia in the conscious patient should be treated with 5 tablespoonfuls of sugar in a cup of tea or water or by 1 mg of glucagon intramuscularly and should be followed by a sandwich after symptoms have improved. Hypoglycaemic coma should be treated by 1 mg of glucagon intramuscularly or subcutaneously and 50–100 ml of 40% glucose or 50% dextrose solution intravenously.

After recovery, the patient should be watched for three

days, and should be questioned so that the circumstances in which the hypoglycaemic attack occurred can be identified and its recurrence prevented.

Warnings: side-effects: Adverse reactions occur infrequently with Gondafon, but the commonest appear to be skin eruptions and gastro-intestinal disorders. Very rarely, leucopenia and purpura have been reported.

Pharmaceutical precautions Store in cool, dry conditions: shelf-life five years.

Legal category POM.

Package quantities Packs of 100 tablets.

Further information Nil.

Product licence number 0053/5004.

LOGYNON* (21-day) ▼

Presentation The memo-pack holds six light-brown tablets containing 30 mcg ethinylloestradiol and 50 mcg levonorgestrel, five white tablets containing 40 mcg ethinylloestradiol and 75 mcg levonorgestrel and ten ochre tablets containing 30 mcg ethinylloestradiol and 125 mcg levonorgestrel.

All tablets have a lustrous, sugar coating. The light-brown tablets bear a black C in a regular hexagon on both sides. The white and the ochre tablets bear a black B in a regular hexagon on both sides.

Uses Oral contraception and the recognised gynaecological indications for such oestrogen-progestogen combinations. The mode of action includes the inhibition of ovulation by suppression of the mid-cycle surge of luteinising hormone, the inspissation of cervical mucus so as to constitute a barrier to sperm, and the rendering of the endometrium unreceptive to implantation.

Dosage and administration *First treatment cycle:* 1 tablet daily for 21 days, starting with the tablet marked number 1, on the first day of the menstrual cycle.

Subsequent cycles: Each subsequent course is started when seven tablet-free days have followed the preceding course.

Changing from another combined oral contraceptive: The first tablet of Logynon should be taken on the first day of the withdrawal bleed which follows the previous oral contraceptive course. Alternatively where it is desirable to retain the previous routine of tablet-taking, Logynon may be started on the same day that the previous combined oral contraceptive would have been resumed, provided the patient has had a withdrawal bleed. In this case, however, additional (non-hormonal) contraceptive precautions, other than the rhythm, temperature or cervical-mucus methods, should also be used for the first 14 days.

Post-partum and post-abortion use: After pregnancy oral contraception is usually started as soon as spontaneous menstruation has been resumed. However, oral contraception can be started within 7–12 days of a vaginal delivery, provided that the patient is fully ambulant and there are no puerperal complications. Starting within 12 days of delivery obviates additional contraceptive precautions. After a first-trimester abortion, oral contraception may be started immediately.

Special circumstances requiring additional contraception: Incorrect administration: If a tablet is delayed, it should be taken as soon as possible, and if it is taken

within 12 hours of the correct time additional contraception is not needed. Further tablets should then be taken at the usual time. However, if the delay exceeds 12 hours, ovulation may occur. In those circumstances, all tablet or tablets delayed more than 12 hours should be omitted, the remaining tablets should be taken on the correct days at the usual time, and extra precaution (except the rhythm, temperature and cervical-mucus methods) should be used until the next withdrawal bleed.

Gastro-intestinal upset: Vomiting or diarrhoea may reduce the effectiveness of the tablets by preventing them from being fully absorbed. Therefore, it is advisable that an additional method of contraception be used throughout the remainder of the course concerned. Mild laxatives do not impair contraceptive action.

Interaction with other drugs: Some drugs accelerate the metabolism of oral contraceptives taken concurrently. Drugs suspected of having the capacity to reduce the efficacy of oral contraceptives include barbiturate, phenylbutazone, phenytoin, rifampicin, ampicillin and other antibiotics. It is, therefore, advisable to use non-hormonal methods of contraception (except the rhythm, temperature or cervical-mucus methods) in addition to the oral contraceptive as long as an extremely high degree of protection must be provided during treatment with such drugs.

Contra-indications, warnings, etc

Contra-indications: Pregnancy. Thrombotic disorders and a history of these conditions, sickle-cell anaemia and disorders of lipid metabolism and other conditions in which, in individual cases, there is known or suspected to be a much increased risk of thrombosis. Acute or severe chronic liver diseases. Dubin-Johnson syndrome. Rotor syndrome. History, during pregnancy, of idiopathic jaundice or severe pruritus. History of herpes gestationis. Mammary or endometrial carcinoma, or a history of these conditions. Abnormal vaginal bleeding of unknown cause. Deterioration of otosclerosis during pregnancy.

Warnings: There is a general opinion, based on statistical evidence, that users of combined oral contraceptive experience, more often than non-users, venous thromboembolism, arterial thrombosis, including cerebral and myocardial infarction, and subarachnoid haemorrhage. Full recovery from such disorders does not always occur and it should be realised that in a few cases they are fatal. How often these disorders occur in users of the modern low-dose pills is not known, but there are reasons for suggesting that they may occur less often than with older pills.

Certain factors may entail some risk of thrombosis, e.g. smoking, obesity, varicose veins, cardiovascular diseases, diabetes and migraine. The suitability of combined oral contraceptive should be judged according to the severity of such conditions in the individual case and should be discussed with the patient before she decides to take it. The risk of arterial thrombosis associated with oral contraceptives increases with age and this risk is aggravated by cigarette-smoking. The use of combined oral contraceptives by women in the older age-group, especially those who are cigarette-smokers should therefore be discouraged, and alternative methods advised.

The possibility cannot be ruled out that certain chronic diseases may occasionally deteriorate during the use of combined oral contraceptives (see 'Precautions'). Hepatic tumours have been reported very rarely in women

ing combined oral contraceptives, generally for a protracted period of time. A hepatic tumour should be considered in the differential diagnosis when upper abdominal pain, enlarged liver or signs of intra-abdominal hemorrhage occur.

Reasons for stopping oral contraception immediately: Onset or recurrence of migraine in patients who have never previously suffered from it. Exacerbation of pre-existing migraine. Any unusually frequent or unusually severe headaches. Any kind of acute disturbance of vision. Suspicion of thrombosis or infarction. Six weeks before elective operations and during immobilisation, e.g. after accidents, etc. Significant rise in blood-pressure. Jaundice. Clear exacerbation of conditions known to be capable of deteriorating during oral contraception or pregnancy. Pregnancy is a reason for stopping immediately because it has been suggested by some investigations that oral contraceptives taken in early pregnancy may slightly increase the risk of foetal malformations. Earlier investigations have failed to support these findings. The possibility therefore cannot be excluded, but it is stated that if a risk exists at all, it is very small.

Examinations: Examination of the pelvic organs, breasts & blood-pressure should precede the prescribing of a combined oral contraceptive, and should be repeated regularly. Before starting treatment, pregnancy must be excluded.

The following conditions require careful consideration: a history of severe depressive states, varicose veins, diabetes, hypertension, epilepsy, otosclerosis, multiple sclerosis, porphyria, tetany, disturbed liver function, gallstones, cardiovascular diseases, renal diseases, leukaemia, uterine fibroids, asthma, the wearing of contact lenses, or any disease that is prone to worsen during pregnancy. The first appearance or deterioration of any of these conditions may indicate that the oral contraceptive should be stopped.

The risk of the deterioration of chloasma, which is often not fully reversible, is reduced by the avoidance of excessive exposure to sunlight.

Side-effects: Occasional side-effects may include nausea, vomiting, headaches, breast tension, changed body weight or libido, depressive moods and chloasma.

Menstrual changes:

Reduction of menstrual flow: This is not abnormal and it is to be expected in some patients. Indeed, it may be beneficial where heavy periods were previously experienced.

Missed menstruation: Occasionally, withdrawal bleeding may not occur at all. If the tablets have been taken correctly, pregnancy is very unlikely, but should be ruled out before a new course of tablets is started.

Intermenstrual bleeding: Very light 'spotting' or heavier breakthrough bleeding may occur during tablet-taking, especially in the first few cycles. It appears to be generally of no significance, except where it indicates errors of tablet-taking, or where the possibility of interaction with her drugs exists (q.v.). However, if irregular bleeding persists, an organic cause should be considered.

Effect on adrenal and thyroid glands: Oral contraceptives have no significant influence on adrenocortical function. The ACTH function test for the adrenal cortex remains unchanged. The reduction in corticosteroid excretion and the elevation of plasma corticosteroids are due to an increased cortisol-binding capacity of the plasma proteins.

The response to metyrapone is less pronounced than

in untreated women and is thus similar to that during pregnancy.

The radio-iodine uptake shows that thyroid function is unchanged. There is a rise in serum protein-bound iodine, similar to that in pregnancy and during the administration of oestrogens. This is due to the increased capacity of the plasma proteins for binding thyroid hormones, rather than to any change in glandular function. In women taking oral contraceptives, the content of protein-bound iodine in blood serum should, therefore, not be used for evaluation of thyroid function.

Effect on blood chemistry: Oral contraceptives may accelerate erythrocyte sedimentation in the absence of any disease. This effect is due to a change in the proportion of the plasma protein fractions. Increases in plasma copper, iron and alkaline phosphatase have also been recorded.

Overdosage: There have been no reports of serious ill-effects from overdosage, even when a considerable number of tablets have been taken by a small child. In general, it is, therefore, unnecessary to treat overdosage. However, if overdosage is discovered within two or three hours and is so large that treatment seems desirable, gastric lavage can be safely used.

There are no specific antidotes and further treatment should be symptomatic.

Pharmaceutical precautions Store in cool, dry conditions: shelf-life five years.

Legal category POM.

Package quantities All Schering combined oral contraceptives are available in packs containing one month's supply.

Further information Nil.

Product licence number 0053/0085.

LOGYNON® ED ▼

Presentation The memo-pack holds six light-brown tablets containing 30 mcg ethinylloestradiol and 50 mcg levonorgestrel, five white tablets containing 40 mcg ethinylloestradiol and 75 mcg levonorgestrel, ten ochre tablets containing 30 mcg ethinylloestradiol and 125 mcg levonorgestrel and seven white placebo tablets.

All tablets have a lustrous, sugar coating. The light-brown tablets bear a black C in a regular hexagon printed on both sides. The white and the ochre tablets bear a black B in a regular hexagon on both sides. The white placebo tablets are larger and bear a black O in a regular hexagon.

Uses Oral contraception and the recognised gynaecological indications for such oestrogen-progestogen combinations. The mode of action includes the inhibition of ovulation by suppression of the mid-cycle surge of luteinising hormone, the inspissation of cervical mucus so as to constitute a barrier to sperm, and the rendering of the endometrium unresponsive to implantation.

Dosage and administration *First treatment cycle:* 1 tablet daily for 28 days, starting in the red sector on the first day of bleeding, the initial tablet being the one marked with the appropriate day of the week. In the first cycle only, an additional form of contraception (except the rhythm, temperature or cervical-mucus methods) must be used for the first 14 days of tablet-taking.

Subsequent cycles: Each subsequent course is started in the red sector on the day after the previous one has been finished. Pack, therefore, follows pack without interval.

Changing from high-dosed to low-dosed preparations: Additional (non-hormonal) precautions, other than the rhythm, temperature or cervical mucus methods, should also be used for the first 14 days when changing products.

Post-partum and post-abortion use: After pregnancy oral contraception is usually started as soon as spontaneous menstruation has been resumed. However, oral contraception can be started within 7–12 days of a vaginal delivery, provided that the patient is fully ambulant and there are no puerperal complications. Starting within 12 days of delivery obviates additional contraceptive precautions. After a first-trimester abortion, oral contraception may be started immediately.

Special circumstances requiring additional contraception: Incorrect administration: If a tablet is delayed, it should be taken as soon as possible, and if it is taken within 12 hours of the correct time additional contraception is not needed. Further tablets should then be taken at the usual time. However, if the delay exceeds 12 hours, ovulation may occur. In those circumstances, any tablet or tablets delayed more than 12 hours should be omitted, the remaining tablets should be taken on the correct days at the usual time, and extra precautions (except the rhythm, temperature and cervical-mucus methods) should be used until the next withdrawal bleed.

Gastro-intestinal upset: Vomiting or diarrhoea may reduce the effectiveness of the tablets by preventing them from being fully absorbed. Therefore, it is advisable that an additional method of contraception be used throughout the remainder of the course concerned. Mild laxatives do not impair contraceptive action.

Interaction with other drugs: Some drugs accelerate the metabolism of oral contraceptives taken concurrently. Drugs suspected of having the capacity to reduce the efficacy of oral contraceptives include barbiturates, phenylbutazone, phenytoin, rifampicin, ampicillin and other antibiotics. It is, therefore, advisable to use non-hormonal methods of contraception (except the rhythm, temperature or cervical-mucus methods) in addition to the oral contraceptive as long as an extremely high degree of protection must be provided during treatment with such drugs.

Contra-indications, warnings, etc

Contra-indications: Pregnancy. Thrombotic disorders and a history of these conditions, sickle-cell anaemia, disorders of lipid metabolism and other conditions in which, in individual cases, there is known or suspected to be a much increased risk of thrombosis. Acute or severe chronic liver diseases, Dubin-Johnson syndrome, Rotor syndrome. History, during pregnancy, of idiopathic jaundice or severe pruritus. History of herpes gestationis. Mammary or endometrial carcinoma, or a history of these conditions. Abnormal vaginal bleeding of unknown cause. Deterioration of otosclerosis during pregnancy.

Warnings: There is a general opinion, based on statistical evidence, that users of combined oral contraceptives experience, more often than non-users, venous thromboembolism, arterial thrombosis, including cerebral and myocardial infarction, and subarachnoid haemorrhage. Full recovery from such disorders does not always occur, and it should be realised that in a few cases they are

fatal. How often these disorders occur in users of the modern low-dose pills is not known, but there are reasons for suggesting that they may occur less often than with older pills.

Certain factors may entail some risk of thrombosis, e.g. smoking, obesity, varicose veins, cardiovascular diseases, diabetes and migraine. The suitability of combined oral contraceptive should be judged according to the severity of such conditions in the individual case and should be discussed with the patient before she decides to take it. The risk of arterial thrombosis associated with oral contraceptives increases with age and this risk is aggravated by cigarette-smoking. The use of combined oral contraceptives by women in the older age-group, especially those who are cigarette-smokers, should therefore be discouraged, and alternative methods advised.

The possibility cannot be ruled out that certain chronic diseases may occasionally deteriorate during the use of combined oral contraceptives (see 'Precautions'). Hepatic tumours have been reported very rarely in women taking combined oral contraceptives, generally for protracted period of time. A hepatic tumour should be considered in the differential diagnosis when upper abdominal pain, enlarged liver or signs of intra-abdominal haemorrhage occur.

Reasons for stopping oral contraception immediately

Occurrence of migraine in patients who have never previously suffered from it. Exacerbation of pre-existing migraine. Any unusually frequent or unusually severe headaches. Any kind of acute disturbance of vision. Suspicion of thrombosis or infarction. Six weeks before elective operations and during immobilisation, e.g. after accidents, etc. Significant rise in blood-pressure. Jaundice. Clear exacerbation of conditions known to be capable of deteriorating during oral contraception or pregnancy. Pregnancy is a reason for stopping immediately because it has been suggested by some investigations that oral contraceptives taken in early pregnancy may slightly increase the risk of foetal malformations. Other investigations have failed to support these findings. The possibility therefore cannot be excluded, but it is certain that if a risk exists at all, it is very small.

Precautions: Examination of the pelvic organs, breast and blood-pressure should precede the prescribing of any combined oral contraceptive, and should be repeated regularly. Before starting treatment, pregnancy must be excluded.

The following conditions required careful consideration: a history of severe depressive states, varicose veins, diabetes, hypertension, epilepsy, otosclerosis, multiple sclerosis, porphyria, tetany, disturbed liver function, gallstones, cardiovascular diseases, renal diseases, chloasma, uterine fibroids, asthma, the wearing of contact lenses, or any disease that is prone to worsen during pregnancy. The first appearance or deterioration of any of these conditions may indicate that the oral contraceptive should be stopped.

The risk of the deterioration of chloasma, which is often not fully reversible, is reduced by the avoidance of excessive exposure to sunlight.

Side-effects: Occasional side-effects may include nausea, vomiting, headaches, breast tension, changed body weight or libido, depressive moods and chloasma.

Menstrual changes:

1. **Reduction of menstrual flow:** This is not abnormal and it is to be expected in some patients. Indeed, it may

be beneficial where heavy periods were previously experienced.

2. Missed menstruation: Occasionally, withdrawal bleeding may not occur at all. If the tablets have been taken correctly, pregnancy is very unlikely, but should be ruled out before a new course of tablets is started.

Intermenstrual bleeding: Very light 'spotting' or heavier breakthrough bleeding may occur during tablet-taking, especially in the first few cycles. It appears to be generally of no significance, except where it indicates errors of tablet-taking, or where the possibility of interaction with other drugs exists (q.v.). However, if irregular bleeding is persistent, an organic cause should be considered.

Effect on adrenal and thyroid glands: Oral contraceptives have no significant influence on adrenocortical function. The ACTH function test for the adrenal cortex remains unchanged. The reduction in corticosteroid excretion and the elevation of plasma corticosteroids are due to an increased cortisol-binding capacity of the plasma proteins.

The response to metyrapone is less pronounced than in untreated women and is thus similar to that during pregnancy.

The radio-iodine uptake shows that thyroid function is unchanged. There is a rise in serum protein-bound iodine, similar to that in pregnancy and during the administration of oestrogens. This is due to the increased capacity of the plasma proteins for binding thyroid hormones, rather than to any change in glandular function. In women taking oral contraceptives, the content of protein-bound iodine in blood serum should, therefore, not be used for evaluation of thyroid function.

Effect on blood chemistry: Oral contraceptives may accelerate erythrocyte sedimentation in the absence of any disease. This effect is due to a change in the proportion of the plasma protein fractions. Increases in plasma copper, iron and alkaline phosphatase have also been recorded.

Overdosage: There have been no reports of serious ill-effects from overdosage, even when a considerable number of tablets have been taken by a small child. In general, it is, therefore, unnecessary to treat overdosage. However, if overdosage is discovered within two or three hours and is so large that treatment seems desirable, gastric lavage can be safely used.

There are no specific antidotes and further treatment should be symptomatic.

Pharmaceutical precautions Store in cool, dry conditions: shelf-life five years.

Legal category POM.

Package quantities All Schering combined oral contraceptives are available in packs containing one month's supply.

Further information Nil.

Product licence number 0053/0115.

NEOGEST*

Presentation Each round, dark brown, sugar-coated tablet bears a printed white D in a white regular hexagon on both sides and contains 37.5 mcg levonorgestrel (formerly known as D-norgestrel) contained in 75 mcg norgestrel.

Uses Oral contraception.

Mode of action: The contraceptive action of Neogest may be explained as follows.

It changes the cervical mucus so that a barrier is formed against the migration of sperm into the uterine cavity. Nidation is impeded because of changes in the structure of the endometrium. As a rule there is no inhibition of ovulation. Evidence suggests that a reduction in corpus-luteum function may also contribute to the contraceptive action.

Dosage and administration The first tablet is taken on the first day of menstrual bleeding at a time chosen by the patient. All subsequent tablets must then be taken at this time. The contraceptive effect is likely to be reduced if a tablet is delayed more than three hours. The tablets are taken daily and pack follows pack without interruption for as long as protection against conception is required. The contraceptive action begins after 14 tablets have been taken.

When starting oral contraception with Neogest, additional precautions other than the rhythm or temperature methods must be used for the first 14 days of tablet-taking.

Use after delivery or abortion: Although after delivery or abortion it is customary to start oral contraception at the end of the first biphasic menstrual cycle, Neogest may be started as early as the 7th day post partum.

Use during breast feeding: There is no evidence that Neogest diminishes the yield of breast milk. Radio-activity can be found in the milk after the administration of labelled levonorgestrel. However, it is not known whether the metabolites which appear in minute amounts in the milk and do not accumulate in the infant's tissues are biologically active.

Contra-indications, warnings, etc

Contra-indications: History during pregnancy, of idiopathic jaundice or severe pruritus. Dubin-Johnson and Rotor syndromes, acute and severe chronic liver diseases; pregnancy. History of herpes gestationis. Although no association between progestogen-only oral contraceptives and thromboembolic disorders has been shown, it is at present required that a history of such disorders be described as a contra-indication to Neogest, as it is to oestrogen-containing oral contraceptives.

Warnings/side-effects: Clinical investigations indicate that, in general, Neogest is very well tolerated. Symptoms reported in isolated cases include nausea, vomiting, dizziness, headaches, migraine, depressive moods, disturbances of appetite, allergic reactions. Amenorrhoea and changes in the pattern of the menstrual cycle have also been observed (For details see 'Menstrual pattern').

Circumstances requiring additional contraceptive precautions, other than the temperature, rhythm and cervical-mucus methods.

1. If a tablet is taken more than three hours late (i.e. if it is more than 27 hours since the last tablet was taken), protection against conception may be impaired. From the time of such an error, extra nonhormonal methods must be employed until 14 consecutive tablets have been taken in the correct manner.

2. When changing over to Neogest from other hormonal contraceptives, additional contraceptive measures must be employed until 14 consecutive tablets have been taken regularly.

3. Vomiting or diarrhoea may reduce the effectiveness of the tablets by preventing them from being fully absorbed. If vomiting occurs shortly after a tablet has

been taken, the contraceptive protection may be maintained if a second tablet is taken within three hours of the normal time, provided that vomiting does not recur. It is advisable to take the last tablet of the pack for this purpose, so as to avoid confusion.

In the case of repeated vomiting, or continued diarrhoea, additional contraceptive measures should be employed for a further 14 days after the symptoms have subsided.

4. Interaction with other drugs. Some drugs accelerate the metabolism of oral contraceptives taken concurrently. Drugs suspected of having the capacity to reduce the efficacy of oral contraceptives include barbiturates, phenylbutazone, phenytoin, rifampicin, ampicillin and other antibiotics. It is, therefore, advisable to use non-hormonal methods of contraception (except the rhythm, temperature or cervical-mucus methods) during treatment with such drugs.

Menstrual pattern: A usual feature of all progestogen-only oral contraceptives is that they produce an initial irregularity of the bleeding pattern, but such irregularity tends to decrease with time.

The patient should be informed before starting Neogest that her menstrual pattern is likely to alter.

Procedure in the case of cycle disturbances: Irregular bleeding is from a medical point of view no reason for discontinuing therapy, as long as organic causes and pregnancy can be ruled out.

If amenorrhoea lasts longer than three months, or occurs repeatedly, administration of Neogest should be suspended until regular cyclical bleeding has been re-established.

No attempt must be made to control irregular cycles by the additional administration of oestrogens since they would reverse the effect of Neogest on the cervical mucus, thus seriously reducing the contraceptive efficacy.

Reasons for stopping oral contraception immediately: First signs of thrombophlebitis or thromboembolism. Jaundice. Pregnancy.

Overdosage: There have been no reports of serious ill-effects from overdosage even when a considerable number of tablets have been taken by a small child. In general, it is, therefore, unnecessary to treat overdosage. However, if overdosage is discovered within two or three hours and is so large that treatment seems desirable, gastric lavage can be safely used. There are no specific antidotes and further treatment should be symptomatic.

Pharmaceutical precautions *Storage:* Cool, dry conditions.

Shelf-life: Seven years.

Legal category POM.

Package quantities Memo-pack containing 35 tablets.

Further information Nil.

Product licence number 0053/0062.

NERISONE* CREAM, OILY CREAM AND OINTMENT

Presentation *Cream* (oil-in-water emulsion), *oily cream* (water-in-oil emulsion) and *ointment* (anhydrous base): 1 g of each Nerisone presentation contains 1 mg (0.1%) diflucortolone valerate.

Uses Corticoid-responsive dermatoses in the absence of infection.

Dosage and administration Initially 2–3 applications daily, according to the severity of the condition. For maintenance, one application daily.

Nerisone is available in three bases. The base chosen for an individual case should depend on the physical characteristics of the lesion. For example, in very dry and chronic skin conditions, the occlusive effect of the Nerisone ointment base aids the healing process.

Contra-indications, warnings, etc

Contra-indications: Rosacea and peri-oral dermatitis. Viral infections. Bacterial or fungal infections of the skin in the absence of appropriate anti-infective therapy. Nerisone is not suitable for the treatment of ophthalmic conditions.

Warnings/side-effects: In infants, long-term continuous therapy with topical corticosteroids should be avoided. Adrenal suppression can occur, even without occlusion. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical steroids should not be used extensively during the first trimester of pregnancy, i.e. in large amounts or for prolonged periods.

In common with all other topical corticoids, side-effects may occur when Nerisone is applied to large areas of the body (10% or more) and for long periods of time (more than four weeks), especially if the ointment or an occlusive dressing is being used. These may be local signs such as atrophy of the skin, telangiectasia, striae and acneiform changes, or systemic corticoid effects caused by absorption. Therefore, caution should be exercised when using occlusive dressings, as there is a possibility that natural steroid production may be depressed.

Babies and children up to the age of 4 years should not be treated with Nerisone for longer than three weeks – particularly on skin areas covered by nappies.

Nerisone may be applied under an occlusive dressing. However, each dressing should not be left on for more than 24 hours. Although occlusive dressings may be used repeatedly, it should be noted that systemic corticoid absorption is likely to be increased with a consequent increased risk of adrenal suppression. Should secondary infection occur during treatment, the use of occlusive dressings should be postponed until the infection has been controlled.

Pharmaceutical precautions Store in cool, dry conditions.

Shelf-life: Five years.

Legal category POM.

Package quantities 30 g tubes.

Further information Nil.

Product licence numbers

Nerisone Cream	0053/0075
Nerisone Oily Cream	0053/0073
Nerisone Ointment	0053/0074

NERISONE* FORTE OILY CREAM AND OINTMENT

Presentation *Oily cream* (water-in-oil emulsion) and *ointment* (anhydrous base). 1 gram of each Nerisone Forte presentation contains 3 mg (0.3%) diflucortolone valerate.

Uses Initial and intermittent treatment of severe and recalcitrant corticoid-responsive dermatoses in the absence of infection. These include psoriasis, neurodermatitis (endogenous eczema, atopic dermatitis), lichen planus, discoid lupus erythematosus and severe chronic eczema.

Dosage and administration Initially, two or three thin applications daily, according to the severity of the condition. Once the clinical picture has improved, the patient should be changed from Nerisone Forte to Nerisone, for maintenance therapy.

Nerisone Forte is available in two bases.

Nerisone Forte Oily Cream: This is an emulsion of water in oil. Because it is an emulsion, it allows heat and exudate to pass freely through, while the oil component protects against undesirable drying out of the skin.

Nerisone Forte Ointment: This has an anhydrous fatty base, which is particularly indicated in chronic and dry skin conditions. The softening and occlusive properties of this base often aid the healing process.

Contra-indications, warnings, etc

Contra-indications: Rosacea, acne and peri-oral dermatitis. Viral infections. Bacterial or fungal infections of the skin in the absence of appropriate anti-infective therapy. Nerisone is not suitable for the treatment of ophthalmic conditions.

Warnings/side-effects: In infants, long-term continuous therapy with topical corticosteroids should be avoided. Adrenal suppression can occur, even without occlusion. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of these findings to human beings has not been established. However, topical steroids should not be used extensively during the first trimester of pregnancy, i.e. in large amounts or for prolonged periods.

Only in rare cases, and preferably under the guidance of a dermatologist, should Nerisone Forte be considered for use on the face, or in babies and children up to the age of four, and then only briefly for the initial control of very severe lesions.

In view of the high efficacy and potency of Nerisone Forte, no more than 60 g a week should be applied, and it is suggested that treatment for one or two weeks should generally be sufficient to obtain control of even the most refractory lesion, after which a change to Nerisone can usually be made if maintenance therapy is necessary.

Since prolonged therapy with potent topical corticosteroids may cause local atrophic changes such as striae, thinning and telangiectasia, particularly in skin folds and where occlusive dressings are used, it is recommended that the progress of patients under treatment for more than one week with Nerisone Forte be reviewed weekly, and that repeat prescriptions be written only when the prescribing physician has again seen the patient.

Since absorption is increased with the use of occlusive dressings, these should not be left on for more than 24 hours. If secondary infection occurs during treatment, the use of occlusive dressings should be stopped until the infection has been eliminated, and appropriate treatment of the infection should be instituted if it persists.

Pharmaceutical precautions Store in cool, dry conditions.

Shelf-life: Five years.

Legal category POM.

Package quantities 15 g tubes.

Further information Nerisone Forte preparations contain neither parabens nor lanolin.

Product licence numbers

Nerisone Forte Oily Cream	0053/0099
Nerisone Forte Ointment	0053/0100

NOCTAMID* ▼

Presentation Round, white, scored tablets. Those marked CG in a regular hexagon contain 0.5 mg lormetazepam. Those marked CF in a regular hexagon contain 1.0 mg lormetazepam.

Uses Noctamid is indicated for the short-term treatment of insomnia including difficulty in falling asleep and/or frequent nocturnal awakenings.

Dosage and administration

Adults: Normally 1.0 mg orally before retiring. In elderly patients 0.5 mg is recommended. Subsequently, the initial dosage may be doubled in individual cases if this proves necessary.

Children: Noctamid has not been evaluated for the treatment of children.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to benzodiazepines. Myasthenia gravis.

Precautions and warnings: Noctamid and other centrally-acting drugs such as phenothiazines enhance each other's actions, and hence careful monitoring of dosage is advised during co-prescription.

The effects of Noctamid are potentiated by alcohol.

Metabolic interactions between Noctamid and other drugs have not been studied and a close watch should be kept for possible interactions.

Prolonged use of benzodiazepines, especially in high dosage, may occasionally result in the development of some psychological dependence, with withdrawal symptoms on sudden discontinuation. Treatment in these cases should be withdrawn gradually. Careful usage seldom results in the development of dependence.

Patients taking Noctamid should be warned about the possible hazard from dizziness or drowsiness when driving or operating machinery. Elderly patients are particularly susceptible to these effects, and to confusion, as are those with organic brain disease.

The use of Noctamid during pregnancy is not recommended, both in accordance with the general principle that drugs should not be administered to pregnant women unless essential, and because the possibility of a harmful effect on the human foetus cannot be totally ruled out, although extensive animal tests have shown no teratogenic actions.

Side-effects: In general, Noctamid is very well tolerated. However the common side-effects of benzodiazepines, including headaches, nausea, drowsiness, blurring of vision, dizziness and ataxia may occur on the following day, particularly in unusually sensitive patients or when dosage has been excessive.

Rare behavioural adverse effects of benzodiazepines include paradoxical aggressive outbursts, excitement, confusion, and the uncovering of depression with suicidal tendencies. Even more rare side-effects reported with some benzodiazepines have been hypotension, gastrointestinal and visual disturbances, skin rashes,

urinary retention, changes in libido, blood dyscrasias, and jaundice, but they have not been reported with Noctamid.

Overdosage: As with other benzodiazepines, overdoses should not present a threat to life. General supportive measures should be used. Treatment is symptomatic, and gastric lavage may be of use if performed shortly after ingestion. If the patient is conscious, an emetic such as ipecacuanha may be given. The patient is likely to sleep, and a clear airway should be maintained.

Pharmaceutical precautions Store in a cool, dry place.

Shelf-life: five years.

Legal category POM.

Package quantities 1 mg-30 tablets and 100 tablets (blister packs), 0.5 mg-30 tablets and 100 tablets (blister packs).

Further information Lormetazepam is rapidly absorbed from the gastrointestinal tract and is conjugated in a simple one-step process to a pharmacologically inactive glucuronide.

There are no major metabolites.

Product licence numbers

0.5 mg tablets 0053/0117

1 mg tablets 0053/0118

NORGESTON*

Presentation Each round, white, sugar-coated tablet bears a printed black E in a black regular hexagon on both sides and contains 30 mcg levonorgestrel (formerly known as D-norgestrel).

Uses Oral contraception.

Mode of action: The contraceptive action of Norgeston may be explained as follows:

It changes the cervical mucus so that a barrier is formed against the migration of sperm into the uterine cavity. Nidation is impeded because of changes in the structure of the endometrium. As a rule there is no inhibition of ovulation. Evidence suggests that a reduction in corpus-luteum function may also contribute to the contraceptive action.

Dosage and administration The first tablet is taken on the first day of menstrual bleeding at a time chosen by the patient. All subsequent tablets must then be taken at this time. The contraceptive effect is likely to be reduced if a tablet is delayed more than three hours. The tablets are taken daily and pack follows pack without interruption for as long as protection against conception is required. The contraceptive action begins after 14 tablets have been taken.

When starting oral contraception with Norgeston, additional precautions other than the rhythm or temperature methods must be used for the first 14 days of tablet-taking.

Use after delivery or abortion: Although after delivery or abortion it is customary to start oral contraception at the end of the first biphasic menstrual cycle, Norgeston may be started as early as the seventh day post-partum.

Use during breast feeding: There is no evidence that Norgeston diminishes the yield of breast milk. Radioactivity can be found in the milk after the administration

of labelled levonorgestrel. However, it is not known whether the metabolites which appear in minute amount in the milk, and do not accumulate in the infant's tissues are biologically active.

Contra-indications, warnings, etc

Contra-indications: History, during pregnancy, of idiopathic jaundice or severe pruritus; Dubin-Johnson and Rotor syndromes; acute and severe chronic liver diseases; pregnancy. History of herpes gestationis. Although no association between progestogen-only oral contraceptives and thromboembolic disorders has been shown, it is at present required that a history of such disorders be described as a contra-indication to Norgeston, as it is to oestrogen-containing oral contraceptives. **Warnings/side-effects:** Clinical investigations indicate that, in general, Norgeston is very well tolerated. Symptoms reported in isolated cases include nausea, vomiting, dizziness, headaches, migraine, depressive moods, disturbances of appetite, allergic reactions. Amenorrhoea and changes in the pattern of the menstrual cycle have been observed. (For details, see 'Menstrual pattern'.)

Circumstances requiring additional contraceptive precautions, other than the temperature, rhythm and cervical-mucus methods.

1. If a tablet is taken more than three hours late (i.e. if it is more than 27 hours since the last tablet was taken), protection against conception may be impaired. From the time of such an error, extra non-hormonal methods must be employed until 14 consecutive tablets have been taken in the correct manner.

2. When changing over to Norgeston from other hormonal contraceptives, additional contraceptive measures must be employed until 14 consecutive tablets have been taken regularly.

3. Vomiting or diarrhoea may reduce the effectiveness of the tablets by preventing them from being fully absorbed. If vomiting occurs shortly after a tablet has been taken, the contraceptive protection may be maintained if a second tablet is taken within three hours of the normal time, provided that vomiting does not recur. It is advisable to take the last tablet of the pack for this purpose, so as to avoid confusion.

In the case of repeated vomiting, or continued diarrhoea, additional contraceptive measures should be employed for a further 14 days after the symptoms have subsided.

4. Interaction with other drugs. Some drugs accelerate the metabolism of oral contraceptives taken concurrently. Drugs suspected of having the capacity to reduce the efficacy of oral contraceptives include barbiturates, phenylbutazone, phenytoin, rifampicin, ampicillin and other antibiotics. It is, therefore, advisable to use non-hormonal methods of contraception (except the rhythm, temperature or cervical-mucus methods) during treatment with such drugs.

Menstrual pattern: A usual feature of all progestogen-only oral contraceptives is that they produce an initial irregularity of the bleeding pattern, but such irregularity tends to decrease with time.

The patient should be informed before starting Norgeston that her menstrual pattern is likely to alter.

Procedure in the case of cycle disturbances: Irregular bleeding is, from a medical point of view, no reason for discontinuing therapy, as long as organic causes and pregnancy can be ruled out.

If amenorrhoea lasts longer than three months, or

occurs repeatedly, administration of Norgeston should be suspended until regular cyclical bleeding has been re-established.

No attempt must be made to control irregular cycles by the additional administration of oestrogens, since they would reverse the effect of Norgeston on the cervical mucus, thus seriously reducing the contraceptive efficacy.

Reasons for stopping oral contraception immediately: First signs of thrombophlebitis or thromboembolism. Jaundice. Pregnancy.

Overdosage: There have been no reports of serious ill-effects from overdosage, even when a considerable number of tablets have been taken by a small child. In general, it is, therefore, unnecessary to treat overdosage. However, if overdosage is discovered within two or three hours and is so large that treatment seems desirable, gastric lavage can be safely used. There are no specific antidotes and further treatment should be symptomatic.

Pharmaceutical precautions *Storage:* Cool, dry conditions.

Shelf-life: Five years.

Legal category POM.

Package quantities Memo-pack containing 35 tablets.

Further information Nil.

Product licence number 0053/0068.

PRIMOLUT N*

Presentation Each white, uncoated tablet is impressed with 'AN' in a regular hexagon on one side and contains 5 mg norethisterone BP.

Uses Metropathia haemorrhagica. Premenstrual syndrome. Postponement of menstruation. Endometriosis. Menorrhagia. Dysmenorrhoea.

A total dose of about 100–150 mg Primolut N (10–15 mg on each of 10 consecutive days) will produce complete secretory transformation of an endometrium which has been pretreated with oestrogens.

A particular advantage is that the menstruation-like withdrawal bleeding occurs consistently two to three days after stopping Primolut N.

During treatment with Primolut N the basal body temperature rises, as it does under the influence of endogenous progesterone in the second half of the menstrual cycle.

Dosage and administration The use of Primolut N is restricted to patients in whom there is no possibility of early pregnancy in the cycle concerned.

Metropathia haemorrhagica (dysfunctional uterine bleeding): 1 tablet 3 times daily for 10 days. Bleeding is arrested usually within 1–3 days. A withdrawal bleeding resembling normal menstruation occurs within 2–4 days after discontinuing treatment.

Prophylaxis against recurrence of dysfunctional bleeding: If there are no signs of resumption of normal ovarian function (no rise in the second half of the cycle of the morning temperature, which should be measured daily) recurrence must be anticipated. Cyclical bleeding can be established with 1 tablet twice daily from the 19th to the 26th day of the cycle.

Premenstrual syndrome (including premenstrual mastalgia): Premenstrual symptoms such as headache,

migraine, breast discomfort, water retention, tachycardia and psychic disturbances may be relieved by the administration of 2–3 tablets daily from the 19th to the 26th day of the cycle. Treatment should be repeated for several cycles. When treatment is stopped, the patient may remain symptom-free for a number of months.

Postponement of menstruation: In cases of too frequent menstrual bleeding, and in special circumstances (e.g. operations, travel, sports) the postponement of menstruation is possible, 1 tablet Primolut N three times daily, starting 3 days before the expected onset of menstruation. A normal period should occur 2–3 days after the patient has stopped taking tablets.

Dysmenorrhoea: Functional or primary dysmenorrhoea is almost invariably relieved by the suppression of ovulation. 1 tablet three times daily for 20 days, starting on the fifth day of the cycle (the first day of menstruation counting as day 1). Treatment should be maintained for three to four cycles followed by treatment-free cycles. A further course of therapy may be employed if symptoms return.

Endometriosis (pseudo-pregnancy therapy): Longterm treatment is commenced on the 5th day of the cycle with 2 tablets Primolut N daily for the first few weeks. In the event of spotting, the dosage is increased to 4 and, if necessary, 5 tablets daily.

After bleeding has ceased, the initial dose is usually sufficient. Duration of treatment: 4–6 months continuously, or longer if necessary.

Menorrhagia (hypermenorrhoea): 1 tablet 2–3 times a day from the 19th to the 26th day of the cycle (counting the first day of menstruation as day 1).

Note: If menstrual bleeding should fail to follow a course of Primolut N, the possibility of pregnancy must be ruled out before a further course is given.

Contra-indications, warnings, etc

Contra-indications: Pregnancy. Severe disturbance of liver function. Dubin-Johnson and Rotor syndromes. History during pregnancy of idiopathic jaundice, severe pruritus or herpes gestationis.

Warnings/side-effects: Rarely occur in doses of 15 mg daily. Amongst those recorded are slight nausea, exacerbation of epilepsy and migraine. With extremely high dosage there may be cholestatic liver changes.

Overdosage: There have been no reports of ill-effects from overdosage and treatment is generally unnecessary. If overdosage is discovered within two or three hours and is so large that treatment seems desirable, gastric lavage can safely be used.

There are no special antidotes, and further treatment should be symptomatic.

Pharmaceutical precautions Store in cool dry conditions: shelf-life five years.

Legal category POM.

Package quantities Bottles of 100 tablets. Containers of 500 tablets.

Further information Nil.

Product licence number 0053/5033.

PRIMOTESTON* DEPOT 250 mg

Presentation Primoteston Depot 250 mg contains testosterone oenanthate 250 mg per ml in clear non-aqueous solution for intramuscular injection.

Uses Mammary carcinoma in the female. Androgen deficiency in the male.

Primoteston Depot is a depot androgen for use when male sex hormones are indicated. Testosterone enanthate has not only a sustained androgenic effect but also a very powerful one, since testosterone in this depot form is particularly well utilised by the body.

Dosage and administration *In the female. Advanced mammary carcinoma:* In advanced mammary carcinoma with metastases or recurrences, high-dosage therapy causes objective remission in some cases and frequently subjective improvement. In responsive cases, pain is diminished and the general condition considerably improved. Bone metastases are often affected favourably. In order to sustain a remission for as long as possible, it is sometimes necessary after a time to shorten the interval between injections. If hypercalcaemia occurs, treatment must be discontinued. In women over 60 years of age, treatment with oestrogens is often more effective.

Dosage: 250 mg Primoteston Depot intramuscularly every two weeks.

In the male: Hypogonadism: To stimulate development of underdeveloped androgen-dependent organs and for initial treatment of deficiency symptoms, 250 mg Primoteston Depot intramuscularly every two to three weeks.

For maintenance treatment: 250 mg Primoteston Depot intramuscularly every three to six weeks, according to individual requirement.

Contra-indications, warnings, etc

Contra-indications: Prostatic carcinoma and pregnancy.

Warnings/side-effects: With high dosage and prolonged testosterone therapy, an increased tendency to fluid retention and oedema is seen occasionally. In patients with a tendency to oedema, therefore, caution is indicated unless the oedema is due to lack of protein, when the protein-anabolic effect of Primoteston Depot is beneficial.

With prolonged use and high dosage of androgens in women, symptoms of virilisation must be expected. Regular examination of the prostate is advisable for men receiving androgen therapy.

Pharmaceutical precautions Store in cool, dry conditions away from strong sunlight: shelf-life five years.

Legal category POM.

Package quantities Ampoules of 250 mg, 3 × 1 ml.

Further information Nil.

Product licence number 0053/5037.

PROGYNOVA* 1 mg PROGYNOVA* 2 mg

Presentation *Progynova 1 mg:* Each beige, sugar-coated tablet bears a printed black B in a black regular hexagon and contains 1 mg of oestradiol valerate.

Progynova 2 mg: Each pale blue, sugar-coated tablet bears a printed red B in a red regular hexagon and contains 2 mg of oestradiol valerate.

Uses The treatment of climacteric symptoms in the short term in postmenopausal women (i.e. who have had no uterine bleeding for at least 12 months).

Dosage and administration One tablet of Progynova 1 mg daily for 21 days, followed by an interval of at least seven days before the next course. If the response is inadequate, Progynova 2 mg may be substituted, but the lowest dose compatible with the control of symptom should always be used, and an attempt should be made to revert to Progynova 1 mg after symptoms have been satisfactorily controlled. However, it should be realised that the appropriate dosage will be determined by the individual patient's rate of metabolism of Progynova rather than by the initial severity of the symptoms.

Alternatively, if the response to Progynova 1 mg is inadequate, Cyclo-Progynova can be substituted and in general when high-dose oestrogen therapy is required, oestrogen-progestogen combinations are recommended.

Bleeding: If possible, a dosage should be found that will abolish climacteric symptoms without inducing endometrial bleeding. Non-recurrent bleeding of short duration in the tablet-free intervals is usually due to oestrogen withdrawal. Any recurrent bleeding occurring during tablet-taking should be investigated to exclude endometrial hyperplasia or carcinoma. If recurrent bleeding is found to be non-pathological, then Cyclo-Progynova which produces controlled shedding of the endometrium should be substituted. (For further information, see the data sheet for Cyclo-Progynova.)

The treatment of recurrences: If, after completion of short-term treatment and the withdrawal of Progynova climacteric symptoms should recur, further treatment should be with Cyclo-Progynova (except in hysterectomised patients, who may take Progynova without any limit on the duration of treatment, and without intervals).

Contra-indications, warnings, etc

Contra-indications: Pregnancy. Severe disturbances of liver function, jaundice or general pruritus during a previous pregnancy, Dubin-Johnson syndrome, Rotor syndrome, existing or previous thromboembolic processes, sickle-cell anaemia, suspected or existing hormone-dependent disorders or tumours of the uterus or breast, congenital disturbances of lipid metabolism or atherosclerosis with deterioration in previous pregnancies.

Warnings/side-effects: Prolonged exposure to unopposed oestrogens may increase the risk of the development of endometrial carcinoma. The following have been reported during treatment: dyspepsia, flatulence, nausea, vomiting, abdominal pain and bloating, weight-gain, breast tension and pain, palpitations, cardiac symptoms, increased libido, headaches, dizziness, vertigo, epistaxis, biliary stasis, hypertension, urticaria and other rashes, thrombophlebitis, uterine bleeding, mucous vaginal discharge, general pruritus.

Diseases that are known to be subject to deterioration during pregnancy (e.g. multiple sclerosis, epilepsy, diabetes, hypertension, porphyria, tetany and otosclerosis) should be carefully observed during treatment.

Precautions and special information: Treatment should be stopped at once if migrainous or frequent and unusually severe headaches occur for the first time, or if there are any other symptoms that are possible prodromata of vascular occlusion.

Treatment should also be stopped if trauma, illness or impending surgery is considered to entail a risk of thrombosis.

Treatment should be stopped at once if jaundice occurs, or if there is a significant rise in blood-pressure.

In patients with mild chronic liver disease, liver function should be checked every 8–12 weeks.

Women with a family history of endometrial carcinoma should be carefully observed.

Examination of the pelvic organs, endometrium, breasts and blood-pressure is advised before and periodically during treatment with Progynova.

Overdosage: There have been no reports of ill-effects from overdosage, which it is, therefore, generally unnecessary to treat. If overdosage is discovered within two or three hours and is so large that treatment seems desirable, gastric lavage can safely be used. There are no specific antidotes, and further treatment should be symptomatic.

Pharmaceutical precautions Store in cool, dry conditions:

Shelf-life:

Progynova 1 mg 5 years.

Progynova 2 mg 7 years.

Legal category POM.

Package quantities Memo-packs of 21 tablets.

Further information Nil.

Product licence numbers

Progynova 1 mg 0053/0057

Progynova 2 mg 0053/0058

PROLUTON® DEPOT

(formerly PRIMULOT DEPOT)

Presentation Hydroxyprogesterone hexanoate BP 250 mg and 500 mg in ampoules and pre-loaded disposable syringe packs for intramuscular injection.

Uses Habitual abortion, when associated with proven progesterone-deficiency.

Dosage and administration 250–500 mg Proluton Depot at weekly intervals during the first half of pregnancy.

Contra-indications, warnings, etc

Contra-indications: A history of herpes gestationis.

Warnings: Many medicinal products, including female sex hormones, have been suspected of being capable of affecting the normal development of a child in the early stages of pregnancy. Many researchers consider that in relation to sex hormones such a suspicion is ill founded but one has to accept that for no medicinal product can a teratogenic activity be excluded with absolute certainty. Therefore, the general principle is now widely accepted that inessential use of drugs during pregnancy should be avoided. Following this general principle, Proluton Depot should be used to maintain pregnancy only if it is strictly indicated, i.e. if there is an urgent desire to have a child, especially if luteal insufficiency is present.

Since Proluton Depot may prevent spontaneous evacuation of a dead foetus (missed abortion) the progress of the pregnancy should be regularly monitored by appropriate means, including immunological tests.

Side-effects: Very rarely, local reactions may occur at the site of injection.

Pharmaceutical precautions Store in cool, dry conditions away from strong sunlight. Shelf-life five years.

Legal category POM.

Package quantities 250 mg: Packs of 3 and 20 ampoules 1 ml.

Preloaded disposable syringes. 1 ml, packed singly.

500 mg: Packs of 3 and 20 ampoules 2 ml.

Preloaded disposable syringes 2 ml, packed singly.

Further information Nil.

Product licence numbers

Proluton Depot 250 mg 0053/5031

Proluton Depot 500 mg 0053/5032

PRO-VIRON®

Presentation Each white tablet has AX in a regular hexagon impressed on one side and is scored on the reverse. It contains 25 mg mesterolone.

Uses Androgen deficiency. Male infertility.

Pro-viron is an orally active androgen with properties quite distinct from those of older products. It offers unusual therapeutic possibilities because it can be given in high dosage over long periods. The presence of a methyl group at C-1 confers special properties on this steroid which, unlike testosterone and all its derivatives that are used for androgen therapy, is not metabolised to oestrogen.

This difference almost certainly accounts for the observation that in its usual therapeutic dosage in normal men, Pro-viron does not significantly depress the release of gonadotrophins from the pituitary. Hence (1) spermatogenesis is unimpaired. (2) unlike other androgens, which suppress and therefore replace endogenous androgens, Pro-viron supplements endogenous androgens.

Furthermore, in contrast to other orally active androgens, liver tolerance is excellent (a fact probably related to the absence of 17-alkyl substitution of the steroid nucleus).

Dosage and administration *Androgen deficiency:* Initially: 1 tablet three to four times daily, i.e. 75–100 mg daily for several months, followed by maintenance therapy of 2–3 tablets (50–75 mg) daily.

Male infertility: 100 mg daily for several months.

Contra-indications, warnings, etc

Contra-indications: In common with other androgens, Pro-viron is contra-indicated in the presence of prostatic carcinoma, since androgens can stimulate the growth of an existing carcinoma.

Warnings/side-effects: Reported side-effects have been rare, transient and minor. Regular examination of the prostate during treatment is advised, in order to exclude prostatic carcinoma.

Overdosage: There have been no reports of ill-effects from overdosage and treatment is generally unnecessary. If overdosage is discovered within two or three hours and is so large that treatment seems desirable, gastric lavage can safely be used.

There are no special antidotes and further treatment should be symptomatic.

Pharmaceutical precautions Store in cool, dry conditions, away from strong sunlight. Shelf-life five years.

Legal category POM.

Package quantities Bottles of 50 tablets.

Further information Nil.

Product licence number 0053/0030.

SCHERIPROCT* OINTMENT AND SUPPOSITORIES

Presentation Each white suppository contains:

Prednisolone hexanoate	1.3 mg
Dibucaine hydrochloride	1.0 mg
Clemizole undecylate	5.0 mg

A white ointment containing in 1 g:

Prednisolone hexanoate	1.9 mg
Dibucaine hydrochloride	5.0
Clemizole undecylate	10.0 mg

Uses Haemorrhoids, fissures, proctitis, pruritus ani and vulvae, and other inflammatory and allergic processes in the anal region.

Dosage and administration *Suppositories:* 1 Scheriproct Suppository to be inserted daily. In severe cases 1 suppository two to three times daily at the beginning of treatment. After complete disappearance of symptoms it is advisable to insert 1 suppository every second day for one further week. The suppositories should be inserted after defaecation.

Ointment: Apply in a thin layer twice daily. In order to obtain a more rapid improvement, Scheriproct Ointment may be applied three to four times on the first day. To avoid relapses, Scheriproct Ointment should be applied once a day for a few days after complete disappearance of the symptoms. The nozzle provided facilitates intra-rectal application.

Contra-indications, warnings, etc

Contra-indications: Viral infections. Bacterial or fungal infections of the skin in the absence of appropriate anti-infective therapy.

Warnings/side-effects: In infants, long-term continuous therapy with topical corticosteroids should be avoided. Adrenal suppression can occur, even without occlusion. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of these findings to human beings has not been established. However, topical steroids should not be used extensively during the first trimester of pregnancy, i.e. in large amounts or for prolonged periods. As with all topical steroids, there is a risk of developing skin atrophy following extensive therapy. The application of unusually large quantities of topical corticoids may result in the absorption of systemically active amounts of corticoid. Infections or secondarily infected dermatoses definitely require additional therapy with antibiotics or chemotherapeutic agents. This treatment can often be topical, but for heavy infections systemic antibacterial therapy may be necessary. If fungal infections are present, a topically active antimycotic should be applied.

Pharmaceutical precautions In order to restore the consistency of suppositories which have become soft owing to warm temperature, they should be put into cold water before the covering is removed.

Store in cool, dry conditions: shelf-life five years.

Legal category POM.

Package quantities *Suppositories:* Packs of 12.
Ointment: Tubes of 10 g.

Further information Nil.

Product licence numbers

Scheriproct Suppositories	0053/5001
Scheriproct Ointment	0053/5002

SH420*

Presentation Each uncoated, white tablet has AR in a regular hexagon impressed on one side, with quarter-scoring on the reverse. It contains 10 mg norethisterone acetate.

Uses Inoperable mammary carcinoma. As an adjunct to surgery and/or radiotherapy.

Note: Hormone therapy can never replace surgery or radiotherapy.

SH420 is a potent progestogen with a clinical efficacy which appears to be at least comparable to that of androgens and oestrogens in the treatment of inoperable mammary carcinoma. It does not, however, have the disadvantage of virilisation as with androgens and is unlikely to cause uterine bleeding as is the case with oestrogens. It may be used in the treatment of both pre- and post-menopausal women.

Although the mode of action of the various classes of hormone in inhibiting the growth of mammary carcinoma is not well understood, the very important role of the pituitary seems to be generally agreed on, as is shown by the response to pituitary ablation and hence to pituitary suppression by hormonal means.

SH420 is a powerful inhibitor of the pituitary. The effect of the progestogen may not depend wholly, however, on pituitary inhibition and it may be that an anti-oestrogenic effect as well as a direct effect on the tumour plays a part. Clinically SH420 has yielded subjective improvement (relief of pain and improvement in the general condition) and objective improvement (regression of tumour and/or bone and soft-tissue metastases).

Dosage and administration The recommended initial dosage of SH420 is 1 tablet three times a day (30 mg norethisterone acetate daily). If, after 6 weeks, no response is apparent, this can be increased to 2 tablets three times daily (60 mg daily).

Any remission obtainable should be apparent by the end of two months. If regression or arrest of tumour growth is obtained, treatment should be maintained as long as it continues to appear beneficial. If after about 9 weeks no response is apparent, none is to be expected and some other form of therapy should be tried.

Contra-indications, warnings, etc

Contra-indications:

Pregnancy. History of herpes gestationis.

Warnings/side-effects: The great advantage of SH420 over oestrogens and androgens is the almost complete freedom from side-effects.

Side-effects such as nausea, uterine bleeding and reversible cholestatic liver changes have occasionally been observed.

Overdosage: There have been no reports of ill-effects from overdosage and treatment is generally unnecessary. If overdosage is discovered within two or three hours and is so large that treatment seems desirable, gastric lavage can safely be used.

There are no special antidotes and further treatment should be symptomatic.

Pharmaceutical precautions Store in cool, dry

conditions, away from strong sunlight. Shelf-life five years.

gal category POM.

ckage quantities Bottles of 100 tablets.

rther information Nil.

oduct licence number 0053/5012.

.TRABASE*

esentation Ultrabase is a white oil-in-water cream for topical application.

omponents: Polyoxyl 40 stearate, white soft paraffin, liquid paraffin, stearyl alcohol, carbopol 934, sodium dioxido, methylhydroxybenzoate (methyl-paraben), propylhydroxybenzoate (propyl-paraben), disodium-ethylate, demineralised water, crematest perfume oil.

ses Ultrabase is intended for general use as an emollient and as a diluent for dermatological preparations and as a vehicle for other medicaments. Additionally, it may be alternated with topical corticosteroids when the latter are being gradually withdrawn, and may be continued after complete withdrawal of the topical corticosteroid.

usage and administration The cream should be rubbed into the skin as often as required.

ontra-indications, warnings, etc There are no specific contra-indications to the use of Ultrabase, other than a known allergy to any of the components.

side-effects: No side-effects have been reported.

pharmaceutical precautions Store in cool, dry conditions, away from strong sunlight: shelf-life five years.

gal category GSL.

ckage quantities Tubes containing 50 g. Jars containing 500 g.

rther information Ultrabase is suitable as a diluent for Schering's corticoid cream preparations and as a vehicle for coal tar solutions, urea, resorcinol, zinc oxide and precipitated sulphur.

oduct licence number 0053/0063.

.TRADIL* OINTMENT PLAIN AND

TEAM PLAIN

.TRALANUM* OINTMENT PLAIN AND

TEAM PLAIN

esentation White creams (oil-in-water emulsions) and ointments (water-in-oil emulsions) with the following ingredients.

tradil Ointment plain and Cream plain: 0.1% fluocortolone pivalate BP and 0.1% fluocortolone hexanoate BP.

tralanum Ointment plain: 0.25% fluocortolone and 0.25% fluocortolone hexanoate BP.

tralanum Cream plain: 0.25% fluocortolone pivalate BP and 0.25% fluocortolone hexanoate BP.

Ultradil plain and Ultralanum plain are dilute and full-strength preparations respectively of the corticoid, corticosterone, and its esters.

ses *Ultradil Cream and Ointment plain:* Most eczemas, dermatoses and other corticoid-responsive skin

conditions in the absence of infection. Ultradil is particularly indicated when the patient is young, the skin area large or the treatment schedule prolonged.

Ultralanum Cream and Ointment plain: More severe corticoid-responsive skin conditions in the absence of infection.

Dosage and administration *Ultradil plain: (ointment and cream):* The usual initial dosage is 1 application three times a day, reducing to 1 application twice daily.

For maintenance one application daily.

Ultralanum plain: (ointment and cream): Initially 2-3 applications daily, according to severity of condition. For maintenance one application daily.

Contra-indications, warnings, etc

Contra-indications: Rosacea and peri-oral dermatitis. Viral infections. Bacterial or fungal infections of the skin in the absence of appropriate anti-infective therapy. Not suitable for the treatment of ophthalmic conditions.

Warnings/side-effects: In infants long-term continuous therapy with topical corticosteroids should be avoided. Adrenal suppression can occur even without occlusion. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of these findings to human beings has not been established. However, topical steroids should not be used extensively during the first trimester of pregnancy, i.e. in large amounts or for prolonged periods. As with all topical steroids, there is a risk of skin atrophy following extensive therapy. The application of unusually large quantities of topical corticoids may result in the absorption of systemically active amounts of corticoid. Infections or secondarily infected dermatoses definitely require additional therapy with antibiotics or chemotherapeutic agents. This treatment can often be topical, but for heavy infections systemic antibacterial therapy may be necessary. If fungal infections are present, a topically active antimycotic should be applied.

Pharmaceutical precautions Store in cool, dry conditions, shelf-life five years.

Legal category POM.

Package quantities *Ultradil Ointment plain:* Tubes of 50 g and 100 g.

Ultradil Cream plain: Tubes of 50 g and 100 g.

Ultralanum Ointment plain: Tubes of 30 g and 50 g.

Ultralanum Cream plain: Tubes of 30 g and 50 g.

Further information Nil.

Product licence numbers

Ultradil Ointment plain 0053/5015

Ultradil Cream plain 0053/5017

Ultralanum Cream plain 0053/5011

Ultralanum Ointment plain 0053/5005

ULTRALANUM* OINTMENT

Presentation A white ointment (water-in-oil emulsion) containing 0.25% fluocortolone and with 0.25% fluocortolone hexanoate BP and 2.5% clemizole hexachlorophane.

Uses Corticoid-responsive skin conditions complicated by bacterial infection.

Dosage and administration Initially, 2-3 applications daily according to the severity of the condition. For maintenance, one application daily.

Contra-indications, warnings, etc

Contra-indications: Rosacea and peri-oral dermatitis. Viral infections. Bacterial or fungal infections of the skin in the absence of appropriate anti-infective therapy. Not suitable for ophthalmic conditions. Since Ultralanum Ointment contains hexachlorophane, it must not be used for babies.

Warnings/side-effects: In infants, long-term continuous therapy with topical corticosteroids should be avoided. Adrenal suppression can occur, even without occlusion. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of these findings to human beings has not been established. However, topical steroids should not be used extensively during the first trimester of pregnancy, i.e. in large amounts or for prolonged periods. As with all topical steroids, there is a risk of skin atrophy following extensive therapy. The application of unusually large quantities of topical corticoids may result in the absorption of systemically active amounts of corticoid. Infections or secondarily infected dermatoses definitely require additional therapy with antibiotics or chemotherapeutic agents. This treatment can often be topical, but for heavy infections systemic antibacterial therapy may be necessary. If fungal infections are present, a topically active antimycotic should be applied.

Pharmaceutical precautions Store in cool dry conditions: shelf-life five years.

Legal category POM.

Package quantities Tubes of 30 g and 50 g.

Further information Nil.

Product licence number 0053/5003.

ULTRAPROCT* OINTMENT ULTRAPROCT* SUPPOSITORIES

Presentation Each white suppository contains:

Fluocortolone pivalate BP	0.61 mg
Fluocortolone hexanoate BP	0.63 mg
Dibucaine hydrochloride	1.00 mg
Clemizole undecylate	5.00 mg

A white ointment containing in 1 g:

Fluocortolone pivalate BP	0.92 mg
Fluocortolone hexanoate BP	0.95 mg
Dibucaine hydrochloride	5.00 mg
Clemizole undecylate	10.00 mg

Uses Haemorrhoids, fissures, proctitis, pruritus ani and vulvae, and other inflammatory and allergic processes in the anal region.

Dosage and administration *Suppositories:* 1 Ultraproct Suppository to be inserted daily. In severe cases 1 suppository two to three times daily at the beginning of treatment. After complete disappearance of symptoms, it is advisable to insert one suppository every second day for one further week. The suppositories should be inserted after defaecation.

Ointment: Apply in a thin layer twice daily. In order to obtain a more rapid improvement, Ultraproct Ointment may be applied three or four times on the first day. To avoid relapses, Ultraproct Ointment should be applied once a day for a few days after complete disappearance

of the symptoms. The nozzle provided facilitates intrarectal application.

Contra-indications, warnings, etc

Contra-indications: Viral infections. Bacterial or fungal infections of the skin in the absence of appropriate anti-infective therapy.

Warnings/side-effects: In infants, long-term continuous therapy with topical corticosteroids should be avoided. Adrenal suppression can occur even without occlusion. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of these findings to human beings has not been established. However topical steroids should not be used extensively during the first trimester of pregnancy, i.e. in large amounts or for prolonged periods. As with topical steroids, there is a risk of skin atrophy following extensive therapy. The application of unusually large quantities of topical corticoids may result in the absorption of systemically active amounts of corticoid. Infections or secondarily infected dermatoses definitely require additional therapy with antibiotics or chemotherapeutic agents. This treatment can often be topical but for heavy infections systemic antibacterial therapy may be necessary. If fungal infections are present, a topically active antimycotic should be applied.

Pharmaceutical precautions In order to restore consistency of suppositories which have become soft owing to warm temperature, they should be put into cold water before the covering is removed.

Store in cool dry conditions: shelf-life five years.

Legal category POM.

Package quantities *Suppositories:* Packs of 12.

Ointment: Tubes of 10 g and 30 g.

Further information Nil.

Product licence numbers

Ultraproct Suppositories	0053/5009
Ultraproct Ointment	0053/5008

UROGRAFIN*

Presentation Ampoules, vials or bottles contain colourless sterile solutions of varying strengths: meglumine diatrizoate and meglumine/sodium diatrizoates.

Urografin 150: An intravenous injection of meglumine diatrizoate 26.1% w/v and sodium diatrizoate 3.9% w/v containing 146 mg iodine per ml.

Urografin 290: An intravascular injection of meglumine diatrizoate 52.1% w/v and sodium diatrizoate 7.9% w/v containing 292 mg iodine per ml.

Urografin 310M: An intravascular injection of meglumine diatrizoate 65% w/v, containing 306 mg iodine per ml.

Urografin 325: An intravenous injection of meglumine diatrizoate 18% w/v and sodium diatrizoate 40% w/v containing 325 mg iodine per ml.

Urografin 370: An intravascular injection of meglumine diatrizoate 66% w/v and sodium diatrizoate 10% w/v containing 370 mg iodine per ml.

Uses X-ray contrast media for the delineation of vascular and renal systems.

Dosage and administration See table on pages 9 and 983.

Contra-indications, warnings, etc

Contra-indications: Proven or suspected hypersensitivity to iodine-containing contrast media, manifest thyrotoxicosis and decompensated cardiac insufficiency.

Hysterosalpingography must not be carried out during pregnancy or in patients with acute inflammatory conditions in the pelvic cavity.

Warnings/side-effects: For patients with severe impairment of hepatic or renal function, cardiac or circulatory sufficiency, cerebral arterial sclerosis, epilepsy, poor general health, hyperthyroidism or multiple myeloma the need for examination with X-ray contrast media merits careful consideration.

This also applies to patients with a history of allergy, e.g. bronchial asthma, since experience shows that they may exhibit hypersensitivity to drugs. Because of possible precipitation, X-ray contrast media and prophylactic agents must not be injected as mixed solutions.

Particular caution should be exercised in allergic persons who have previously tolerated an injectable iodine-containing contrast medium without any complication because they may have become sensitized to these substances in the meantime.

The patient should be recumbent during the administration of Urografin. Thereafter, the patient must be kept under close observation for at least 15 minutes, since about 90% of all severe incidents occur within that time. The administration does not take place on the X-ray table, any patient with a labile circulation should be brought to the X-ray machine sitting or lying down.

In patients with multiple myeloma the fluid supply could not be restricted. This also applies to infants and young children, in whom disturbances of the balance of water and electrolytes must be corrected before the administration of a hypertonic contrast medium solution. X-ray examinations should if possible be avoided during pregnancy. It has not yet been proved beyond question that Urografin may be used without hesitation in pregnant patients. Therefore an examination with a contrast medium during pregnancy should be carried out only if considered absolutely necessary by the physician.

If iodine isotopes are to be administered for diagnosing thyroid disease, it should be borne in mind that after the administration of iodised contrast media which are excreted via the kidneys, the capacity of the thyroid tissue to take up iodine will be reduced for a few days, and sometimes up to 6 weeks.

Mild subjective symptoms, such as a feeling of heat and nausea, occur very seldom and disappear rapidly when the injection is slowed down or briefly interrupted. Persistent pain may occur, in particular during the

examination of peripheral vascular regions. Extravasations give rise to serious tissue reactions only in very rare cases.

If marked side-effects or suspected allergic reactions occur during injection and do not disappear, or even get worse, when the injection is briefly interrupted, it is probable that the patient has such a hypersensitivity and the investigation must be abandoned. Even relatively minor symptoms such as itching of the skin, sneezing, violent yawns, tickling in the throat, hoarseness or attacks of coughing may be early signs of a severe reaction and, therefore, merit careful attention.

Very rarely, severe or even life-threatening side-effects such as severe hypotension and collapse, circulatory failure, ventricular fibrillation, cardiac arrest, pulmonary oedema, anaphylactic shock or other allergic manifestations, convulsions, or other cerebral symptoms may occur.

Ready availability of all drugs and equipment for emergency treatment and familiarity with the respective procedures are prerequisites for the effective management of contrast-medium incidents. Some guidance in the treatment of such incidents is contained in the leaflet supplied with the pack.

Pharmaceutical precautions *Storage:* Protect from light and heat. Shelf-life five years.

Legal category POM.

Package quantities

Urografin 150: Packs of 4 × 5 × 10 ml ampoules.

Urografin 150 for Infusion: Packs of 1 × 250 ml bottles.

Urografin 290: Packs of 4 × 5 × 20 ml ampoules and 4 × 5 × 50 ml vials.

Urografin 310M: Packs of 4 × 5 × 20 ml ampoules and 4 × 5 × 50 ml vials.

Urografin 325: Packs of 4 × 5 × 20 ml ampoules and 4 × 5 × 50 ml vials.

Urografin 370: Packs of 4 × 5 × 20 ml ampoules and 4 × 5 × 50 ml vials. In addition packs of 1 × 100 ml vials and 1 × 200 ml vials.

Further information Nil.

Product licence numbers

Urografin 150	0053/5041
Urografin 150 for infusion	0053/5007
Urografin 290	0053/5043
Urografin 310M	0053/5018
Urografin 325	0053/5006
Urografin 370	0053/5044

UROGRAFIN MEDIA – DOSAGE AND ADMINISTRATION**Adults only**

The table below shows the medium/media Schering suggest for each investigation. Alternative medium/media (shown by asterisk) may be used in the same dose. Schering media may be used at the discretion of the radiologist or other established permutations of medium and examination which, for the sake of simplicity, have been omitted from the table.

Examination	150	290	310M	325	370
Intravenous urography		Up to 70 ml	Up to 70 ml	Up to 70 ml	
High-dose urography		100 ml	100 ml	100 ml	
Infusion urography	2–4 ml/kg body wt up to 250 ml				

[cont.]

Examination	150	290	310M	325	370
Retrograde urography	5–10 ml				
Cystography	Up to 400 ml				
Angiocardiography			*		30–50 ml
Right-heart catheterisation			*		40–80 ml
Left-heart catheterisation			*		40–60 ml
Pulmonary angiography			*		30–40 ml
Coronary arteriography			DO NOT USE		4–8 ml per artery ^a
Renal arteriography		*	5–8 ml		*
Coeliac-axis arteriography		*	35–50 ml		*
Superior mesenteric arteriography		*	20–30 ml		
Inferior mesenteric arteriography		*	15–20 ml		
Peripheral arteriography (leg)		*	15–25 ml		
Peripheral arteriography (arm)					
Subclavian			20 ml		
Axillary			15 ml		
Brachial			10 ml		
Hepatic arteriography		*	25 ml		
Thoracic aortography			*		
Percutaneous retrograde abdominal aortography		*	25–30 ml. No more than 2 inj.		30–60 ml
Pelvic aortography			*		20–25 ml
Lower limb aortography		*	35–50 ml		
Translumbal abdominal aortography			*		20–30 ml
Placentography			25 ml		*
Carotid angiography (internal)			8–10 ml		
Carotid angiography (external)			6–8 ml.		
			Not more than 3 inj. per artery		
Vertebral angiography			6 ml. Not more than 2 inj. per vessel		
Pelvic venography			25–30 ml	*	
Venacavography					
Inferior			30–50 ml	*	
Superior			25–35 ml	*	
Renal venography		*	10–15 ml		
Peripheral venography					
Leg			30–50 ml		
Arm			20–30 ml per injection		
Splenoportography			40–50 ml		40–50 ml
Splenoportography – indirect		*	30–50 ml		
			Higher doses required to demonstrate splenic and portal veins		
Hysterosalpingography			*		4–7 ml
Arthrography		*		1–10 ml	
Percutaneous cholangiography		20–30 ml			

^a100 ml and 200 ml vials are available for coronary arteriography

(Other indications include selective visceral angiography, limb venography, jugular venography, vesiculography, sialography, sinusography, amniography, lymphangiography, intramuscular urography, operative cholangiography, fistulography, oesophageal anal atresia.)

Urografin media are not suitable for myelography

Children and neonates

Intravenous urography: The fact that urograms of infants and young children generally show a lower contrast density than those of adults is explained by the physiologically less effective function of the immature nephron. Relatively high doses of media are therefore indicated.

	<i>Urografin 310M/290</i>		<i>Urografin 325/370</i>
Up to 1 year	8–12 ml	Up to 1 year	7–10 ml
–2 years	12–15 ml	1–2 years	10–12 ml
–6 years	15–20 ml	2–6 years	12–15 ml
–10 years	20–25 ml	6–12 years	15–20 ml
–15 years	25–30 ml	over 12 years	adult dose

Drip-infusion urography: Dosage of Urografin 150 should not exceed 4 ml/kg body weight.

Angiocardiography: In neonates up to 5 kg body weight, 8 ml of Urografin 310M or Urografin 370. Infants over 5 kg body weight, 1 ml/kg body weight up to 25 ml per injection.

Right and left-heart catheterisation: 1–1.2 ml/kg body weight of Urografin 310M or Urografin 370, with a maximum of 15 ml per injection for the right heart and 25 ml per injection for the left heart.

Pulmonary angiography: 0.5–0.6 ml/kg body weight up to 8 ml Urografin 310M or Urografin 370 per injection.

**Trade Mark*

Searle Pharmaceuticals
Lane End Road
High Wycombe
Bucks HP12 4HL

SEARLE

ALDACTIDE® 50
ALDACTIDE® 25

Presentation *Aldactide 50:* Buff, film-coated tablets engraved SEARLE 180 on one side containing Spironolactone BP 50 mg and Hydroflumethiazide BP 50 mg.

Aldactide 25: Buff, film-coated, scored tablets engraved SEARLE 101 on one side containing Spironolactone BP 25 mg and Hydroflumethiazide BP 25 mg.

Uses Hypertension. Congestive heart failure.

Dosage and administration *Adults: Essential hypertension:* Aldactide 50 – 1 or 2 tablets with breakfast or the first main meal of the day.

Aldactide 25 – 1 to 4 tablets with breakfast or the first main meal of the day.

Congestive heart failure: The requirements of most patients will be met by an initial dosage of 4 tablets Aldactide 25 or 2 tablets Aldactide 50 daily. The dosage should be adjusted as necessary and may range from 1 tablet Aldactide 25 to 8 tablets Aldactide 25 or 4 tablets Aldactide 50 daily.

Children: Although clinical trials using Aldactide have not been carried out in children, as a guide, a daily dosage providing 1.5 to 3 mg of spironolactone per kilogram body weight, given in divided doses, may be employed.

Contra-indications, warnings, etc Aldactide is contra-indicated in patients with anuria, acute renal insufficiency, rapidly progressing impairment of renal function, hyperkalaemia and in patients who are hypersensitive to either component. Aldactide should not be administered concurrently with other potassium-conserving diuretics as hyperkalaemia may be induced. For the same reason the use of potassium supplements in association with Aldactide therapy is also not recommended, except in cases of initial potassium depletion. If potassium supplementation is considered essential, serum electrolytes should be monitored.

Carcinogenicity: Spironolactone has been shown to produce tumours in rats when administered at high doses over a long period of time. The significance of these findings with respect to clinical use is not certain. However the long term use of spironolactone in young patients requires careful consideration of the benefits and the potential hazard involved.

Precautions: Patients receiving Aldactide therapy should be carefully evaluated for possible disturbances of fluid and electrolyte balance.

Hyperkalaemia may occur in patients with impaired renal function or excessive potassium intake and can cause cardiac irregularities which may be fatal. Should hyperkalaemia develop Aldactide should be discontinued, and if necessary, active measures taken to reduce the serum potassium to normal.

Hypokalaemia may develop as a result of profuse diuresis, particularly when Aldactide is used concurrently with loop diuretics, glucocorticoids or ACTH.

Caution should be observed in patients with severe liver disease as overvigorous diuretic therapy precipitate encephalopathy in susceptible patients. Periodic estimation of serum electrolytes is desirable.

Reversible increases in blood urea have been reported particularly accompanying vigorous diuresis or in presence of impaired renal function.

Dilutional hyponatraemia may be induced, especially when Aldactide is administered in combination with other diuretics.

Thiazides may cause hyperuricaemia and precipitate attacks of gout in some patients.

Thiazides may aggravate existing diabetes. Diabetes mellitus which has been latent may become manifest during thiazide administration.

Drug interactions: Potentiation of the effect of certain antihypertensive drugs occurs and their dosage need to be reduced by about 50% when Aldactide is added to the treatment regime, and then adjusted as necessary.

Pregnancy: Spironolactone or its metabolites may, hydroflumethiazide does, cross the placental barrier. Use of Aldactide in pregnant women requires that anticipated benefit be weighed against the possible hazards to the mother and foetus. These hazards include foetal or neonatal jaundice, thrombocytopenia, possibly other adverse effects that have been reported in adults.

Nursing mothers: Canrenone, a metabolite of spironolactone, and hydroflumethiazide appear in breast milk. Use of Aldactide is considered essential, an alternative method of infant feeding should be instituted.

Adverse effects: Gynaecomastia may develop in association with the use of spironolactone. Development appears to be related to both dosage level and duration of therapy and is normally reversible when Aldactide is discontinued. Other adverse reactions reported in association with spironolactone include: gastrointestinal intolerance, drowsiness, headache, mental confusion, skin rashes, menstrual irregularities, impotence and androgenic effects. Adverse reactions reported in association with thiazides include: gastrointestinal upset, skin rashes, blood dyscrasias, muscle cramps, headache, dizziness, vertigo, jaundice, orthostatic hypotension, impotence and paraesthesia. Rarely, hyperkalaemia has been reported in association with thiazides, usually in patients with pre-existing metabolic bone disease or parathyroid dysfunction.

Overdosage: Acute overdosage may be manifested by drowsiness, mental confusion, nausea, vomiting, diarrhoea or diarrhoea. Hyponatraemia, hypokalaemia, hyperkalaemia may be induced, or hepatic coma may be precipitated in patients with severe liver disease,

associated with acute
haemia may manifest
paralysis or muscle
wasting clinically from

is the earliest specific
No specific antidote
may be expected after
supportive measures
and electrolytes may be

Aldactide should be

50: Calendar pack of
100 and 500 tablets.
100 and 500 tablets.

Chlorthalidone induces
which lasts for 12-18

is an aldosterone antag-
onist whilst reducing potas-
sium. It has a gradual and
onset being usually

100 mg: Buff, film-coated
tablets, one side, containing

100 mg tablets engraved
with 100 mg Spironolactone BP

hepatic cirrhosis with
ascites; Nephrotic syn-
drome including premenstrual
oedema of primary aldoster-

Adults: Congestive
heart failure. In difficult or
gradually increased up-
take controlled, the usual
dose.

Idiopathic oedema: If urinary
output 100 mg per day. If the
output 100 mg/day. Maintenance
dose 100-200 mg.

usually 100-200 mg. In
gradually increased up-
take controlled, mainte-
nance determined.

100-200 mg/day.
It is an anti-inflam-
matory process. Its
effects by themselves are

Idiopathic oedema including premenstrual oedema:
Usual dose - 100 mg/day.

Diagnosis and treatment of primary aldosteronism:
Aldactone may be employed as an initial diagnostic
measure to provide presumptive evidence of primary
hyperaldosteronism while patients are on normal diets.

Long test: Aldactone is administered at a daily dosage of
400 mg for three to four weeks. Correction of hypoka-
laemia and of hypertension provides presumptive evi-
dence for the diagnosis of primary hyperaldosteronism.

Short test: Aldactone is administered at a daily dosage
of 400 mg for four days. If serum potassium increases
during Aldactone administration but drops when Aldac-
tone is discontinued, a presumptive diagnosis of primary
hyperaldosteronism should be considered.

After the diagnosis of hyperaldosteronism has been
established by more definitive testing procedures, Al-
dactone may be administered in doses of 100 mg to
400 mg daily in preparation for surgery. For patients who
are considered unsuitable for surgery, Aldactone may be
employed for long-term maintenance therapy at the
lowest effective dosage determined for the individual
patient.

Essential hypertension: Usual dose - 50-100 mg per
day, which for difficult or severe cases may be gradually
increased at two weekly intervals up to 200 mg/day.

Treatment should be continued for two weeks or
longer since an adequate response may not occur before
this time. Dosage should subsequently be adjusted
according to the response of the patient.

Children: Initial daily dosage should provide 3 mg of
spironolactone per kilogram body weight, given in
divided doses. Dosage should be adjusted on the basis
of response and tolerance. If necessary a suspension
may be prepared by crushing Aldactone tablets. A
suitable suspending vehicle is Cologel® 20% v/v, purified
water to 100%. Such a suspension is stable for one
month when refrigerated.

Contra-indications, warnings, etc Aldactone is
contra-indicated in patients with anuria, acute renal
insufficiency, rapidly progressing impairment of renal
function, hyperkalaemia, and in patients who are hyper-
sensitive to spironolactone. Aldactone should not be
administered concurrently with other potassium-con-
serving diuretics as hyperkalaemia may be induced. For
the same reason the use of potassium supplements in
association with Aldactone therapy is also not recom-
mended, except in cases of initial potassium depletion.
If potassium supplementation is considered essential,
serum electrolytes should be monitored.

Carcinogenicity: Spironolactone has been shown to
produce tumours in rats when administered at high doses
over a long period of time. The significance of these
findings with respect to clinical use is not certain.
However the long-term use of spironolactone in young
patients requires careful consideration of the benefits
and the potential hazard involved.

Precautions: Patients receiving Aldactone therapy
should be carefully evaluated for possible disturbances
of fluid and electrolyte balance.

Hyperkalaemia may occur in patients with impaired
renal function or excessive potassium intake and can
cause cardiac irregularities which may be fatal. Should
hyperkalaemia develop Aldactone should be discontin-
ued, and if necessary, active measures taken to reduce
the serum potassium to normal.

Reversible increases in blood urea have been reported in association with Aldactone therapy, particularly in the presence of impaired renal function.

Dilutional hyponatraemia may be induced, especially when Aldactone is administered in combination with other diuretics.

Drug interactions: Potentiation of the effect of other antihypertensive drugs occurs and their dosage may need to be reduced by about 50% when Aldactone is added to the treatment regime, and then adjusted as necessary.

Pregnancy: Spironolactone or its metabolites may cross the placental barrier. The use of Aldactone in pregnant women requires that the anticipated benefit be weighed against the possible hazards to the mother and foetus.

Nursing mothers: Canrenone, a metabolite of spironolactone, appears in breast milk. If use of Aldactone is considered essential, an alternative method of infant feeding should be instituted.

Adverse effects: Gynaecomastia may develop in association with the use of spironolactone. Development appears to be related to both dosage level and duration of therapy and is normally reversible when Aldactone is discontinued. Other adverse reactions reported in association with spironolactone include: gastrointestinal intolerance, drowsiness, headache, mental confusion, skin rashes, menstrual irregularities, impotence and mild androgenic effects.

Overdosage: Acute overdosage may be manifested by drowsiness, mental confusion, nausea, vomiting, dizziness or diarrhoea. Hyponatraemia or hyperkalaemia may be induced but these effects are unlikely to be associated with acute overdosage. Symptoms of hyperkalaemia may manifest as paraesthesia, weakness, flaccid paralysis or muscle spasm and may be difficult to distinguish clinically from hypokalaemia. Electrocardiographic changes are the earliest specific signs of potassium disturbances. No specific antidote has been identified. Improvement may be expected after withdrawal of the drug. General supportive measures including replacement of fluids and electrolytes may be indicated. For hyperkalaemia, reduce potassium intake, administer potassium-excreting diuretics, intravenous glucose with regular insulin, or oral ion-exchange resins.

Pharmaceutical precautions Aldactone should be stored in a cool, dry place.

Legal category POM.

Package quantities *Aldactone 100 mg:* Calendar pack of 28 tablets and bottles containing 100 and 500 tablets.

Aldactone 25 mg: Bottles containing 100 and 500 tablets.

Further information Aldactone as a competitive aldosterone antagonist increases sodium excretion whilst reducing potassium loss at the distal renal tubule. It has a gradual and prolonged action, maximum response being usually attained after 2-3 days' treatment.

Combination of Aldactone with a conventional, more proximally acting diuretic usually enhances diuresis without excessive potassium loss.

Product licence numbers

Aldactone 100 mg 0020/0048

Aldactone 25 mg 0020/5000

CONOVA* 30

Presentation White, film-coated tablets engraved SEARLE 930 on one side containing Ethynodiol Diacetate BP 2 mg and Ethinyloestradiol PhEur 0.03 mg.

Uses Oral contraception.

Dosage and administration One tablet daily for days, starting on Day 5 of the menstrual cycle (whilst Day 1 is the first day of bleeding). The next course of tablets should be started after seven tablet-free days. This 'three weeks on, one week off' regimen is continued for as long as contraception is required. Patients should be advised to use an additional form of contraception during the first 14 days of the first pack.

Missed tablets: Patients who miss a single tablet should be instructed to take the missed tablet as soon as they remember, even though this may mean taking two tablets on one single day. The regular tablet for that day should be taken at the usual time. An additional method of contraception (a sheath or a cap plus spermicide) should be used for the remainder of the cycle. If two consecutive tablets are missed, patients should be instructed to take two tablets each day for the next two days and use an additional method of contraception for the rest of the cycle. Those who miss more than two tablets should resume as soon as they remember, ignoring the tablets they have missed, and should use additional contraceptive precautions for the rest of the cycle.

Contra-indications, warnings, etc The contra-indications for combined oral contraceptives are: thrombophlebitis, thromboembolic disorders, cerebral vascular disease, myocardial infarction, coronary artery disease or a past history of these conditions, known, suspected or a past history of breast, genital or hormone dependent cancer; past or present, benign or malignant liver tumours; impaired liver function; active liver disease disorders of lipid metabolism; haemoglobinopathies, undiagnosed abnormal vaginal bleeding or amenorrhoea known or suspected pregnancy.

It has been established that the use of combined oral contraceptives is associated with an increase in the risk of thromboembolic and thrombotic disease.

Recent studies have indicated that combined oral contraceptives may be associated with an increased risk of myocardial infarction. The risk of arterial thrombosis associated with combined oral contraceptives increases with age, and this risk is aggravated by cigarette smoking. The use of combined oral contraceptives by women in the older age group, especially those who are cigarette smokers, should therefore be discouraged, and alternative methods advised.

Conova 30 should be discontinued at least six weeks before elective surgery or during periods of prolonged immobilisation. It would be reasonable to resume combined oral contraceptives two or three weeks after surgery provided the patient is ambulant. Every patient, however, should be considered individually with regard to the nature of the operation, the extent of immobilisation, the presence of additional risk factors and the chance of unwanted conception.

Discontinue treatment if there is a gradual or sudden partial or complete loss of vision or any evidence of ocular changes, onset or aggravation of migraine development of headache of a new kind which is recurrent, persistent or severe.

Patients with a history of jaundice during pregnancy

ve an increased risk of recurrence. Discontinue Conova 30 if jaundice occurs.

Precautions: Patients receiving treatment with oestrogen progestogen or both, should be kept under regular surveillance.

Caution should be exercised where there is the possibility of an interaction between a pre-existing disorder and a known or suspected side-effect. The use of Conova 30 in patients suffering from epilepsy, or with a history of migraine, or cardiac dysfunction may result in exacerbation of these disorders, because of fluid retention. Caution should also be observed in patients who wear contact lenses, patients with impaired carbohydrate tolerance, hypertension, asthma, varicose veins, any disease that is prone to worsen during pregnancy, and in young patients in whom the growth period has not yet ended.

Vomiting or diarrhoea may reduce the effectiveness of the tablets, particularly if this should occur at or around the time of ovulation.

Drug interactions: Conova 30 may be rendered less effective and increased incidence of breakthrough bleeding may occur by virtue of drug interaction with imipenem, isoniazid, ampicillin, neomycin, penicillin V, loramphenicol, sulphonamides, nitrofurantoin, barbiturates, phenytoin, primidone, anti-arthritics, analgesics, tranquilisers and anti-migraine preparations. Conova 30 may alter the effectiveness of other types of drugs, such as oral anticoagulants, anticonvulsants, tricyclic antidepressants, antihypertensive agents (e.g. guanethidine), aminoglycosides and hypoglycaemic agents. Therefore, the possibility of a drug interaction occurring in patients on any of these therapeutic agents should be considered when prescribing Conova 30.

Breast-feeding mothers: Active ingredients of oral contraceptives have been detected in the milk of mothers taking these drugs. The effect of Conova 30 on breast-fed infants has not been determined.

Adverse effects: Known or suspected side-effects of oral contraceptives include nausea, vomiting, other gastrointestinal symptoms, irregular vaginal bleeding, amenorrhoea, certain skin disorders, chloasma, breast and weight changes, ocular changes, headache, hypertension, migraine, depression, change in libido and appetite, increase in the size of uterine myofibromata, fluid retention, infertility after discontinuation, and changes in carbohydrate, lipid and vitamin metabolism.

Tests of endocrine, hepatic and thyroid function, as well as coagulation tests, may be affected by this preparation.

The use of oral contraceptives has also been associated with a possible increased incidence of gallbladder disease.

Benign hepatic adenomas, although rare, have been reported with long-term use of oral contraceptives.

Overdosage: Fatal overdosage has not been reported. Overdosage may be manifested by nausea, vomiting, breast engorgement and vaginal bleeding. Gastric lavage may not be necessary but demulcents such as milk, egg white or bismuth hydroxide may be helpful.

Pharmaceutical precautions Conova 30 should be stored in a cool dry place.

Legal category POM.

Packaging quantities Carton containing one strip of 21 tablets, with instructions.

Further information Conova 30 provides effective, low oestrogenic contraception in a form acceptable to most women. It is particularly suitable for new patients or patients switching from another oral contraceptive. Patients switching in this way should start Conova 30 seven days after finishing their current pack.

Product licence number 0020/0066.

DIATENSEC®

Presentation Off-white, film coated tablets engraved SEARLE 916. Each tablet contains Spironolactone BP 50 mg.

Uses Essential hypertension and hypertension associated with diabetes.

Dosage and administration *Adults:* Usual dose – 50–100 mg per day, which for difficult or severe cases may be gradually increased at two weekly intervals up to 200 mg/day.

Treatment should be continued for two weeks or longer since an adequate response may not occur before this time. Dosage should subsequently be adjusted according to the response of the patient.

Children: Initial daily dose should provide 3 mg of spironolactone per kilogram body weight, given in divided doses. Dosage should be adjusted on the basis of response and tolerance. If necessary a suspension may be prepared by crushing Diatensec tablets.

Contra-indications, warnings, etc Diatensec is contra-indicated in patients with anuria, acute renal insufficiency, rapidly progressing impairment of renal function, hyperkalaemia, and in patients who are hypersensitive to spironolactone. Diatensec should not be administered concurrently with other potassium-conserving diuretics as hyperkalaemia may be induced. For the same reason the use of potassium supplements in association with Diatensec therapy is also not recommended, except in cases of initial potassium depletion. If potassium supplementation is considered essential, serum electrolytes should be monitored.

Carcinogenicity: Spironolactone has been shown to produce tumours in rats when administered at high doses over a long period of time. The significance of these findings with respect to clinical use is not certain. However the long term use of spironolactone in young patients requires careful consideration of the benefits and the potential hazard involved.

Precautions: Patients receiving Diatensec therapy should be carefully evaluated for possible disturbances of fluid and electrolyte balance.

Hyperkalaemia may occur in patients with impaired renal function or excessive potassium intake and can cause cardiac irregularities which may be fatal. Should hyperkalaemia develop, Diatensec should be discontinued, and if necessary, active measures taken to reduce the serum potassium to normal.

Reversible increases in blood urea have been reported in association with Diatensec therapy, particularly in the presence of impaired renal function.

Dilutional hyponatraemia may be induced, especially when Diatensec is administered in combination with other diuretics.

Drug Interactions: Potentiation of the effect of other antihypertensive drugs occurs and their dosage may

need to be reduced by about 50% when Diatensec is added to the treatment regime, and then adjusted as necessary.

Pregnancy: Spironolactone or its metabolites may cross the placental barrier. The use of Diatensec in pregnant women requires that the anticipated benefit be weighed against the possible hazards to the mother and foetus.

Nursing mothers: Canrenone, a metabolite of spironolactone, appears in breast milk. If use of Diatensec is considered essential, an alternative method of infant feeding should be instituted.

Adverse effects: Gynaecomastia may develop in association with the use of spironolactone. Development appears to be related to both dosage level and duration of therapy and is normally reversible when Diatensec is discontinued. Other adverse reactions reported in association with spironolactone include: gastrointestinal intolerance, drowsiness, headache, mental confusion, skin rashes, menstrual irregularities, impotence and mild androgenic effects.

Overdosage: Acute overdosage may be manifested by drowsiness, mental confusion, nausea, vomiting, dizziness or diarrhoea. Hyponatraemia or hyperkalaemia may be induced but these effects are unlikely to be associated with acute overdosage. Symptoms of hyperkalaemia may manifest as paraesthesia, weakness, flaccid paralysis or muscle spasm and may be difficult to distinguish clinically from hypokalaemia. Electrocardiographic changes are the earliest specific signs of potassium disturbances. No specific antidote has been identified. Improvement may be expected after withdrawal of the drug. General supportive measures including replacement of fluids and electrolytes may be indicated. For hyperkalaemia, reduce potassium intake, administer potassium-excreting diuretics, intravenous glucose with regular insulin, or oral ion-exchange resins.

Pharmaceutical precautions Diatensec should be stored in a cool, dry place.

Legal category POM.

Package quantities Bottles containing 100 tablets.

Further information Diatensec as a competitive aldosterone antagonist increases sodium excretion whilst reducing potassium loss at the distal renal tubule. It has a gradual and prolonged action, maximum response being usually attained after 2-3 days' treatment. Combination of Diatensec with a conventional, more proximally acting diuretic usually enhances diuresis without excessive potassium loss.

Product licence number 0020/0089.

DRAMAMINE*

Presentation Yellow, scored tablets engraved SEARLE on one side. Each tablet contains Dimenhydrinate BP 50 mg.

Uses Motion sickness. Vertigo, nausea and vomiting associated with Ménière's disease and other labyrinthine disorders.

Dosage and administration For prevention of motion sickness the first dose should be taken 30 minutes before the journey.

Adults and children over 12 years: 1-2 tablets two or three times daily.

Children: 1-6 years: $\frac{1}{4}$ - $\frac{1}{2}$ tablet two or three times daily
7-12 years: $\frac{1}{2}$ -1 tablet two or three times daily.

Contra-indications, warnings, etc Dramamine contra-indicated in patients with a hypersensitivity to dimenhydrinate, diphenhydramine and other antihistamines of similar chemical structure. May cause drowsiness. Patients affected in this way should not drive or operate machinery.

Precautions: Dramamine may mask ototoxic symptom associated with certain antibiotics.

Patients should be advised to avoid alcoholic drinks

Drug Interactions: In common with other antihistamines Dramamine may potentiate the sedative effects of CNS depressants including alcohol, barbiturates, narcotic analgesics, tranquillisers, and may enhance the effect of anticholinergics such as atropine and tricyclic antidepressants.

Pregnancy: The use of Dramamine in pregnant women requires that the benefits of therapy be weighed against the possible hazards to the mother and foetus.

Nursing mothers: Diphenhydramine, a metabolite of dimenhydrinate, has been detected in breast milk. The benefits of therapy should be weighed against the possible hazards to the child.

Adverse effects: Sedation is the most commonly reported. Gastrointestinal disturbances such as nausea and vomiting and atropine-like effects may be associated with antihistamines. Occasionally allergy and anaphylaxis have been reported.

Overdosage: The anticholinergic effects of antihistamines are most prominent in cases of mild poisoning with dryness of the mouth, headache, nausea, tachycardia and urinary retention. In massive overdosage the central effects of antihistamines may both stimulate and depress the nervous system. In infants and children symptoms of overdosage may include convulsion, hallucinations, excitement, incoordination, fixed dilated pupils, a flushed face and hyperthermia. Subsequent coma and respiratory depression may develop. Symptoms of stimulation may also arise in adults. Treatment should consist of gastric aspiration and lavage and supportive measures. Diazepam may be required for the treatment of convulsions.

Pharmaceutical precautions Dramamine may be powdered and dissolved in any acceptable aqueous fluid medium, provided that a concentration of 3 mg/ml is not exceeded. Above this concentration not all of the active constituent may dissolve.

Dramamine should be stored in a cool dry place.

Legal category P.

Package quantities Bottles containing 100 and 50 tablets.

Further information Nil.

Product licence number 0020/5011.

FEMULEN*

Presentation White tablets engraved SEARLE on both sides, containing Ethynodiol Diacetate BP 0.5 mg

Uses Oral contraception.

Dosage and administration Starting on the first day of menstruation, 1 tablet every day, without a break in

indication for as long as contraception is required. If Femulen is being taken for the first time, additional contraceptive precautions should be taken for the first 7 days of the first pack. Tablets should be taken at the same time each day.

Missed tablets: If the patient misses one tablet or takes later than the usual time, contraceptive efficacy may be reduced and additional contraceptive precautions (a condom or a cap plus spermicide) should be taken until the next period occurs. Patients who miss a single tablet should be instructed to take the missed tablet as soon as they remember, even though this may mean taking two tablets on one single day. The regular tablet for that day should be taken at the usual time. If two or more consecutive tablets are missed, Femulen should be discontinued and alternative contraceptive measures should be taken until menstruation occurs and the possibility of pregnancy is excluded.

Contra-indications, warnings, etc. The contra-indications for progestogen-only contraceptives are: known, suspected, or a past history of breast, genital or hormone dependent cancer; past or present, benign or malignant liver tumours; impaired liver function; active liver disease; disorders of lipid metabolism; undiagnosed abnormal vaginal bleeding or amenorrhoea; known or suspected pregnancy.

It has been established that the use of combined oestrogen/progestogen preparations is associated with an increase in the risk of thromboembolic and thrombotic disease. Although from these studies it has not yet been possible to evaluate the involvement of the progestogen component, it is at present required that the existence, a history of thrombophlebitis, thromboembolic disorders, cerebral vascular disease, myocardial infarction, coronary artery disease or a haemoglobinopathy be described as a contra-indication to Femulen, as it is to oestrogen-containing oral contraceptives.

Discontinue treatment if there is a gradual or sudden, partial or complete loss of vision or any evidence of ocular changes, onset or aggravation of migraine or development of headache of a new kind which is current, persistent or severe.

Patients with a history of jaundice during pregnancy have an increased risk of recurrence. Discontinue Femulen if jaundice occurs.

Progestogen-only oral contraceptives may offer less protection against ectopic pregnancy than against intra-uterine pregnancy.

Precautions: Patients receiving treatment with Femulen should be kept under regular medical surveillance.

Although it has not yet been possible to evaluate the involvement of the progestogen component of oral contraceptives and thromboembolic disorders, at present it is advisable to discontinue Femulen at least six weeks before elective surgery or during periods of prolonged immobilisation. It would be reasonable to resume Femulen two or three weeks after surgery provided the patient is ambulant. Every patient, however, should be considered individually with regard to the nature of the operation, the extent of immobilisation, the presence of additional risk factors and the chance of unwanted conception.

Caution should be exercised where there is the possibility of an interaction between a pre-existing disorder and a known or suspected side-effect. The use of Femulen in patients suffering from epilepsy, or with a history of migraine, or cardiac dysfunction may result in exacerbation of these disorders, because of fluid reten-

tion. Caution should also be observed in patients who wear contact lenses, patients with impaired carbohydrate tolerance, varicose veins, hypertension, asthma or any disease that is prone to worsen during pregnancy.

Vomiting or diarrhoea may reduce the effectiveness of the tablets, particularly if this should occur at or around the time of ovulation. If an episode of vomiting and/or diarrhoea occurs, additional contraceptive measures should be used until the next menstrual period occurs.

If a patient does not have a menstrual period within 45 days of her last menstrual period, the possibility of pregnancy should be investigated.

Drug interactions: Femulen may be rendered less effective and increased incidence of breakthrough bleeding may occur by virtue of drug interaction. At present, drugs suspected to interact in this way include barbiturates, anticonvulsants, antibiotics and antiarthritics. In common with oestrogen-containing oral contraceptives, Femulen may alter the metabolism of other drugs such as oral anticoagulants, anticonvulsants, tricyclic antidepressants, antihypertensive agents (e.g. guanethidine), vitamins and hypoglycaemic agents.

Nursing mothers: Available data suggest that progestogen-only oral contraceptives exert little effect on milk yield. Norethisterone, a metabolite of Femulen, has been detected in breast milk. In a study of infants breast fed by mothers taking Femulen, no adverse effects of the drug were observed.

Adverse effects: Patients taking progestogen-only oral contraceptives for the first time may initially experience menstrual irregularity. This may include amenorrhoea, prolonged bleeding and/or spotting and should decrease with time. Clinical investigations with Femulen indicate that side-effects are infrequent and tend to decrease as treatment continues. Known or suspected side-effects of progestogen-only oral contraceptives include nausea, vomiting, other gastrointestinal symptoms, certain skin disorders, chloasma, breast and weight changes, ocular changes, headache, migraine, depression, change in libido and appetite, increase in size of uterine myofibromata, and changes in carbohydrate, lipid, or vitamin metabolism. Tests of endocrine, hepatic and thyroid function, as well as coagulation tests, may be affected by this preparation.

The use of oral contraceptives has also been associated with a possible increased incidence of gall-bladder disease.

Benign hepatic adenomas, although rare, have been reported with long-term use of oral contraceptives.

Overdosage: Fatal overdosage has not been reported. Overdosage may be manifested by nausea, vomiting, breast engorgement and vaginal bleeding. Gastric lavage may not be necessary but demulcents such as milk, egg white or bismuth hydroxide may be helpful.

Pharmaceutical precautions Femulen should be stored in a cool dry place.

Legal category POM.

Package quantities Carton containing one strip of 28 tablets, with instructions.

Further information Femulen does not necessarily inhibit ovulation but it is believed to discourage implantation of the fertilised ovum by altering the endometrium. Cervical mucus viscosity is also changed which may render the passage of sperm less likely.

Product licence number 0020/0054.

GRAVIGARD® MINI-GRAVIGARD®

Presentation Two sizes of Gravigard intrauterine device are available:

Gravigard – Transverse arm 26 mm; vertical arm 36 mm.

Mini-Gravigard – Transverse arm 22 mm; vertical arm 28 mm.

Each device consists of pure electrolytic copper wire, surface area approximately 200 mm², wound onto the vertical arm of a plastic carrier which approximates the shape of the number 7. The plastic carrier is composed of polypropylene homopolymer impregnated with barium sulphate to render it radio-opaque, with a monofilament thread attached to the base of the vertical arm. Each device is presented partially loaded in its inserter tube and instructions for use are included with each sterile pack.

Uses Intrauterine contraception.

Dosage and administration Gravigard is recommended for women with a uterine size measurement from external os to fundus greater than 6.5 cm. Mini-Gravigard is recommended for women with a uterine size measurement from external os to fundus of 5.5 to 6.5 cm. Gravigard and Mini-Gravigard should be replaced every two years. The procedure for insertion is fully detailed in the instructions for use leaflet included with each sterile pack. Insertion is not recommended if uterine size from external os to fundus measures less than 5.5 cm.

Although IUCDs may be inserted at any time during the menstrual cycle, insertion during or shortly after the menstrual period reduces the possibility of an existing undiagnosed pregnancy. Postpartum insertion is usually delayed until involution of the uterus is complete. The benefits of immediate post abortion insertion should be weighed against the risks due to the relatively soft structure of the uterus.

Contra-indications, warnings, etc Contra-indications for IUCDs are pregnancy, history of ectopic pregnancy, postpartum endometritis or septic abortion within the past three months, abnormalities of the uterine cavity including developmental abnormalities, large or multiple fibroids, acute pelvic inflammatory disease or a history of repeated pelvic inflammatory disease, acute cervicitis, cervical dysplasia, endometrial disease such as hyperplasia or uterine polyps, suspected or proven malignancy of the genital organs, severe dysmenorrhoea, menorrhagia and/or intermenstrual bleeding. Contra-indicated in women with Wilson's disease or hypersensitivity to copper.

Medical diathermy to the abdominal and sacral regions is contra-indicated in Gravigard or Mini-Gravigard users because of the possibility of heat injury to the surrounding tissue.

An increased incidence of pelvic inflammatory disease and menorrhagia associated with the use of IUCDs has been reported. Pelvic infection may result in future infertility. Women with certain known or suspected heart diseases are more susceptible to development of sub-acute bacterial endocarditis. Appropriate precautions including administration of antibiotics should be observed when inserting an IUCD in such cases.

Syncope or bradycardia may occur in some women during insertion or removal of an IUCD.

Post-insertion cramps are usually of only a few minutes

duration, but some women experience cramps for several hours or days. Cramps may be associated with or increased menstrual flow, or increased menstrual bleeding or pain. Removal of the device may be required.

Gravigard or Mini-Gravigard may be inserted at any time during the menstrual cycle. In the event of partial expulsion or perforation of the uterine wall, the device should be removed. Infection, foreign body reaction, or perforation may result if an IUCD is inserted into the uterine cavity. Removal is advised if there is an infection resistant to treatment, or if there is significant anaemia, or

Precautions: A complete medical history including measurement of haemoglobin prior to insertion of the device and examination of the cervix and uterus should be examined within the first 12 months and annually thereafter.

After insertion the patient should be advised to ascertain the position of the retrieval thread. Advise the patient to report if pregnancy is suspected. Intrauterine devices should not be used in women with anaemia, a history of a previous pelvic infection of the uterus and those undergoing chemotherapy or having a coagulopathy.

The possibility of a patient suffering from a uterine infection at the time of insertion of an IUCD, should be considered.

Lost threads: If the retrieval thread is not visible at the cervix on follow-up, the device may be drawn up into the uterine cavity. If the device does not reappear during the next menstrual period, the device may usually be located by using a retrieval instrument. If it cannot be located, the device may have been expelled or may have been used to locate the cervix.

Pregnancy: The risk of a pregnancy occurring while using an IUCD is greater in women with a history of ectopic pregnancy than in those without. If a woman becomes pregnant while using an IUCD, the pregnancy should be carefully evaluated for complications.

There have been reports of a higher incidence of septic abortion in women using an IUCD in situ. Patients with an IUCD in situ should be closely monitored. If all abortion symptoms, fever, crampy discharge, as the onset of septic abortion may be rather than initial signs. The incidence of spontaneous abortion is increased over that in women not using contraception occurs with an IUCD.

If pregnancy occurs while using an IUCD, the thread is visible then the device should be removed. If the thread is not visible, the IUCD may go to term or until a miscarriage occurs. If the patient is pregnant, careful observation of the effects of intrauterine contraception should be reported.

Adverse effects: Uterine infection, discharge, embedment, perforation, and expulsion have been reported.

Pharmaceutical precautions Gravigard and Minigravigard are supplied in sterile packs which should not be opened until required for insertion. Each device should be handled with aseptic precautions and should be left folded in its inserter tube for more than two minutes, as this may prevent the transverse arm from assuming its correct position. Care should be taken not to damage the sterile packaging which should be stored in a cool dry place.

Legal category POM.

Package quantities *Gravigard*: Pack containing one sterile device.

Minigravigard containing five packs.

ii-Gravigard: Pack containing one sterile device. *Minigravigard* containing five packs.

Other information The average amount of copper released from copper IUCDs is well below the daily dietary intake of copper. Small increases of endometrial copper levels have been noted in the presence of copper IUCDs, these are not cumulative. No changes in blood levels of copper have been detected.

Product licence numbers

Gravigard 0020/0062

ii-Gravigard 0020/0085

MOTIL* TABLETS
MOTIL* LIQUID

Presentation *Lomotil Tablets*: White tablets engraved with 'MOTIL' on one side. Each tablet contains Diphenoxylate Hydrochloride BP 2.5 mg with Atropine Sulphate PhEur 0.025 mg.

Lomotil Liquid: Red, cherry flavoured liquid. Each 5 ml measure contains Diphenoxylate Hydrochloride BP 2.5 mg with Atropine Sulphate PhEur 0.025 mg.

Uses Acute and chronic diarrhoea.

Contraindications Control of stool formation after colostomy or ileostomy.

Safe and administration *Caution*: Lomotil should not be given to children under one year. The recommended dosage should not be exceeded.

Adults: The recommended starting dose is four tablets, four 5 ml measures, followed by two tablets or two 5 ml measures every six hours. Once satisfactory control is achieved, dosage should be reduced to suit the requirements of the individual patient.

Children: Recommended dosage guide:

–3 years: 1 tablet or one 5 ml measure twice daily.

–8 years: 1 tablet or one 5 ml measure three times daily.

–12 years: 1 tablet or one 5 ml measure four times daily.

–3–16 years: 2 tablets or two 5 ml measures three times daily.

Once satisfactory control is achieved, dosage should be reduced to suit the requirements of the individual patient.

Contra-indications, warnings, etc Lomotil is contraindicated in children under one year, in patients with known hypersensitivity to diphenoxylate hydrochloride or atropine, in patients with jaundice or intestinal obstruction, and in the treatment of diarrhoea associated with pseudomembranous enterocolitis.

Lomotil should be used with special caution in young

children because of the variability of response in this age group. Appropriate fluid and electrolyte therapy should also be given to protect against dehydration. If severe dehydration or electrolyte imbalance is present, Lomotil should be withheld until appropriate corrective therapy has been initiated.

In some patients with acute ulcerative colitis, agents which inhibit intestinal motility or delay intestinal transit time have been reported to induce toxic megacolon. Patients with acute ulcerative colitis should be carefully observed and Lomotil therapy should be discontinued promptly if abdominal distension or other untoward symptoms develop.

Lomotil should be used with caution in patients with liver disease, since hepatic coma may be precipitated.

Precautions: Because a subtherapeutic dose of atropine is added to Lomotil, atropinic effects may occur.

Drug interactions: Since the chemical structure of diphenoxylate hydrochloride resembles that of meperidine hydrochloride, concurrent use with MAO inhibitors could precipitate hypertensive crisis. Close observation is required when these medications are given concomitantly with diphenoxylate hydrochloride.

Diphenoxylate hydrochloride may potentiate the action of barbiturates, tranquillisers and alcohol.

Pregnancy: The safety of Lomotil in pregnancy has not been established. Animal teratology and reproduction studies have demonstrated no adverse effects. The benefits of therapy must be weighed against the possible hazards to the mother and foetus.

Nursing mothers: Diphenoxylate hydrochloride and atropine sulphate may be excreted in human milk. If a nursing mother is taking Lomotil, the infant may exhibit some effects of the drug.

Adverse effects: Atropine effects, such as dryness of the skin and mucous membrane, tachycardia, hyperthermia and urinary retention may occur, especially in children. Other adverse reactions are uncommon but may include gastrointestinal intolerance, sedation, headache, dizziness, paralytic ileus, toxic megacolon, angioneurotic oedema, restlessness, depression and cutaneous reactions.

Overdosage: Accidental overdosage may produce narcosis with respiratory depression or atropine poisoning or both, particularly in children. Symptoms of overdosage include dryness of the skin and mucous membranes, flushing, hyperthermia and tachycardia, nystagmus, pinpoint pupils and severe respiratory depression. Since the onset of symptoms of overdosage may be considerably delayed and respiratory depression may not become evident until 12 to 30 hours after ingestion, gastric lavage and continuous observation for at least 48 hours are recommended.

If respiratory depression develops, naloxone, a specific antidote, should be administered. The duration of action of naloxone hydrochloride is considerably shorter than that of diphenoxylate hydrochloride, and repeated injections of the antidote may be required. Establishment of a patent airway and artificial ventilation may be needed.

Pharmaceutical precautions Lomotil should be stored in a cool dry place.

Legal category POM.

Package quantities *Lomotil tablets*: Pack of 100 consisting of 5 blister strips, each containing 20 tablets. *Bottles* containing 500 and 1,000 tablets.

Lomotil liquid: Bottles containing 60 ml (with 5 ml measure) and 500 ml.

Further information Nil.

Product licence numbers

Lomotil Tablets 0020/5014

Lomotil Liquid 0020/5015

LOTUSSIN*

Presentation Pale amber, peach flavoured linctus containing Diphenhydramine Hydrochloride BP 10 mg, Dextromethorphan Hydrobromide BP 12.5 mg, Ephedrine Hydrochloride PhEur 15 mg and Guaiphenesin BP 100 mg in each 10 ml.

Uses Cough suppression and nasal or bronchial mucosal decongestion.

Dosage and administration *Adults and children over 12 years:* 10 ml three times daily.

Children: 1–5 years: 2.5 ml to 5 ml three times daily.

6–12 years: 5 ml to 10 ml three times daily.

Contra-indications, warnings, etc Lotussin is contra-indicated in patients with a known hypersensitivity to any of the active constituents, in patients with heart disease including coronary artery disease, hypertension, thyrotoxicosis and in patients receiving monoamine oxidase inhibitor therapy or within 14 days of stopping such treatment.

Lotussin should not be given to children under one year old.

May cause drowsiness. Patients affected in this way should not drive or operate machinery.

Precautions: Use with caution in patients with peripheral vascular disease, bronchial asthma, prostatic enlargement or glaucoma.

When prescribing Lotussin for patients with diabetes mellitus the sucrose content of 6.55 g per 10 ml should be considered.

Drug interactions: Concurrent use of Lotussin with monoamine oxidase inhibitors may precipitate a hypertensive crisis. Lotussin therefore should not be used in a patient receiving MAO inhibitors or within 14 days of stopping such treatment.

Lotussin may potentiate the effect of other drugs acting on the central nervous system such as hypnotics, sedatives and tranquillisers and patients should avoid alcoholic drink during treatment.

The possibility of interaction with other medication should be considered by reference to each active ingredient.

Pregnancy: The safety of Lotussin in pregnancy has not been established. The benefits of therapy must be weighed against the possible hazards to the mother and foetus.

Nursing mothers: Diphenhydramine is, and other constituents of Lotussin may be, excreted in human milk. The benefits of therapy must be weighed against possible hazards to the mother and child.

Adverse effects: Drowsiness may be experienced by some patients. One case of skin rash has been reported.

Overdosage: Treatment of overdosage consists of gastric lavage in the conscious patient and intensive supportive therapy where necessary.

Pharmaceutical precautions Lotussin should be stored in a cool dry place. Recommended diluent – w required for paediatric usage – Syrup BP. When diluted use within 14 days of preparation.

Legal category P.

Package quantities Bottles of 100 ml and 1 litre.

Further information Nil.

Product licence number 0020/0077.

NOVAGARD*

Presentation Novagard is an intrauterine device consisting of pure copper wire with a silver core, surface area approximately 200 mm², wound on to the vertical arm of a T-shaped plastic carrier. The plastic carrier is composed of polyethylene impregnated with bar sulphate, to render it radio-opaque, with a polyethylene thread attached to the base of the vertical arm. The device is presented partially loaded in its insertor and instructions for use are included with each sterile pack.

Novagard dimensions: Transverse arms 32 mm
Vertical arm 32 mm

Uses Intrauterine contraception.

Dosage and administration Novagard is recommended for women with a uterine size measured from external os to fundus greater than 5.5 cm. Novagard should be replaced every four years. The procedure for insertion is fully detailed in the instructions for use leaflet included with each sterile pack.

Although IUCDs may be inserted at any time during the menstrual cycle, insertion during or shortly after menstrual period reduces the possibility of an existing undiagnosed pregnancy. Postpartum insertion is usually delayed until involution of the uterus is complete. The benefits of immediate post abortion insertion should be weighed against the risks due to the relatively simple structure of the uterus.

Contra-indications, warnings, etc Contra-indications are pregnancy, history of ectopic pregnancy, postpartum endometritis or septic abortion within past three months, abnormalities of the uterine cavity including developmental abnormalities, large or multiple fibroids, acute pelvic inflammatory disease or a history of repeated pelvic inflammatory disease, acute cervicitis, cervical dysplasia, endometrial disease such as hyperplasia or uterine polyps, suspected or proven malignancy of the genital organs, severe dysmenorrhoea, menorrhagia and/or intermenstrual bleeding. Contra-indicated in women with Wilson's disease or hypersensitivity to copper.

Medical diathermy to the abdominal and sacral region is contra-indicated in Novagard users because of the possibility of heat injury to the surrounding tissue.

An increased incidence of pelvic inflammatory disease and menorrhagia associated with the use of IUCDs has been reported. Pelvic infection may result in future infertility. Women with certain known or suspected diseases are more susceptible to development of severe acute bacterial endocarditis. Appropriate precautions including administration of antibiotics should be observed when inserting an IUCD in such cases.

Syncope or bradycardia may occur in some women.

ring insertion or removal of an IUCD. Post-insertion cramps are usually of only a few minutes duration, but some women may experience cramps for several hours days. Spotting, intermenstrual bleeding or increased menstrual flow may occur. If heavy or persistent bleeding or persistent cramping occur, removal of the device may be indicated.

Novagard should be removed in the event of partial expulsion and a new device inserted. If perforation of the uterus or cervix is suspected, the device should be removed as soon as medically feasible. Adhesions, foreign body reactions and intestinal obstruction may result if an IUCD is left within the peritoneal cavity. Removal is also indicated in cases of pelvic infection resistant to treatment, menorrhagia producing significant anaemia, or intractable pain.

Precautions: A complete gynaecological examination, including measurement of the uterus, should precede insertion of the device. Ideally the patient should be re-examined within the first three months after insertion and annually thereafter. After insertion the patient should be taught to examine herself to ascertain the continued presence of the retrieval threads. Advise the patient to consult her doctor if pregnancy is suspected.

Intrauterine devices should be used with caution in women with anaemia, menorrhagia, hypermenorrhoea, history of a previous uterine incision or perforation of the uterus and those receiving anticoagulants, steroid therapy or having a coagulopathy.

The possibility of a seizure being precipitated in a patient suffering from epilepsy, at or shortly after the insertion of an IUCD, should also be borne in mind.

Retrieval threads: If the retrieval threads are not visible at the review on follow-up examination, they may have been drawn up into the uterus or cervical canal and may appear during the next menstrual period. The threads may usually be located by gently probing with a suitable instrument. If they cannot be found, they may have broken off, or the device may have been expelled. Ultrasound or X-ray may be used to locate the device.

Pregnancy: The risk of ectopic pregnancy is reported to be greater in women who conceive with an IUCD in situ than in those without an IUCD. Therefore, if a patient becomes pregnant with an IUCD in situ, she should be carefully evaluated for possible ectopic pregnancy.

There have been reports of an increased incidence of ectopic abortion in women who become pregnant with an IUCD in situ. Patients who are pregnant with an IUCD in situ should be closely observed and told to report immediately all abnormal symptoms such as 'flu-like' symptoms, fever, cramping pain, bleeding or excessive discharge, as the onset of septicaemia associated with ectopic abortion may be insidious with general symptoms rather than initial signs of spontaneous abortion. Also, the incidence of spontaneous abortion appears to be increased over that in unprotected women when conception occurs with an IUCD in situ.

If pregnancy occurs with an IUCD in situ and the threads are visible then the device should be removed. If the threads are not visible or device removal would be difficult, the IUCD may be left in situ until the pregnancy goes to term or until a decision is made to terminate the pregnancy. If the patient elects to continue the pregnancy, careful observation is required. The long term effects of intrauterine copper on the foetus are unknown.

Adverse effects: Uterine or cervical perforation, vaginal discharge, embedment and allergic reactions have been reported with copper IUCD's.

Pharmaceutical precautions Novagard is supplied in a sterile pack which should not be opened until required for insertion. Each device should be handled with aseptic precautions and it is advisable that the folded device in the inserter tube should not be left for more than two minutes, as this may prevent the transverse arms from reassuming the correct position.

Care should be taken not to damage the sterile package which should be stored in a cool dry place.

Legal category POM.

Package quantities Pack containing one sterile device.

Outer containing five packs of one sterile device.

Outer containing ten sterile devices.

Further information The average amount of copper eluted from copper IUCDs is well below the daily dietary intake of copper. Small increases of endometrial copper levels have been noted in the presence of copper IUCDs, but these are not cumulative. No changes in blood levels of copper have been detected.

Product licence number 0022/0046.

The product licence is held by KabiVitrum.

OVULEN* 50

Presentation White tablets engraved SEARLE 163 on both sides, containing Ethynodiol Diacetate BP 1 mg and Ethinyloestradiol PhEur 0.05 mg.

Uses Oral contraception.

Dosage and administration One tablet daily for 21 days, starting on Day 5 of the menstrual cycle (where Day 1 is the first day of bleeding). The next course of tablets should be started after seven tablet-free days. This 'three weeks on, one week off' regimen is continued for as long as contraception is required. Patients should be advised to use an additional form of contraception for the first 14 days of the first pack.

Missed tablets: Patients who miss a single tablet should be instructed to take the missed tablet as soon as they remember, even though this may mean taking 2 tablets on one single day. The regular tablet for that day should be taken at the usual time. An additional method of contraception (a sheath or a cap plus spermicide) should be used for the remainder of the cycle. If two consecutive tablets are missed patients should be instructed to take 2 tablets each day for the next two days and use an additional method of contraception for the rest of the cycle. Those who miss more than 2 tablets should resume as soon as they remember, ignoring those they have missed, and should use additional contraceptive precautions for the rest of the cycle.

Contra-indications, warnings, etc The contra-indications for combined oral contraceptives are thrombophlebitis, thromboembolic disorders, cerebral vascular disease, myocardial infarction, coronary artery disease, or a past history of these conditions; known, suspected or a past history of breast, genital or hormone dependent cancer; past or present, benign or malignant liver tumours; impaired liver function; active liver disease; disorders of lipid metabolism; haemoglobinopathies; undiagnosed abnormal vaginal bleeding or amenorrhoea; known or suspected pregnancy.

It has been established that the use of combined oral

contraceptives is associated with an increase in the risk of thromboembolic and thrombotic disease.

Recent studies have indicated that combined oral contraceptives may be associated with an increased risk of myocardial infarction. The risk of arterial thrombosis associated with combined oral contraceptives increases with age, and this risk is aggravated by cigarette smoking. The use of combined oral contraceptives by women in the older age group, especially those who are cigarette smokers, should therefore be discouraged, and alternative methods advised.

Ovulen 50 should be discontinued at least six weeks before elective surgery or during periods of prolonged immobilisation. It would be reasonable to resume oral contraceptives two or three weeks after surgery provided the patient is ambulant. Every patient, however, should be considered individually with regard to the nature of the operation, the extent of immobilisation, the presence of additional risk factors and the chance of unwanted conception.

Discontinue treatment if there is a gradual or sudden, partial or complete loss of vision or any evidence of ocular changes, onset or aggravation of migraine or development of headache of a new kind which is recurrent, persistent or severe.

Patients with a history of jaundice during pregnancy have an increased risk of recurrence. Discontinue Ovulen 50 if jaundice occurs.

Precautions: Patients receiving treatment with oestrogen or progestogen or both, should be kept under regular surveillance.

Caution should be exercised where there is the possibility of an interaction between a pre-existing disorder and a known or suspected side-effect. The use of Ovulen 50 in patients suffering from epilepsy, or with a history of migraine, or cardiac dysfunction may result in exacerbation of these disorders, because of fluid retention. Caution should also be observed in patients who wear contact lenses, patients with impaired carbohydrate tolerance, hypertension, asthma, varicose veins, or any disease that is prone to worsen during pregnancy, and in young patients in whom the growth period has not yet ended.

Vomiting or diarrhoea may reduce the effectiveness of the tablets, particularly if this should occur at or around the time of ovulation.

Drug interactions: Ovulen 50 may be rendered less effective and increased incidence of breakthrough bleeding may occur by virtue of drug interaction with rifampicin, isoniazid, ampicillin, neomycin, penicillin V, chloramphenicol, sulphonamides, nitrofurantoin, barbiturates, phenytoin, primidone, anti-arthritis, analgesics, tranquilisers and anti-migraine preparations. Ovulen 50 may alter the effectiveness of other types of drugs, such as oral anticoagulants, anticonvulsants, tricyclic antidepressants, antihypertensive agents (e.g. guanethidine), vitamins and hypoglycaemic agents. Therefore, the possibility of a drug interaction occurring in patients on any of these therapeutic agents should be considered when prescribing Ovulen 50.

Nursing mothers: Active ingredients of oral contraceptives have been detected in the milk of mothers taking such drugs. The effect of Ovulen 50 on breast-fed infants has not been determined.

Adverse effects: Known or suspected side-effects of oral contraceptives include nausea, vomiting, other gastrointestinal symptoms, irregular vaginal bleeding, amenorrhoea, certain skin disorders, chloasma, breast and

weight changes, ocular changes, headache, hypertension, migraine, depression, change in libido and appetite, increase in the size of uterine myofibromata, fluid retention, infertility after discontinuation, and change in carbohydrate, lipid and vitamin metabolism.

Tests of endocrine, hepatic and thyroid function, well as coagulation tests, may be affected by the preparation.

The use of oral contraceptives has also been associated with a possible increased incidence of gall-bladder disease.

Benign hepatic adenomas, although rare, have been reported with long-term use of oral contraceptives.

Overdosage: Fatal overdosage has not been reported. Overdosage may be manifested by nausea, vomiting, breast engorgement and vaginal bleeding. Gastric lavage may not be necessary but demulcents such as milk, or white or bismuth hydroxide may be helpful.

Pharmaceutical precautions Ovulen 50 should be stored in a cool dry place.

Legal category POM.

Package quantities Carton containing one strip of 7 tablets, with instructions.

Further information Ovulen 50 provides oral contraception at a dosage level acceptable to many women. Patients switching from another oral contraceptive should start Ovulen 50 seven days after finishing the current pack.

Product licence number 0020/5023.

PRO-BANTHINE[®]

Presentation Pink, sugar coated, biconvex tablets printed SEARLE on one side. Each tablet contains Propantheline Bromide BP 15 mg.

Uses *Gastrointestinal:* Peptic ulcer, acute pancreatitis. *Genitourinary:* Enuresis.

Miscellaneous: Diagnostic radiological procedure hyperhidrosis.

Dosage and administration *Caution:* Food has been reported to reduce the bioavailability of Pro-Banthine. Tablets should be taken at least one hour before meals.

Adults: **Peptic ulcer:** The recommended initial starting dose is one tablet before each meal, and two tablets bedtime. Subsequently, dosage should be adjusted according to the patient's individual response and tolerance.

Diagnostic radiological procedures: Two tablets should be given 45 minutes prior to the diagnostic procedure.

Other indications: A dosage of up to eight tablets daily may be required.

Children: For enuresis the usual dosage is one to three tablets taken at bedtime. Although clinical trials using Pro-Banthine tablets for other indications have not been conducted in children, as a guide the total daily dosage should not exceed 2 mg per kilogram body weight, and should be given in divided doses.

Contra-indications, warnings, etc Pro-Banthine is contra-indicated in patients with obstructive diseases of the gastrointestinal or urinary tract, pyloric stenosis, intestinal atony, severe ulcerative colitis or toxic megacolon, hiatus hernia associated with reflux oesophagitis

able cardiovascular adjustment in acute haemorrhage, myasthenia gravis, glaucoma and in patients who are hypersensitive to propantheline bromide.

Some patients, especially those with ileostomy or stoma, diarrhoea may be a symptom of incomplete intestinal obstruction. Pro-Banthine therapy should be used in such patients.

Patients with severe heart disease in whom an increase in heart rate is undesirable should be observed closely if Pro-Banthine is administered.

Pro-Banthine may produce drowsiness or blurred vision. Patients should not drive or operate machinery if affected in this way.

Precautions: Patients with prostatic hypertrophy may experience some urinary hesitancy. This may be minimised if such patients are advised to micturate at the time the medication is taken.

Patients with ulcerative colitis should be treated with caution, since Pro-Banthine may suppress intestinal motility to the point of producing paralytic ileus, thus precipitating or aggravating toxic megacolon.

Pro-Banthine should be used with caution in the elderly and in all patients with autonomic neuropathy, atonic renal disease, hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias or hypertension.

Drug interactions: Concurrent use of Pro-Banthine with slow-dissolving tablets of digoxin may cause increased serum digoxin levels.

Anticholinergics may alter absorption of other medication given concomitantly.

Excessive cholinergic blockade may occur if Pro-Banthine is given concomitantly with belladonna alkaloids or synthetic and semisynthetic anticholinergic agents.

Pregnancy: Animal reproduction and teratology studies have not been performed. The use of Pro-Banthine in pregnant women requires that the anticipated benefit be weighed against the possible hazards to mother and fetus.

Lactating mothers: Whether propantheline bromide is excreted in human breast milk is unknown. No animal studies have been conducted. If use of the drug is considered essential the anticipated benefit should be weighed against the possible hazards to mother and child.

Adverse effects: Varying degrees of drying of salivary secretion may occur, as well as mydriasis, blurred vision and heat stroke. Other adverse reactions reported include: nervousness, drowsiness, dizziness, insomnia, headache, tachycardia, loss of the sense of taste, nausea, vomiting, constipation, urinary hesitancy and retention, incontinence, allergic dermatitis and anaphylaxis.

Overdosage: Intensification of the usual side effects may occur. Severe intoxication may result in disturbances of the central nervous system (from restlessness and excitement to psychotic behaviour), circulatory changes (shaking, fall in blood pressure, circulatory failure), respiratory failure, paralysis and coma.

In the event of overdosage, empty the stomach by vomiting or lavage. Physostigmine salicylate 0.5 to 1 mg should be injected intravenously to control the central and peripheral effects of propantheline bromide. Since it has a brief duration of action of about 1 to 2 hours, it may be necessary to repeat injections up to a total dose of 5 mg.

Excitement may be controlled by small doses of a

short-acting barbiturate such as thiopentone sodium 100 mg.

Supportive therapy may require oxygen and assisted respiration, ice bags or alcohol sponges for hyperpyrexia, especially in children, bladder catheterisation and the administration of fluids.

Pharmaceutical precautions Pro-Banthine tablets should be stored in a cool dry place.

Legal category POM.

Package quantities Bottles containing 100 and 1,000 tablets.

Further information Propantheline bromide is extensively metabolised in man. Some enzymic hydrolysis of the drug may occur in the gastrointestinal tract prior to its absorption.

Studies in healthy men demonstrated that peak plasma levels of unchanged drug were reached within 2 hours of a single, oral dose of propantheline bromide. Following single oral dosing the plasma elimination half-life was about 2–3 hours and some 1–10% of propantheline bromide was excreted in urine as unchanged drug.

In healthy men studies have shown onset of anticholinergic effects within 1 hour of oral administration. Effects persisted for up to 6 hours after oral dosing.

Product licence number 0020/5026

REGULAN®

Presentation Premeasured, single-dose sachet containing 6.4 g of beige rough ground powder. Active Ingredient – 3.6 g Ispaghula Husk BP.

Uses For the treatment of constipation and patients requiring a high fibre regimen.

Dosage and administration

1. Pour measured dosage into a glass.
2. Slowly add 150 ml ($\frac{1}{4}$ pint) cool water.
3. Drink entire contents immediately. An additional glass of liquid may be taken if needed.

Adults and Children over 12 years: The usual dosage is the entire contents of one sachet taken one to three times daily.

Children: A reduced dosage based upon the age of the child should be given.

6–12 years: $\frac{1}{2}$ –1 level 5 ml teaspoonful one to three times daily.

Contra-indications, warnings, etc Regulan should not be given to patients with intestinal obstruction, faecal impaction or hypersensitivity to ispaghula.

Regulan should always be taken as a liquid suspension and should be drunk immediately after mixing.

Precautions: It may be advisable to supervise treatment in the elderly or debilitated and patients with intestinal narrowing or decreased motility, as rare instances of gastrointestinal obstruction have been reported with mucilloid preparations when taken with insufficient liquid, contrary to the administration instructions.

The sucrose content of each 6.4 g dose has a calorific value of approximately 3.5 kilocalories, this should be considered when taken by diabetics.

Pregnancy and Lactation: The benefits of therapy should be weighed against any possible hazards if used during pregnancy and lactation.

Adverse effects: Allergy, gastrointestinal obstruction or impaction have been reported with hydrophilic mucilloid preparations.

Overdosage: No instances of true overdosage have been reported. If overdosage should occur there is no specific treatment and symptomatic measures should be employed.

Pharmaceutical precautions Store in a cool dry place.

Legal category GSL.

Package quantities Box of 30 and 90 sachets.

Further information Regular is gluten-free.

Product licence number 0020/0087.

SERENACE* AMPOULES

SERENACE* TABLETS

SERENACE* LIQUID

SERENACE* CAPSULES

Presentation *Serenace 5 mg and 20 mg Ampoules:* Clear glass ampoules containing Haloperidol BP 5 mg in 1 ml aqueous solution.

Clear glass ampoules containing Haloperidol BP 20 mg in 2 ml aqueous solution.

Serenace 1.5 mg; 5 mg; 10 mg and 20 mg Tablets: White, biconvex, scored tablets engraved SEARLE 41 on one side, containing Haloperidol BP 1.5 mg.

Bright pink, biconvex, scored tablets engraved SEARLE 12 on one side, containing Haloperidol BP 5 mg.

Pale pink, biconvex, scored tablets engraved SEARLE 919 on one side, containing Haloperidol BP 10 mg.

Dark pink, biconvex, scored tablets engraved SEARLE 920 on one side, containing Haloperidol BP 20 mg.

Serenace Liquid: Clear, odourless, colourless liquid containing Haloperidol BP 2 mg per ml.

Serenace Capsules: Two-tone green capsules printed SEARLE on both halves, containing Haloperidol BP 0.5 mg.

Uses Mania and hypomania, acute and chronic schizophrenia, acute psychotic agitation, organic psychoses, Gilles de la Tourette syndrome, childhood behaviour disorders, anxiety neurosis, tension states, psychosomatic conditions associated with anxiety, anxiety associated with depression.

Dosage and administration Daily dosage may range between 1 mg to 200 mg dependent on the patient's condition and the individual's response to treatment. As with all neuroleptic drugs, the dose of haloperidol should be titrated to the needs of each patient. Oral dosage may be given in single or divided doses.

Adults: The maximum and maintenance dose will generally be lower for debilitated or geriatric patients who may be more sensitive to Serenace.

Oral administration: Usually treatment may be started at 10–15 mg daily and progressively increased until satisfactory control is achieved. When maximum improvement is reached the dosage should be gradually reduced to the lowest effective maintenance dose which, for many patients, will be 5–10 mg per day.

Parenteral administration: For rapid emergency control, up to 30 mg may be given by intramuscular injection. A dose of 10 mg will usually be adequate. Further doses

may be repeated six-hourly until control is achieved when oral dosage may be substituted in diminishing doses.

Serenace injection may also be administered by intravenous route.

Anxiety states: Usual adult dosage, 0.5 mg (one capsule) twice daily.

Children: *Oral administration:* Usual maintenance dose 0.05 mg per kg body weight per day. Where control is not urgent treatment may be initiated at 0.025 mg/kg body weight per day and gradually increased to usual maintenance level. Therapy may be initiated at or three times the maintenance dosage, together with antiparkinsonian drugs if required.

Parenteral administration: Not recommended.

Contra-indications, warnings, etc Contra-indicated for comatose patients and for those with Parkinson's disease or a sensitivity to haloperidol.

May cause drowsiness or affect mental concentration. Patients affected in this way should not drive or operate machinery.

Precautions: May be given to epileptics, but with anticonvulsant therapy should be continued.

Administer with care to patients with severe cardiovascular disorders, because of the possibility of transient hypotension. Should hypotension occur and a vasopressor be required, adrenaline should not be used as haloperidol may block its vasopressor activity and paradoxical further lowering of the blood pressure may occur.

Use cautiously in thyrotoxic patients and those with arteriosclerosis who may have occult or manifest lesions of the basal ganglia. Such patients may be more prone to develop extrapyramidal symptoms.

In common with other tranquilisers, Serenace should not be used alone where psychotic depression predominates, but may be combined with antidepressants where there is associated anxiety.

Drug Interactions: Serenace may potentiate the action of other CNS depressants, including alcohol.

Enhanced CNS effects (sedation, mental disturbances) have been reported with the combined use of methyldopa and haloperidol.

Severe neuromuscular symptoms with impairment of consciousness and fever have been reported with combined use of lithium and haloperidol. A causal relationship has not been established; however, patients receiving such combined therapy should be carefully observed for early evidence of neurological toxicity and treatment should be discontinued if such signs appear.

Pregnancy: The safety of Serenace in pregnancy has not been established.

Reproduction studies in rodents have shown increased incidence of resorption, reduced fertility and pup mortality. No specific teratogenic effect has been reported in rats, rabbits or dogs but cleft palate and eye syndrome have been observed in mice.

No well controlled studies of haloperidol use in pregnant women have been conducted. Two cases of foetal limb malformation have been reported following maternal use of haloperidol combined with other drugs during the first trimester. No causal relationship has been established. Use of Serenace during pregnancy requires that the anticipated benefit be weighed against possible hazards to mother and foetus.

Nursing mothers: Haloperidol has been detected

ast milk. If use of Serenace is considered essential, an alternative method of infant feeding should be instituted.

Adverse effects: Extrapyramidal symptoms such as parkinson-like symptoms, akinesia, akathisia, dyskinesia, dystonia may develop during Serenace treatment. Very rarely dystonia has been reported to produce laryngeal/pharyngeal spasm associated with gagging, stridor, respiratory distress and asphyxia. Such symptoms may be promptly controlled by parenteral administration of a short-acting barbiturate, an antihistamine or an antiparkinsonian drug. The occurrence and severity of most extrapyramidal symptoms are generally, but not always, dose related. Extrapyramidal reactions have occasionally been reported during treatment at relatively low dose levels in both children and adults. Administration of antiparkinsonian drugs may be required for control of such reactions.

It is common with certain other antipsychotic agents that haloperidol has been associated with persistent tardive dyskinesia. Tardive dyskinesia may develop in some patients on long-term therapy or may develop after drug therapy has been discontinued. The risk is reported to be greater in elderly patients on high-dose therapy. Characteristic symptoms are rhythmical involuntary movements of the tongue, face, mouth or jaw sometimes accompanied by involuntary movements of the extremities. They may persist for many months or even years and, while they gradually disappear in some patients, they may appear to be permanent in others. Gradual reduction of dosage to reveal persisting dyskinesia has been suggested, so that treatment may be stopped if necessary. Antiparkinsonian agents have proved of little value in this syndrome.

Other adverse reactions reported include insomnia, depression, drowsiness, blurred vision, hypotension and gastrointestinal effects. Impairment of liver function, cardiac arrhythmias, blood dyscrasias, skin reactions including photosensitisation are rarely reported as are severe reactions related to endocrine effects.

Overdosage: Intensification of the known pharmacological and adverse effects may occur. The most prominent could be severe extrapyramidal symptoms, hypotension and sedation. The patient may appear comatose with respiratory depression and hypotension which could be severe enough to produce a shock-like state. Extrapyramidal reactions may include muscular weakness or rigidity and a generalised or localised tremor. With accidental overdosage hypothermia, bradycardia, sinus bradycardia and hypertension have been reported in young children.

No specific antidote has been identified.

In the event of overdosage the stomach should be emptied by aspiration and lavage. Emetics should not be used. Establishment of a patent airway and artificial ventilation may be needed. Hypotension may be counteracted by placing the patient in the head-down position and by use of a plasma expander and careful use of a vasopressor agent such as noradrenaline. Adrenaline

should not be used. Severe extrapyramidal reactions should be treated with parenteral antihistamines or antiparkinsonian drugs. The relatively long plasma elimination half-life of haloperidol should be considered.

Pharmaceutical precautions Serenace Ampoules should be stored in a cool place and protected from light.

Serenace Tablets and Capsules should be stored in a cool, dry place.

Serenace Liquid should be stored in a cool place.

Dilution: Serenace liquid may be diluted 50% with either distilled water or Syrup BP. The diluted solution should be stored in amber bottles and is stable for 8 weeks at room temperature.

Legal category POM.

Package quantities 5 mg Ampoules: Boxes of 6.

20 mg Ampoules: Boxes of 10.

1.5 mg Tablets: Bottles of 50, 250 and 1,000.

5 mg Tablets: Bottles of 50, 250 and 1,000.

10 mg Tablets: Bottles of 50, 250 and 1,000.

20 mg Tablets: Bottles of 50 and 250.

2 mg/ml Liquid: Bottles of 100 ml and 500 ml.

0.5 mg Capsules: Bottles of 50, 250 and 1,000.

Further information The pharmacokinetics of haloperidol have been studied in healthy volunteers and patients. In volunteers, following a single intravenous or oral dose, serum elimination half-life ranged from 10 to 19 hours and 12 to 38 hours respectively. Similar elimination half-lives were observed in patients after administration of a single oral or intramuscular dose of the drug or after withdrawal of the drug from patients who were in a steady-state. Steady-state serum levels were usually achieved within 6 days on a fixed oral dosage.

Haloperidol serum concentrations were in the range 0.5–10 ng/ml in patients at steady-state. The free fraction of haloperidol was generally about 8% of the total serum concentration, although some patients showed considerable deviation from this value. A number of other psycho-active drugs caused no measurable interference with the protein binding of haloperidol. The compound was found to be extensively metabolised in man and very little unchanged haloperidol was excreted in urine.

Product licence numbers

5 mg Ampoules 0020/5036

20 mg Ampoules 0020/0078

1.5 mg Tablets 0020/5033

5 mg Tablets 0020/5034

10 mg Tablets 0020/0076

20 mg Tablets 0020/0079

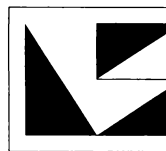
2 mg/ml Liquid 0020/5035

0.5 mg Capsules 0020/5038

*Trade Mark

Servier Laboratories Limited

Fulmer Hall
Windmill Road
Fulmer, Slough SL3 6HH



DIAMICRON* ▼

Presentation *Diamicon tablets*: White, circular tablets with a cross scoring on one side each containing 80 mg gliclazide. Gliclazide is 1-(3-azabicyclo (3,3,0) oct-3-yl)-3-(p-tolylsulphonyl) urea.

Pharmacology Gliclazide is a hypoglycaemic sulphonylurea differing from other related compounds by the addition of an azabicyclo octane ring. The drug is well absorbed and its half-life in man is approximately 10–12 hours. Gliclazide is metabolised in the liver; less than 5% of the dose is excreted unchanged in the urine.

In man, apart from having similar hypoglycaemic effect to the other sulphonylureas, gliclazide has been shown to reduce platelet adhesiveness and aggregation and increase fibrinolytic activity. These factors are thought to be implicated in the pathogenesis of long term complications of diabetes mellitus.

Uses For the treatment of maturity onset diabetes in patients who cannot be controlled on diet alone.

Dosage and administration *Adults*: The total daily dose may vary from 40 to 320 mg taken orally. The dose should be adjusted according to the individual patient's response commencing with 40–80 mg daily ($\frac{1}{2}$ –1 tablet) and increasing until adequate control is achieved. Higher doses should be divided according to the main meals of the day.

In obese patients or those not showing adequate response to Diamicon alone, a biguanide may be added.

Children: Diamicon, as with other sulphonylureas, is not indicated for the treatment of juvenile onset diabetes mellitus.

Contra-indications, warnings, etc

Contra-Indications: Diamicon should not be used in:

1. Juvenile onset diabetes.
2. Diabetes complicated by ketosis and acidosis.
3. Pregnancy.
4. Diabetics undergoing surgery, after severe trauma or during infections.
5. Patients known to have hypersensitivity to other sulphonylureas and related drugs.

Precautions: Diamicon is generally well tolerated but nausea, headache, rashes and gastro-intestinal disturbances have been reported. Care should be exercised in patients with hepatic and/or renal impairment and a small starting dose should be used with careful patient monitoring. As with other sulphonylureas, hypoglycaemia will occur if the patients' dietary intake is reduced or if they are receiving a larger dose of Diamicon than required.

Care should be taken when giving Diamicon with drugs which are known to alter the diabetic state or potentiate the drug's action, such as sulphonamides, salicylates, phenylbutazone, β -blocking agents, MAOI's, thiazide diuretics and steroid hormones.

Overdosage: The symptom to be expected of overdose

would be hypoglycaemia. The treatment is gastric lavage and correction of the hypoglycaemia by appropriate means with continued monitoring of the patient's blood sugar until the effect of the drug has ceased.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Cartons of 60 tablets (contain three push-through blister strips of 20 tablets).

Further information Nil.

Product licence number 0093/0024.

IMOTEST* -TUBERCULIN ▼

Merieux Tuberculin Test Ring (Purified Tuberculin)

Presentation Each Imotest unit consists of a plastic ring with a 9 mm square setting on which is mounted a platform with nine points arranged in three rows of three. A plastic tube fitted over the platform is filled with purified tuberculin (PPD) (0.05 ml) prior to being hermetically sealed. The entire unit has been sterilised. The reactivity of Imotest is comparable to the intermediate strength Mantoux test (5TU PPD). The ring is designed to fit on the thumb of the administrator.

Uses Imotest-Tuberculin is an intradermal test for the detection of tuberculin sensitivity and is used for screening for tuberculosis.

Dosage and administration *Adults and children*: Tuberculin testing may be done during the first year of life. The frequency of repeated testing may be increased in groups where there is a higher risk of tuberculosis. The recommended site for accurate tuberculin testing is the volar surface of the mid-forearm. The skin should be cleansed with alcohol, ether or acetone and allowed to dry.

Method of application: Place the ring on the thumb so the points protrude from the pulp surface. Carefully remove the tube surrounding the points by a slight twist which breaks the seal. Squeeze the tuberculin from the plastic tube onto the Imotest points until they are covered. Grasp the patient's arm firmly with the free hand stretching the skin of the forearm tightly. Press the loaded points firmly into the cleansed site.

Sufficient pressure should be exerted to produce nine visible puncture sites and an imprint of the square base. Do not wipe the puncture site and allow 3 or 4 minutes exposure before the patient dresses.

Reading the reaction: The test should be read at 48 to 72 hours after administration. Slight local erythema may be observed but the sole criterion for a positive reaction is a palpable induration. It is important to measure exactly the broadest transverse diameter of the induration.

mining under adequate light. This procedure is facilitated by using the millimeter callipers which may be obtained from Servier Laboratories on application. Identification of the application site is usually easy because of the distinct imprint of the points.

Positive reaction: The presence of a palpable induration transverse diameter measuring 3 mm and more constitutes a positive reaction.

Positive reaction: If the diameter of induration measures less than 1 mm the reaction is considered negative.

Doubtful reaction: Induration diameters between 1 mm and 3 mm are considered doubtful reactions.

Contra-indications, warnings, etc

Contra-indication: Erythema nodosum.

Precautions: In the case of severe positive reactions, investigations for pathological causes should be carried out.

Tuberculin testing should be carried out with caution in persons with active tuberculosis. However, activation of quiescent lesions is not to be expected.

Reactivity to the test may be suppressed in patients who are receiving corticosteroids or immunosuppressive agents, or those who have recently been vaccinated with a virus vaccine such as measles.

Do not apply Imotest on areas of acne, hairy areas and areas without adequate subcutaneous tissue.

Discard the Imotest ring and the tube containing tuberculin after use. DO NOT RE-USE.

Side effects: Vesiculation, ulceration, or necrosis may occur at the test site in highly sensitive persons. Pain, pruritus and discomfort at the test site may be relieved by cold packs or by a topical corticosteroid preparation.

Pharmaceutical precautions Imotest should be stored at room temperature in the original pack.

Legal category POM.

Package quantities Box of 10 tests.

Further information Nil.

Product licence number 0093/0041.

ISOCABITOL*

Presentation 10 ml of 0.25% solution of fusafungine in a pressurised aerosol container designed to give approximately 200 metered doses. Each metered dose contains approximately 125 mcg fusafungine. Two attachments, one for nasal use, one for oral use, are supplied.

Fusafungine is an antibiotic produced by *Fusarium termitum* strain 437.

Uses A topical antibiotic with anti-inflammatory properties for the treatment of infections and inflammatory conditions of the upper respiratory tract.

Dosage and administration **Administration:** By inhalation using the appropriate attachment.

Dosage: **Adults:** Nasal – 3 metered doses in each nostril 4 times a day.

Oral – 5 metered doses five times a day.

Children	Nasal – in each nostril five times a day	Oral – three times a day
–5 years	1 metered dose	2 metered doses
–12 years	2 metered doses	3 metered doses
12 years	3 metered doses	4 metered doses

Contra-indications, warnings, etc

Contra-indication: Sensitivity to fusafungine or excipients.

Warnings: Avoid directing the spray into the eyes, as aerosol sprays can cause irritation.

Side-effects: Some patients may experience a transient stinging sensation.

Pharmaceutical precautions **Storage:** Store at room temperature.

Note. Do not throw full or empty aerosol containers into a fire or subject them to excessive heat.

Legal category POM.

Package quantities Unit pack of one 10 ml aerosol container with one oral and one nasal attachment.

Further information An insert leaflet for patients is included in each pack.

Product licence number 0093/5003.

MFV-JECT* ▼

Presentation MFV-JECT is available in mono-dose pre-filled syringes and multidose vials. MFV-JECT is Influenza Vaccine BP, purified by zonal ultra-centrifugation and extraction with ether. The strains of influenza virus contained in the vaccine are those currently recommended each year by the World Health Organisation. Each dose also contains not more than 0.05 mg of thiomersal as preservative.

Uses Prophylaxis against influenza.

Dosage and administration By subcutaneous or intramuscular injection.

Adults and children over 13 years: Single dose; 0.5 ml.

Children under 13 years: Not recommended.

The vaccine should be allowed to reach room temperature before use.

Contra-indications, warnings, etc

Contra-indications: Persons known to have sensitivity to egg protein.

Side-effects: The incidence of side-effects with the vaccine is minimal due to the purification method; however, a transient erythema, tenderness or pain at the site of injection or mild fever may appear within the first 48 hours.

Precautions: The vaccine should be used with caution in patients with a history of allergy.

Overdosage: Not applicable.

Pharmaceutical precautions Protect from light and store at 4°C. Do not freeze.

Legal category POM.

Package quantities Monodose in prefilled syringe (0.5 ml); unit dose pack. 10 dose (5 ml) vial; 50 dose (25 ml) vial.

Further information Nil.

Product licence number 0093/0032.

MERIEUX* INACTIVATED RABIES VACCINE (MIRV)

Presentation Human Diploid Cell Rabies Vaccine.

The vaccine is a lyophilised, stabilised suspension of inactivated Wistar rabies virus strain PM/WI 38 1503-3M, cultured on human diploid cells and inactivated by beta-propiolactone. The dry vaccine is coloured off-white but after reconstitution with the diluent supplied it turns a pinkish colour due to the presence of phenol red.

The potency of the reconstituted vaccine is not less than $2.5 \times$ the International Standard per dose (1 ml).

Uses 1. Prophylactic immunisation against rabies.

2. Treatment of patients following suspected rabies contact.

Dosage and administration The dose of reconstituted vaccine in all cases is 1 ml given by deep subcutaneous injection.

Reconstitution: Inject diluent from syringe into vaccine vial, shake to ensure complete reconstitution and withdraw contents back into syringe.

1. **Prophylaxis:** 1 ml of reconstituted vaccine followed by a second dose (1 ml) after a one month interval. A booster dose should be given 6–12 months later. High antibody titres should be maintained by further boosters, the frequency depending on the risk of infection.

2. **Treatment:** The first injection should be given as soon as possible after the suspected contact. Three further doses should be given on the third, seventh and fourteenth day. Booster injections should be given after one month and three months. The treatment schedule may be stopped if the animal concerned is found conclusively to be free of rabies.

Contra-indications, warnings, etc There are no absolute contra-indications to inactivated rabies vaccine cultured on human diploid cells. Redness, swelling or tenderness at the site of injection may occur during the first 48 hours. A mild fever has been reported in about 1% of cases during the first 24 hours. In subjects with a history of allergy there may be an increased risk of side-effects and this possibility should be taken into account.

Pharmaceutical precautions Store at 4°C, do not freeze. Use immediately after reconstituting the vaccine.

Legal category POM.

Package quantities A vial of lyophilised vaccine containing one dose together with a disposable syringe containing 1 ml of diluent.

Further information Nil.

Product licence number 0093/0028.

MERIEUX* ORAL POLIOMYELITIS VACCINE Poliomyelitis Vaccine (Oral) ▼

Presentation The product is available in single dose ampoules and multi-dose vials. The vaccine is a sterile aqueous suspension of suitable live attenuated strains of poliomyelitis virus types 1, 2 and 3 grown in monkey kidney cell cultures. The virus strains are those chosen by Sabin for their antigenic potency and safety.

Each dose contains:

Poliomyelitis virus type 1 $\geq 3 \times 10^5$ TCID₅₀

Poliomyelitis virus type 2 $\geq 1 \times 10^5$ TCID₅₀
Poliomyelitis virus type 3 $\geq 3 \times 10^5$ TCID₅₀

and magnesium chloride and human serum albumin stabilisers. The vaccine may appear pink due to presence of phenol red and may contain traces neomycin.

Uses Prophylaxis against poliomyelitis.

Dosage and administration By oral administration only. The contents of a single dose ampoule (0.5 ml), two drops (0.1 ml) of vaccine from a multi-dose vial, be conveniently administered on a lump of sugar directly into the mouth.

Primary Immunisation – Adults and children: 3 doses; intervals of not less than 4 weeks.

In the United Kingdom, oral polio vaccine is normally given to infants at the same time as routine vaccination against diphtheria, tetanus and pertussis.

Reinforcing doses – Adults: Reinforcing doses may be given to adults if they are likely to be exposed to special risk of contracting the disease.

Children: 1 dose upon school entry and again at 15-years of age or upon leaving school.

Contra-indications, warnings, etc

Contra-indications: Acute febrile illness or any suspected infection, malignant disease, impaired immune responsiveness e.g. steroid treatment, radiotherapy. The vaccine should not be administered to pregnant women, unless they are known to be at definite risk from poliomyelitis.

Precautions: The efficacy of the vaccine may be impaired if given when the subject has diarrhoea or gastrointestinal dysfunction. The vaccine should not generally be administered within 3–4 weeks of another live vaccine.

Warnings: The vaccine may contain trace amounts neomycin. Administration of vaccine to subjects known to be hypersensitive to this antibiotic should be avoided.

The vaccine may contain minute traces of penicillin carried over from the original Sabin strains but this does not normally contra-indicate use except in extreme cases of hypersensitivity.

Other unvaccinated members of the household, including adults, are advised to have a vaccination at the same time as the vaccinee.

Overdosage: Not applicable.

Pharmaceutical precautions If stored at –20°C, the vaccine can be expected to retain its potency up to the expiry date indicated on the pack. After thawing, store at +4°C for no longer than 6 months. Do not re-freeze. Once opened, any unused vaccine must be discarded after 4 hours.

Legal category POM.

Package quantities Single-dose snap-open ampoules (0.5 ml) unit dose pack. 10 dose (1 ml) vial.

Box of 10 droppers for use with multi-dose vials.

Further information Nil.

Product licence number 0093/0042.

NATRILIX* ▼

Presentation Pink biconvex sugar-coated tablets each containing 2.5 mg indapamide hemihydrate.

Uses For the treatment of hypertension.

atrilix may be used as sole therapy or combined with antihypertensive agents.

Dosage and administration *Adults:* The dosage is 1 tablet, containing 2.5 mg indapamide hemihydrate, daily taken in the morning. The action of Natrilix is progressive and the reduction in blood pressure may continue and not reach a maximum until several months after the start of therapy. A larger dose than 2.5 mg Natrilix daily is not recommended as there is no appreciable additional antihypertensive effect but a diuretic effect may become apparent. If a single daily tablet of Natrilix does not achieve a sufficient reduction in blood pressure, another antihypertensive agent may be added; those which have been used in combination with Natrilix include beta-blockers, methyldopa, clonidine and other adrenergic blocking agents. The combination of Natrilix with diuretics which may cause hypokalaemia is not recommended. There is no evidence of rebound hypertension on withdrawal of Natrilix.

Children: There is no experience of the use of this drug in children.

Contra-indications, warnings, etc There are no absolute contra-indications to the use of Natrilix but caution should be exercised when prescribing it in cases of severe renal or hepatic impairment.

As with all new drugs, the administration of Natrilix should be avoided during pregnancy although no teratological effects have been seen in animals.

At doses of higher than that recommended, Natrilix has a diuretic effect, therefore it is not recommended to combine it with a diuretic agent which may cause hypokalaemia. Also, slight weight loss has been reported in some patients taking Natrilix. Reported side-effects include nausea and headache, but they are generally uncommon and mild in nature. Serum uric acid levels may rise slightly but there is no evidence that uric acid tolerance is adversely affected.

Overdosage: Symptoms of overdosage would be those associated with a diuretic effect: electrolyte disturbances, hypotension and muscular weakness. Treatment should be symptomatic, directed at correcting the electrolyte abnormalities and gastric lavage or emesis should be considered.

Pharmaceutical precautions Nil.

Legal category POM.

Packaging quantities Cartons of 30 tablets (containing 10 push-through blister strips of 15 tablets) and cartons of 60 tablets (containing three push-through blister strips of 20 tablets).

Other information No interactions have been reported between Natrilix and oral hypoglycaemic agents, anticoagulants, uricosurics and anti-inflammatory agents.

Product licence number 0093/0022.

ONDERAX PACAPS* PONDERAX* 20 mg **ONDERAX* 40 mg**

Description *Ponderax Pacaps:* Prolonged action formulation in hard gelatin capsule, size 3 with clear body and opaque blue cap, printed in black with Px PA containing small white pellets. Each prolonged action capsule contains 60 mg fenfluramine hydrochloride BP.

Ponderax 20 mg: Pale blue sugar-coated tablet containing 20 mg fenfluramine hydrochloride BP.

Ponderax 40 mg: White sugar-coated tablet, containing 40 mg fenfluramine hydrochloride BP.

Uses

1. Obesity.
2. Maturity-onset diabetes.

For the control of post-prandial hyperglycaemia in maturity onset diabetics who achieve marginal control either with diet alone or diet plus sulphonylureas.

Dosage and administration *Dosage: (1) Obesity: Adults:* 1–2 mg per kg of desirable body weight according to the severity of obesity.

Ponderax Pacaps: The recommended adult daily dose of 60 mg capsules is 1 or 2 capsules taken at the same time, once daily, according to the severity of obesity. When a dosage of 2 capsules is prescribed the dosage for the first and last week of treatment should be 1 capsule daily.

Ponderax 20 mg and Ponderax 40 mg: The recommended adult dose of Ponderax tablets is as follows:

Severe obesity: (1st week) 20 mg twice a day; (2nd week) 40 mg twice a day; (maintenance) 40 mg three times a day.

Moderate obesity: (1st week) 20 mg twice a day; (maintenance) 40 mg twice a day.

Mild obesity: (1st week) 20 mg twice a day; (maintenance) 20 mg three times a day.

On stopping treatment the dosage should be gradually reduced.

Dosage: Children: Recommended children's daily dose of 20 mg Ponderax tablets:

6–10 years: 20 mg.

10–12 years: 40 mg (in divided doses). This may be increased to 60 mg if the child is grossly obese.

A gradual build-up and reduction of dosage is advised.

Ponderax Pacaps: The capsule form is not suitable for children's dosage.

Dosage: (2) Maturity Onset Diabetes: Adults: The dosage must be adjusted to the needs of the individual patient and may vary between 80–120 mg daily, taken either as tablets or Ponderax Pacaps. Ponderax may be given together with sulphonylureas.

Children: Not applicable.

Administration: Ponderax tablets and Pacaps should be taken orally. Ponderax tablets should be taken in divided daily doses and Ponderax Pacaps, because of the slow release of the active constituent, need be taken only once daily; preferably before breakfast. If possible the tablets or capsules should be taken half an hour before food.

Contra-indications, warnings, etc Should not be used concomitantly with MAOIs. There should be an interval of three weeks between stopping MAOIs and starting Ponderax. Care should be exercised when giving Ponderax to depressed patients or those receiving antidepressant therapy.

Following sudden withdrawal of high therapeutic doses of Ponderax occasional reports of depression, lasting a few days, have been received. This effect may be avoided by a gradual reduction of dosage.

Ponderax may potentiate the action of antihypertensive, antidiabetic and sedative drugs. The dosage of

these drugs should be reassessed when Ponderax is prescribed.

In those patients who experience sedation with Ponderax care should be taken when driving, working machinery or taking alcohol.

It is recommended that Ponderax is not given concomitantly with other appetite suppressants. There should be an interval of two weeks before stopping any other appetite suppressant and starting Ponderax to allow for any possible withdrawal symptoms to subside.

Although both human and animal studies have demonstrated that there are no harmful effects on the foetus, it is not recommended that Ponderax be administered during the first trimester of pregnancy unless the physician considers that the benefits outweigh any possible risk.

Side-effects: In some patients looseness of the bowels, mild sedation and giddiness may occur. Nausea and headache have been reported. Side-effects may be reduced or avoided by using a gradual build up of dosage; in other patients the effects are often transient and a temporary reduction of dosage will usually eliminate them. Side-effects only rarely necessitate any interruption of therapy.

Overdosage: The following symptoms have been reported: dilated pupils, tachycardia, facial flushing, hypertension, agitation, fine tremor. The symptoms can progress to vomiting, convulsions, unconsciousness, hyperpyrexia. Depression of respiration, cardiac arrhythmias, ventricular fibrillation and death may occur following very high overdosage.

Action to be taken in the event of an overdose: i) monitor ECG continuously; ii) use diazepam to control convulsions; iii) reduce hyperthermia; iv) use anti-arrhythmic drugs (e.g. beta-blockers) to control cardiac tachyarrhythmias.

Pharmaceutical precautions *Storage:* Ponderax PACAPS should be stored in a cool, dry place.

Legal category POM.

Package quantities *Ponderax Pacaps:* Push-through blister strips of 10 capsules.

Carton of 60 capsules (6 strips).

Ponderax 20 mg and Ponderax 40 mg: Push-through blister strips of 20 tablets.

Carton of 100 tablets (5 strips).

Further information Although fenfluramine is chemically allied to amphetamine the introduction of a CF₃ group into the molecule alters the pharmacological characteristics of the compound which are evident from its lack of central nervous system stimulation and its lack of abuse or dependence potential.

Ponderax is not a controlled drug under the Misuse of Drugs Act 1971 or the Misuse of Drugs Regulations 1973.

Product licence numbers

Ponderax PACAPS 0093/0013

Ponderax 20 mg 0093/5004

Ponderax 40 mg 0093/0026

SYN-ERGEL*

Presentation Synergel is a white gel with an odour and flavour of orange. It contains two gels – one aluminium phosphate and the other a natural gel of pectin and agar. Each dose is presented in the form of a 20 g sachet the active constituents of which are aluminium phosphate gel (11 g), with a pectin agar (9 g).

Aluminium phosphate gel is in the form of a microcolloid which has a high adsorptive capacity. A suspension of the gel is neutral (pH 6.5–7) and neither weakly ionised bases nor acids can attack it. The insoluble gel acts as a buffer in the pH range corresponding to that of the gastric contents.

The natural gel is a molecular colloid which adheres to the walls of the digestive tract, as is the case with natural mucin, providing protection for the mucosa and a dispersal medium for the aluminium phosphate gel.

Uses Dyspepsia, gastritis, oesophagitis, gastric ulcer, duodenal ulcer, heartburn in pregnancy, hiatus hernia, hyperacidity, flatulence.

Dosage and administration The usual adult dose is 1 sachet two or three times daily or as directed by a physician. The medication can be taken directly from the sachet or diluted in water. The dosage for children is 5 ml measure per 24 hours for each 4.5 kg weight, to be taken in divided doses.

Contra-indications, warnings, etc There are no known contra-indications to Synergel. Synergel is physico-chemical in its action; it acts locally and is not absorbed. It is not habit forming and may be used over long periods of time without untoward effect.

Pharmaceutical precautions Synergel should be stored in a cool dry place.

Legal category P.

Package quantities Packs of 25 sachets.

Further information Nil

Product licence number 0093/0025.

* Trade Mark

Seton Products Limited

Tubiton House
Medlock Street
Oldham, OL1 3HS

CALABAND*

Presentation Calaband is Zinc paste with calamine bandage (Drug Tariff) and consists of an open-wave bleached cotton bandage impregnated evenly with a paste of:

Zinc Oxide BP	9.25%
Calamine BP	5.75%
Modified Starch	19.15%
Boric Acid BP	2.0%
Glycerine BP	27.0%
Castor Oil BP	1.0%
Propyl Hydroxybenzoate BP	0.2%
Water to	100%

The bandage is pink in colour and supplied rolled ready for use. It is presented wrapped in waxed paper, sealed in an air tight polythene pouch within a cardboard carton.

Uses

1. Varicose and gravitational ulcers, in conjunction with a compression bandage such as Lestreflex* where protection and treatment of an accompanying subacute eczema is required.
2. All non exudative subacute eczemas particularly where erythema predominates.
3. Dermatitis sometimes experienced after removal of Plaster of Paris casts and protecting areas of contact dermatitis from further irritation.

Dosage and administration The bandage is for topical application and may be renewed as frequently as the condition requires.

Contra-indications, warnings, etc Allergy to an ingredient of the paste.

Pharmaceutical precautions The bandage should be stored in a cool place.

Legal category POM.

Package quantities Calaband is supplied as a single bandage 7.5 cm x 6 m in a carton.

Further information Calaband is intended to be covered, by a compression bandage for the treatment of leg ulcers, or by a tubular bandage for other conditions in order to prevent the soiling of clothes and to reduce drying out of the bandage.

The incidence of hyper-sensitivity reaction is extremely rare.

Product licence number 0223/5003.

ICTHABAND*

Presentation Ichthaband is Zinc paste and ichthammol bandage BPC (Drug Tariff) and consists of an open-wave bleached cotton bandage impregnated evenly with a paste of:

Zinc Oxide BP	15.0%
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Modified Starch	18.5%
Glycerine BP	27.0%
Castor Oil BP	1.0%
Boric Acid BP	2.0%
Ichthammol BP	2.0%
Propyl Hydroxybenzoate BP	0.2%
Water to	100%

The bandage is beige in colour and supplied rolled ready for use. It is presented wrapped in waxed paper, sealed in an air tight polythene pouch within a cardboard carton.

Uses

1. Subacute eczematous conditions.
2. Chronic eczema, where tar is not tolerated.
3. Subacute gravitational eczemas and all other forms of leg eczema.
4. Varicose and gravitational ulcers, in conjunction with a compression bandage such as Lestreflex*, when a protective barrier to thin and fragile skin is required.

Dosage and administration The bandage is for topical application and may be renewed as frequently as the condition requires.

Contra-indications, warnings, etc Allergy to an ingredient of the paste.

Pharmaceutical precautions The bandage should be stored in a cool place.

Legal category GSL.

Package quantities Ichthaband is supplied as a single bandage 7.5 cm x 6 m in a carton.

Further information The formulation of Ichthaband is intended to overcome the drying tendency of ichthammol. It is intended that the bandage be covered, by a compression bandage in the treatment of leg ulcers, or by a tubular bandage for other conditions in order to prevent soiling of clothes and to reduce drying out of the bandage.

The incidence of hyper-sensitivity reaction is extremely rare.

Product licence number 0223/5001.

QUINABAND*

Presentation Quinaband is Zinc paste, calamine and clioquinol bandage (Drug Tariff) and consists of an open-wave bleached cotton bandage impregnated evenly with a paste of:

Zinc Oxide BP	9.25%
Clioquinol	1.0%
Calamine BP	5.75%
Modified Starch	18.5%
Boric Acid BP	2.0%
Glycerine BP	27.0%
Castor Oil BP	1.0%

Propyl Hydroxybenzoate BP	0.0625%
Water to	100%

The bandage is yellow in colour and supplied rolled ready for use. It is presented wrapped in a waxed paper, sealed in an air tight polythene pouch within a cardboard carton.

Uses

1. Varicose and gravitational ulcers, in conjunction with a compression bandage such as Lestreflex*. Quinaband will reduce the odour often associated with leg ulcers and is particularly useful if the ulcer is infected.

2. Conditions liable to become secondary infected such as burns and scalds.

Dosage and administration The bandage is for topical application and may be renewed as frequently as the condition requires.

Contra-indications, warnings, etc Allergy to an ingredient of the paste.

Pharmaceutical precautions The bandage should be stored in a cool place.

Legal category GSL.

Package quantities Quinaband is supplied as a single bandage 7.5 cm x 6 m in a carton.

Further information Quinaband is impregnated with cloquinol 1.0%. This antibacterial agent has a low sensitising potential and a wide spectrum of action. Resistance on the part of organisms does not occur.

It is intended that the bandage be covered, by a compression bandage for the treatment of leg ulcers, or by a tubular bandage for other conditions in order to prevent soiling of clothes and to reduce drying out of the bandage.

The incidence of hyper-sensitivity reactions is extremely rare.

Product licence number 0223/5005.

TARBAND*

Presentation Tarband is Zinc paste and coal tar bandage BP (Drug Tariff) and consists of an open-wave bleached cotton bandage impregnated evenly with a paste of:

Zinc Oxide BP	15.0%
Prep. Coal Tar BP 1973	3.0%
Glycerine BP	27.0%
Propyl Hydroxybenzoate BP	0.2%
Modified Starch	18.5%
Castor Oil BP	1.0%
Water to	100%

The bandage is grey in colour and supplied rolled ready for use. It is presented wrapped in a waxed paper, sealed in an air tight polythene pouch within a cardboard carton.

Uses

1. All forms of chronic eczema.
2. Lichenification (lichen simplex) and lichenified eczema.

3. Infantile eczema.

4. Atopic dermatitis.

5. Varicose and gravitational ulcers, in conjunction with a compression bandage such as Lestreflex*, where protection and treatment of an accompanying eczema is required.

Dosage and administration The bandage is for topical application and may be renewed as frequently as the condition requires.

Contra-indications, warnings, etc Allergy to an ingredient of the paste and acute eczematous lesions.

Pharmaceutical precautions The bandage should be stored in a cool place.

Legal category GSL.

Package quantities Tarband is supplied as a single bandage 7.5 cm x 6 m in a carton.

Further information Tarband is intended to be covered, by a compression bandage for the treatment of leg ulcers, or by a tubular bandage for other conditions in order to prevent soiling of clothes and to reduce drying out of the bandage.

The incidence of hyper-sensitivity reaction is extremely rare.

Product licence number 0223/5004.

ZINCABAND*

Presentation Zincaband is Zinc paste bandage BP (Drug Tariff) and consists of an open-wave bleached cotton bandage impregnated evenly with a paste of:

Zinc Oxide BP	15.0%
Modified Starch	18.5%
Glycerine BP	27.0%
Castor Oil BP	1.0%
Boric Acid BP	2.0%
Propyl Hydroxybenzoate BP	0.2%
Water to	100%

The bandage is off-white in colour and supplied rolled ready to use. It is presented wrapped in waxed paper, sealed in an air tight polythene pouch within a cardboard carton.

Uses

1. Varicose ulcers, where protection and a soothing application is indicated, in conjunction with a compression bandage such as Lestreflex*.

2. Subacute and chronic eczema.

3. Dermatitis of the hand or wrist.

4. Lichenification.

Dosage and administration The bandage is for topical application and may be renewed as frequently as the condition requires.

Contra-indications, warnings, etc Allergy to an ingredient of the paste.

Pharmaceutical precautions The bandage should be stored in a cool place.

Legal category GSL.

Package quantities Zincaband is supplied as a single bandage 7.5 cm x 6 m in a carton.

Further information Zincaband is especially formulated to retain its smoothness and consistency. It is intended that the bandage be covered, by a compression bandage for the treatment of leg ulcers, or by a tubular bandage for other conditions in order to prevent soiling of clothes and reduce drying out of the bandage.

The incidence of hyper-sensitivity reaction is extremely rare.

Product licence number 0223/5000.

*Trade Mark

Sinclair Pharmaceuticals Limited

3orough Road
3odalming
3urrey GU7 2AB



ALUHYDE*

Presentation Each off-white scored tablet contains:
Dried Aluminium Hydroxide Gel BP 245 mg
Magnesium Trisilicate BP 245 mg
Belladonna Extract, Liquid BPC 7.8 mg
The alkaloids of belladonna have a spasmolytic action in the smooth muscle in the treatment of intestinal and biliary colic.

As in contrast to other antacids, Magnesium Trisilicate does not give rise to alkalosis and its antacid action is prolonged; the compound is of great value in the treatment of gastric and duodenal ulcers.

Dried Aluminium Hydroxide Gel as a slow-acting antacid, provides symptomatic relief in gastric and duodenal ulcer, in reflux eosophagitis and is used in the treatment of hyperchlorhydria.

Uses Antacid and antispasmodic, gastric and duodenal ulcer, gastritis, pylorospasm, hyperchlorhydria, functional dyspepsia, gall bladder dyspepsia, and irritable bowel syndrome.

Dosage and administration 2 tablets to be taken after each meal, preferably with a cupful of milk, or before each meal according to the discretion of the physician.

Contra-indications, warnings, etc *Contra-indications:* Glaucoma and acute intermittent porphyria.

Precautions: Caution should be observed in patients with prostatic enlargement, angina pectoris, cardiac failure, and in patients with impaired hepatic or renal function.

Side-effects: These are rare and include Xerostomia and disturbances of vision.

Overdose: Treatment should be directed towards the elimination of the injected material by emesis, aspiration and gastric lavage. General supportive measures should be applied with particular reference to the cardiovascular and respiratory system.

Pharmaceutical precautions *Storage:* No special storage requirements.

Legal category POM.

Package quantities Containers of 50 and 500 tablets.

Further information Nil.

Product licence number 0622/5906.

CAPRIN*

Presentation Each pink tablet of Caprin contains 324 mg (5 grains) of compacted acid resistant acetylsalicylic acid.

Caprin has been designed to minimise or eliminate the gastric side-effects of aspirin and will be useful in rheumatoid arthritis or when long term salicylate therapy is indicated.

Caprin tablets are produced under very heavy pressure resulting in a compacted tablet which will not disintegrate in the stomach. The possibility of surface erosion or diffusion in an acid medium has been overcome by the application of a long chain polymer to the aspirin prior to compression. The polymer has the property of being resistant to acid but it swells on contact with alkali. This, together with the acid-alkali interaction between aspirin and the alkaline medium of the duodenum, provides rapid disintegration and absorption.

Uses Caprin is especially valuable in acute and chronic rheumatic states when long-term aspirin therapy is necessary.

Dosage and administration 1-4 tablets. 3-4 times daily as required.

This is identical with ordinary Aspirin. The tablets must not be chewed or crushed and Caprin tablets are best taken before meals.

Dosage should be adjusted according to the daily salicylate requirements. 15 tablets are equivalent to 5 grammes of Aspirin.

Contra-indications, warnings, etc *Side-effects and precautions:* Caprin is contra-indicated in aspirin allergy. The side-effects of gastric irritation and occult bleeding are eliminated. Caprin should not be taken with concurrent antacid therapy.

Overdosage should be treated initially by aspiration and lavage and a saline purgative such as sodium sulphate, 30 g in 250 ml of water should be given to promote peristalsis. Otherwise treat as for aspirin poisoning.

Pharmaceutical precautions

Storage: No special storage requirements.

Legal category GSL.

Package quantities Containers of 100 and 1000 tablets.

Further information Nil.

Product licence number 0622/5000.

CLAIRVAN* INJECTION

Presentation Clairvan Injection is presented as 2 ml ampoules, containing a 5% solution of Ethamivan BPC. It is also available as Clairvan Oral Solution for use in infants.

Uses Clairvan is a respiratory stimulant which is useful in reversal of barbiturate anaesthesia; management of carbon dioxide narcosis, and to alleviate respiratory depression in patients with chronic obstructive pulmonary disease receiving oxygen therapy; treatment of barbiturate poisoning; neonatal asphyxia (oral solution).

Clairvan increases the rate and depth of respiration by

action through the respiratory centre. This activity is complemented by a stimulant effect on the vasomotor centre which causes peripheral vasoconstriction.

Clairvan has an immediate onset of action but, because it is rapidly metabolised, its stimulant action is short. Repeated dosage is therefore necessary.

Dosage and administration Clairvan is given intravenously except to very young children when it may be given lingually, in the form of the oral solution.

Children: The drug is usually administered by the lingual route and the effect on respiration is comparable to that of the same dose given by intravenous injection. Response to treatment usually begins within one minute and lasts for about five to ten minutes.

Full term infant: 12 drops (to graduation mark on dropper – 25 mg.)

Premature infant: 6 drops (12.5 mg).

Clairvan Oral Solution should be administered after routine aspiration of the air passages. If there is no response to the recommended dose within two minutes, the respiratory depression may be assumed to be irreversible by any available safe chemotherapeutic agent. Intubation should be carried out.

Adults: Reversal of barbiturate anaesthesia: intravenous injection of 1 ml (5% solution) repeated in one minute if necessary. In some cases, 3 to 5 ml is required and should be administered over 10 to 15 minutes.

Barbiturate poisoning: initially, injection of 5 to 10 mg/kg, an average of 10 ml (5% solution) in adults; repeat if required.

Barbiturate poisoning should be treated with measures to maintain respiration, correct electrolyte imbalance and by removal of any drug from stomach. Severe cases of phenobarbitone poisoning should in addition be given forced alkaline diuresis. Clairvan is a useful adjunct to treatment particularly in the less severe cases.

Carbon dioxide narcosis: Intermittent intravenous injection of 2 ml (5% solution).

Contra-indications, warnings, etc Clairvan should not be given to epileptic patients or to those with respiratory failure caused by a convulsant drug. It should not be given to patients who are being treated with a monoamine oxidase inhibitor such as isocarboxazid, nialamide, phenelzine or tranylcypromine, or within two weeks of the discontinuation of such treatment.

Side-effects: Spontaneous motor activity – limb movement, coughing, yawning or hiccoughing – is a sign of response to treatment with Clairvan. A repeat dose should then only be administered with caution, as overdose may lead to convulsions.

Overdose treatment: The drug is rapidly metabolised and no specific treatment is usually necessary apart from general supportive measures. Short acting barbiturates, e.g. thiopentone, counteract the convulsive effect of Clairvan.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Clairvan is supplied in boxes containing 6 x 2 ml ampoules; also 5 ml dropper bottles of Oral Solution for infants.

Further information Nil.

Product licence number 0622/0008.

CLAIRVAN* ORAL

Presentation Clairvan Oral Solution is available in glass dropper bottles. Each bottle contains 5 ml solution of Ethamivan BPC 5% (50 mg/ml) in 25% ethyl alcohol.

Uses Clairvan Oral is a respiratory stimulant, specifically designed for simple administration to neonates. It is indicated in neonatal asphyxia, cyanotic attacks (as seen in premature infants), respiratory distress syndrome (hyaline membrane disease).

Ethamivan increases the rate and depth of respiration by action through the respiratory centre and reflexly through the carotid body. This activity is complemented by a stimulant effect on the vasomotor centre which causes peripheral vasoconstriction.

Clairvan has an immediate onset of action as a result of its rapid absorption from the mucous membrane of the tongue and mouth. It is rapidly metabolised in the tissue. The effect on respiration by the lingual route is comparable to that of the same dose given by intravenous injection. Response to treatment usually begins within one minute and lasts for about five to ten minutes.

Dosage and administration

Full term infant: 12 drops (to graduation mark on dropper – 25 mg).

Premature infant: 6 drops (12.5 mg).

Clairvan Oral Solution should be administered after routine aspiration of the air passages. If there is no response to the recommended dose within two minutes the respiratory depression may be assumed to be irreversible by any available safe chemotherapeutic agent. Intubation should be carried out.

Contra-indications, warnings, etc

Side-effects and overdose: Symptoms of overdose are irritability, gasping respiration and muscle twitching. Clairvan Oral Solution should therefore be administered with care, if these symptoms start to appear.

Contra-indications: None.

Pharmaceutical precautions No special storage precautions are required. After use, the bottle should be re-closed with the original cap, to prevent evaporation.

Legal category POM.

Package quantities Bottle containing 5 ml supplied with a separate dropper.

Further information Nil.

Product licence number 0622/0009.

FERFOLIC*

Presentation Each dark orange sugar-coated tablet contains:

Folic Acid BP	5 mg
Ferrous Gluconate BP (equivalent to 30 mg Fe)	250 mg
Thiamine Hydrochloride BP	3 mg
Nicotinamide BP	10 mg
Riboflavin BP	1 mg
Ascorbic Acid BP	10 mg

Folic acid is necessary for normal production of red blood-cells; it is readily absorbed from the gastrointestinal tract and rapidly appears in the blood. It is usually well tolerated.

In iron-deficiency anaemia, the daily haemoglobin increase and the iron utilisation coefficient have been found to be much higher after the treatment with Ferrous Gluconate than with various other iron preparations. The combination with Ascorbic Acid proved to be more effective than a comparable tablet without Ascorbic Acid. As anaemias in numerous animal trials proved to be partly due to deficiencies in vitamins, other members of the vitamin B-group, such as Thiamine, Riboflavine and Nicotinamide, are included in the preparation, in order to re-establish a healthy blood-picture and to maintain a normal basal metabolism. The vitamins of the B-group play an essential role in the oxygenation-reduction processes in the organism.

Uses For the prevention and treatment of iron and folic acid deficiency anaemias.

Dosage and administration Three tablets daily for the treatment of anaemia and one to three tablets daily for prophylaxis. The tablets should be administered with food. Therapy in patients with iron deficiency should be continued for 3–6 weeks after the haemoglobin level has returned to normal.

Ferfolic is unsuitable for children.

Contra-indications, warnings, etc

Contra-indications: Patients with known hypersensitivity to iron. Macrocytic anaemia due to vitamin B12 deficiency. Use with caution in patients with haemochromatosis and haemolytic anaemia.

Side-effects: Those associated with oral iron therapy, i.e. nausea, vomiting, diarrhoea or constipation. These are reduced by giving iron preparations with food.

Precautions:

1. The absorption of iron salts is decreased in the presence of antacids.
2. As with all iron preparations, oral tetracycline therapy should be avoided as iron diminishes the absorption of the antibiotic from the gastro intestinal tract.

Overdosage: Excessive iron will produce a corrosive effect in the gastro intestinal tract, with abdominal pain, vomiting and sometimes haematemesis. Treatment is by gastric lavage with 1% sodium bicarbonate followed by oral desferrioxamine 5 g. In very severe cases with high serum levels intravenous desferrioxamine therapy should be used in addition to the oral dose.

Pharmaceutical precautions

Storage: No special storage requirements.

Legal category POM.

Package quantities Containers of 100 and 500.

Further information Nil.

Product licence number 0622/5015.

FERFOLIC* S.V.

Presentation Each pink sugar-coated tablet contains:

Folic Acid BP	5 mg
Ferrous Gluconate BP	250 mg
(equivalent to 30 mg Fe)	
Ascorbic Acid BP	10 mg

Ferfolic S.V. contains iron, folic acid and vitamin C, thus omitting the vitamins of the B group contained in Ferfolic. Thus its suffix S.V. (*sine vitaminis*).

Folic Acid is necessary for normal production of red blood-cells; it is readily absorbed from the gastro-

intestinal tract and rapidly appears in the blood. It is usually well tolerated.

In iron-deficiency anaemia, the daily haemoglobin increase and the iron utilisation coefficient have been found to be much higher after the treatment with Ferrous Gluconate than with various other iron preparations. The combination with Ascorbic Acid proved to be more effective than a comparable tablet without Ascorbic Acid.

Uses For the treatment and prevention of Anaemias associated with folic acid deficiency.

Dosage and administration Three tablets daily for the treatment of anaemia and one to three tablets daily for prophylaxis. The tablets should be administered with food. Therapy in patients with iron deficiency should be continued for 3–6 weeks after the haemoglobin level has returned to normal.

Ferfolic S.V. is unsuitable for children.

Contra-indications, warnings, etc

Contra-indications: Patients with known hypersensitivity to iron. Macrocytic anaemia due to vitamin B12 deficiency. Use with caution in patients with haemochromatosis and haemolytic anaemia.

Side-effects: Those associated with oral iron therapy, i.e. nausea, vomiting, diarrhoea or constipation. These are reduced by giving iron preparations with food.

Precautions:

1. The absorption of iron salts is decreased in the presence of antacids.
2. As with all oral iron preparations, oral tetracycline therapy should be avoided as iron diminishes the absorption of the antibiotic from the gastrointestinal tract.

Overdosage: Excessive iron will produce a corrosive effect in the gastro intestinal tract, with abdominal pain, vomiting and sometimes haematemesis. Treatment is by gastric lavage with 1% sodium bicarbonate followed by oral desferrioxamine 5 g. In very severe cases with high serum levels intravenous desferrioxamine therapy should be used in addition to the oral dose.

Pharmaceutical precautions

Storage: No special storage requirements.

Legal category POM.

Package quantities Containers of 100 and 500.

Further information Nil.

Product licence number 0622/5016.

FERGLUVITE*

Presentation Each yellow sugar-coated tablet contains:

Ferrous Gluconate BP	250 mg
(equivalent to 30 mg Fe)	
Thiamine Hydrochloride BP	3 mg
Nicotinamide BP	10 mg
Riboflavine BP	1 mg
Ascorbic Acid BP	10 mg

In iron-deficiency anaemia, the daily haemoglobin increase and the iron utilisation coefficient have been found to be much higher after the treatment with Ferrous Gluconate than with various other iron preparations.

The combination with Ascorbic Acid proved to be more effective than a comparable tablet without Ascorbic Acid.

As anaemias in numerous animal trials proved to be partly due to deficiencies in vitamins, members of the vitamin B-group, such as Thiamine, Riboflavine and Nicotinamide, are included in the preparation, in order to re-establish a healthy blood-picture and to maintain a normal basal metabolism. The vitamins of the B-group play an essential role in the oxygenation – reduction processes in the organism.

Uses Hypochromic and microcytic anaemias.

Dosage and administration One to two tablets 3 times daily after meals.

Contra-indications, warnings, etc

Side-effects and precautions: The tablets are well tolerated at the recommended dosage, and side-effects are uncommon. Therapeutic doses of iron may cause gastro-intestinal discomfort and diarrhoea, but may not necessitate stopping treatment. Overdosage with iron-preparations have a corrosive effect on the stomach, illustrated by epigastric pain, diarrhoea, vomiting, and haematemesis. In acute poisoning, induce emesis, followed by gastric lavage with a 1% solution of sodium bicarbonate.

Pharmaceutical precautions

Storage: No special storage requirements.

Legal category GSL.

Package quantities Containers of 100 and 500.

Further information Nil.

Product licence number 0622/5018.

GLYKOLA*

Presentation A dark red syrupy liquid with a pleasant sweet fruity taste.

Each 5 ml contains:

Caffeine Alkaloid	20 mg
Calcium Glycerophosphate	30 mg
Kola Extract, Liquid	0.12 ml
Chloroform Spirit	0.12 ml
Ferric Chloride Solution	0.01 ml
Alcohol 95%	0.5 ml

Caffeine stimulates the central nervous system and acts on the cardiac muscle and on the kidneys.

The Glycerophosphate, a constituent of lecithin, contained in the brain, for many years has been widely used as a tonic in debilitated conditions and in convalescence.

The Kola drug, known to the medical profession for over 100 years, contains caffeine and has a peculiar stimulating effect in so far, as it does not leave the secondary depression, unlike the after-effects of the ordinary stimulants, which gradually develop into an irresistible desire for continuation of the use of the drug. Thus Kola is not habit-forming, a point of inestimable value in its favour. The physiological action of Kola differs from that of caffeine in so far as it is more pronounced and prolonged; the reason being, that the glycoside kolamin has to be hydrolyzed into caffeine and tannine by the metabolism.

Ferric Chloride Solution is included in the preparation, as iron is fundamentally needed for haemoglobin formation and for the oxidative processes of living tissues.

Uses A powerful general tonic and restorative pick me-up, useful in post-operative and post-influenza Convalescence, Asthenia, Debility and Depressive States.

Dosage and administration 1–2 teaspoonful 3 times daily after meals.

Contra-indications, warnings, etc

Contra-indications: None.

Precautions: The preparation should be given with care to patients with a history of peptic ulceration. The oral administration of iron preparations sometimes produce gastro-intestinal irritation with vomiting and diarrhoea which may be reduced by administration immediately after food.

Pharmaceutical precautions

Storage: No special storage requirements.

Legal category GSL.

Package quantities Bottles of 1 litre.

Further information Nil.

Product licence number 0622/5020.

GLYKOLA* INFANS

Presentation A dark reddish-brown liquid with a pleasant sweet fruity taste.

Each 5 ml contains:

Manganese Glycerophosphate	10 mg
Ferric Chloride Solution	0.016 ml
Kola Extract, Liquid	0.066 ml
Compound Gentian Infusion	1.000 ml
Citric Acid	40 mg

Manganese, being a normal component of the body plays an important physiological role in the metabolism especially as a catalyst for iron it increases its haematinic action.

The Ferric Chloride Solution is included in the preparation, as iron is fundamentally needed for the haemoglobin formation and for the oxidative processes of living tissues.

The Glycerophosphate, a constituent of lecithin contained in the brain, has for many years been widely used as a tonic in debilitated conditions and in convalescence.

The Kola drug, known to the medical profession for over 100 years, contains caffeine and has a peculiar stimulating effect in so far as it does not leave the secondary depression, unlike the after-effects of the ordinary stimulants, which gradually develop into an irresistible desire for a continuation of the use of the drug. Thus Kola is not habit-forming, a point of inestimable value in its favour. The physiological action of Kola differs from that of caffeine, in so far, as it is more pronounced and prolonged, the reason being, that the glycoside kolamin has to be hydrolyzed into caffeine and tannine by the metabolism.

Gentian is the most important of the *amara* and is used to stimulate gastric secretion and, thus, improve the appetite; it contains the bitter glycoside gentiopicrin.

Furthermore, it has been proved that, even after small doses of Gentian, an increase in the white and red blood-corpuscles took place.

Uses A tonic for children, useful in post-operative and post-influenza Convalescence, Asthenia, Debility and Depressive States.

Dosage and administration

Children of 6 months to 2 years: 1–2 ml.

Children over 2 years: 2–5 ml.

Both: 3 times daily, well diluted with water, after meals.

Contra-indications, warnings, etc

Contra-indications: None.

Precautions: The preparation should be given with care to children with a history of peptic ulceration. The oral administration of iron preparations sometimes produces gastro-intestinal irritation with vomiting and diarrhoea, which may be reduced by administration immediately after food.

Pharmaceutical precautions

Storage: No special storage requirements.

Legal category GSL.

Package quantities Bottles of 1 litre.

Further information Nil.

Product licence number 0622/5021.

LEDCLAIR* INJECTION

Presentation Each 5 ml ampoule contains 1 g Sodium Calciumedetate BP in water for injection.

Uses Ledclair Injection is indicated in the treatment of lead and other heavy metal poisoning.

Sodium calciumedetate is the calcium chelate of disodium ethylenediamine tetra-acetic acid (E.D.T.A.). E.D.T.A. combines with polyvalent metallic ions to form a non-ionised water-soluble complex or chelate. When this complex is given either by injection or orally, the calcium is exchanged for lead in the plasma; compounds of E.D.T.A. do not enter the erythrocytes. Lead is mobilised from the bones and other tissues into the plasma where the exchange occurs. It is also gradually lost from the erythrocytes probably due to migration of lead into the plasma. The chelate of lead (and certain other heavy metals) is water-soluble and is readily excreted via the kidneys.

Ledclair may be used for the diagnosis of early and mild cases of lead poisoning. In this test the total amount and concentration of lead excreted in the urine during the 24 hours after drug administration is determined. The output of a normal child after treatment average 165 mcg/Litre. Concentrations in excess of 500 mcg/Litre indicate the presence of potentially toxic amounts of lead in the body and the patient should be investigated further.

Dosage and administration

Adults and Children: The injection may be given by either the intravenous or intramuscular route.

Intravenous therapy: The contents of a 5 ml (1 g) ampoule should be diluted with 250 to 500 ml of Injection of Sodium Chloride BP or Injection of Dextrose BP 5% and the dilute solution given over a period of at least one hour. The concentration of Ledclair should not exceed 3% in the infusate (one ampoule diluted with at least 33 ml fluid).

The dose is 60–80 mg/kg per day given in two equal divided doses with 8–12 hours between each treatment. This therapy is continued for up to 5 days followed at least 48 hours later, by a further course of up to 80 mg/kg/day for a maximum of 5 days.

It is important not to exceed the maximum daily dose of 80 mg/kg or to give more than a total of 800 mg/kg in the two 5-day treatment periods. If the patient's condition necessitates further treatment with Ledclair after the two five day courses have been completed, there must be an interval of at least 7 days before recommending therapy.

Intramuscular therapy: The same limitations on dosage apply as for intravenous therapy. Procaine (without a preservative) should be added to give a concentration of 1.5% of the anaesthetic. The total daily dose should be divided into two or four injections.

Diagnostic Use: The dose of Ledclair for diagnostic purposes is 75 mg/kg intramuscularly and divided into three equal doses given at 8-hourly intervals. Procaine should be added as described above for intramuscular therapy.

Contra-indications, warnings, etc

Contra-indications: None.

Precautions: Overdosage can lead to nephro-toxicity and, therefore, considerable care must be exercised in patients with impaired renal function. The doses recommended above should be halved for patients with moderate impairment, the whole dose being given in a single daily injection. It is recommended that smaller and less frequent doses should be used with more severe renal dysfunction.

Side-effects: Nausea and cramp can occur, particularly during intravenous injection.

Overdosage: General supportive measures should be applied and the patient monitored for signs of renal impairment.

Pharmaceutical precautions No special storage requirements.

Legal category POM.

Package quantities Boxes of 6 × 5 ml ampoules (0.2 g/ml).

Further information Nil.

Product licence number 0622/5900.

LIMCLAIR* INJECTION

Presentation Limclair is the trisodium salt of ethylenediamine tetra-acetic acid (E.D.T.A.).

Each 5 ml ampoule contains 0.2 g/ml of Trisodium Edetate in water for injection.

Uses Limclair is indicated for hypercalcaemia, parathyroidism, digitalis arrhythmias and, by local application, for calcareous corneal opacities resulting from lime burns and band keratitis.

When given by injection, sodium ions are exchanged for calcium ions. The resulting sodium/calcium E.D.T.A. complex formed is excreted via the kidneys. The serum calcium concentration is decreased. The speed with which the calcium level is lowered varies with the route of administration, concentration of the solution and the rapidity of the injection. If the injection is too rapid and the serum calcium level is reduced too quickly, hypocalcaemic tetany can result. Development of systemic hypocalcaemia from the administration of Limclair indicates that calcium chelation is proceeding faster than replacement from calcium reserves.

Dosage and administration

Adults: The average dose is 5 g per day. This is administered by slow intravenous infusion up to 70 mg/kg body weight daily.

Children: Up to 60 mg/kg (1 g/35 lb) body weight daily, by slow intravenous infusion.

The dose is best given in 500 ml of 5 per cent glucose or normal saline solution. The intravenous drip is regulated so that from 2 to 3 hours are required for total infusion.

Important: Too rapid intravenous infusion of Limclair or too high concentration, may lower the serum calcium level precipitously and cause hypocalcaemic tetany. This can be fatal if it is of sufficient severity.

Intravenous infusion of Limclair must therefore be undertaken cautiously, slowly, and with dilute solutions.

Contra-indications, warnings, etc

Side-effects: Renal damage, haemorrhagic tendency and damage of the reticuloendothelial system have been reported from excessive dosage. Toxic skin and mucous membrane reactions have been noted, but these disappeared when medication was stopped.

Nausea, diarrhoea and abdominal cramping pains may occur during intravenous treatment.

Caution: Limclair should be used with caution in tuberculosis.

Contra-indication: Renal disease.

Overdosage: Repeated serum calcium determinations are important for control and maintenance of normal calcium levels. Patients should be under constant observation for signs of tetany, when the infusion rate should be decreased or administration discontinued.

Pharmaceutical precautions

Storage: No special storage precautions are required.

Preparation of dilute solution of Limclair for ophthalmic purposes: A 0.4% solution is recommended, and this is obtained by straightforward dilution of 1 in 50 using distilled water as the diluent (i.e. 1 ml. Limclair made up to 50 ml). This solution can be autoclaved.

Legal category POM.

Package quantities Boxes of 6 × 5 ml ampoules (0.2 g/ml).

Further information Nil.

Product licence number 0622/0006.

MYELOBROMOL* TABLETS

Presentation Myelobromol are plain white tablets containing 125 mg of Mitobronitol.

Myelobromol is a cytostatic agent. It is a halogenated derivative of mannitol which has been shown to have a cytotoxic effect on tumour cells and a selective action on the myeloid system.

Myelobromol is an anti-leukaemic agent which differs from other biological alkylating agents in its mode of action.

Animal experiments and *in vitro* studies have shown clearly that it is effective in inhibiting the growth of solid tumours, but its main clinical application to date has been in the treatment of general myeloproliferative disorders and in particular chronic myeloid leukaemia.

In vitro, Myelobromol exhibits the properties of strong alkylating agent but the drug represents transitional form between alkylating agents and antimetabolites.

Myelobromol shows an alkylating behaviour *in vitro* to that of busulphan, but since Myelobromol release two bromine-containing C3 radicals after enzymatic splitting of the molecule it could well exert an epoxidic alkylating effect and thus the presence of the hydroxy groups may play an important part in its cytostatic effectiveness.

Myelobromol is completely absorbed from the gastro intestinal tract and after passing the liver it is secreted in high concentration in the bile.

A maximum initial level is followed, 24 hours later, by a second peak. After reabsorption from the small intestine the agent remains for a prolonged period in a high concentration in the blood, being excreted in the urine over a period of days for the most part unchanged but partly as bromine-containing metabolites.

Uses Chronic myeloid leukaemia. Myelobromol is indicated in newly presenting cases of chronic myeloid leukaemia and also in those cases which have developed resistance to Busulphan therapy.

Dosage and administration Dependent on the severity of the disease:

Initially: 2 tablets daily until the leucocyte count reduces to 20,000/c.mm.

Maintenance: The dosage used will depend upon blood picture and degree of remission. The suggested dosage is between 1 tablet daily and 1 tablet on alternate days. The duration of treatment is usually 8–12 weeks but may be prolonged or resumed as indicated by the leucocyte count.

Myelobromol should only be given by or under the supervision of a physician experienced in the use of anti-leukaemic agents, and haematological monitoring should be carried out at regular intervals.

This product should not normally be administered to patients who are pregnant or to mothers who are breast-feeding.

Contra-indications, warnings, etc Myelobromol is contra-indicated in severe thrombocytopenia subsequent to previous cytotoxic agents.

Daily blood-count monitoring should be performed until haematological values are stable on a given dose of Myelobromol. Subsequent fortnightly examinations of Hb, stained film, total and differential leucocyte counts and a platelet count should be performed.

Myelobromol may exert a non-selective bonemarrow depressant effect. Blood counts should be carried out frequently during Myelobromol therapy. The appearance of severe thrombocytopenia warrants temporary reduction or discontinuation of Myelobromol therapy. Side-effects of Myelobromol are few; those reported include gastro-intestinal disturbances, alopecia, skin pigmentation, skin rashes and menstrual abnormalities.

Treatment of overdosage: Gastric lavage, whole blood transfusion may be necessary.

Pharmaceutical precautions **Storage:** No special requirements.

Legal category POM.

Package quantities Containers of 50 tablets.

Product licence number 0622/0007.

as brown tablets with

400 mg
500 mg
100 mg
25 mg

treatment of peptic ulcer
normal X-ray findings.
es not produce fluid
cularly indicated in the
less severe forms of

One or two tablets
daily after meals and
ely, the tablets may be
n water, tea or milk. A
onths is recommended.
gradually over a period

s, etc
with renal impairment;
rolonged. Caution is
re oedema or severe

ntomatic and suppor-

Storage: No special

cs of 60, 150 and 600.

5/5000.

3 white, sugar-coated
lamine tartrate (1, 2, 3,
l-2-azafluorene hydro-

ne drug, gives sympto-
t differs from most other
rat it rarely produces
/, has a mild stimulant

for the symptomatic
ch as hay fever, allergic
stings.

Adults: 1 to 2 tablets

blet one to three times

t, the last dose on any
r than 4 pm.
idministration.

s, etc

with other drugs acting
n, patients should be

instructed to avoid alcohol while under treatment, since the individual response cannot be foreseen. In exceptional cases, Thephorin may produce sedation and modify patients' reactions (driving ability, operation of machinery, etc.).

Side-effects: Thephorin is very well tolerated. Side-effects such as dryness of the mouth and gastro-intestinal complaints are uncommon and can usually be avoided by reducing the dose. Stimulation or, very rarely, drowsiness may occur.

Treatment of overdosage: In toxic doses, the anti-histamines produce a complex of central nervous system excitatory and depressant effects. The excitatory effects may produce delirium, excitement and convulsions. Children are apt to exhibit convulsions with hyper-reflexia.

Gastric lavage should be performed, followed by a saline cathartic, and general supportive measures employed. Convulsions or marked excitement may be controlled by injection of diazepam or a short-acting barbiturate. If respiratory depression and coma occur, oxygen and artificial respiration should be used and normal blood pressure maintained with vasopressor agents. Stimulants should not be given.

Pharmaceutical precautions *Storage:* Thephorin tablets should be stored in well-closed containers.

Legal category P.

Package quantities Thephorin tablets in packings of 50.

Further information Nil.

Product licence number 0622/0025.

TOSMILEN* EYE DROPS

Presentation Clear aqueous solution: demecarium bromide 0.25% and 0.5%.

Uses Cholinesterase inhibitor for treatment of chronic primary glaucoma, concomitant convergent strabismus, as an adjunct after cataract extraction, to correct mydriasis due to atropine medication, in ocular myasthenia gravis.

Dosage and administration *Adults:* To initiate therapy, 1 or 2 drops of 0.25% solution instilled into affected eye.

Children: Initial dose 1 drop.

If the patient has not received the drug before, tonometric measurements should then be made at intervals for two to four hours after the first instillation to detect any paradoxical rise in intra-ocular pressure.

Contra-indications, warnings, etc Asthmatic bronchitis, digestive disorders, gastric and duodenal ulcers, bradycardiac disturbances.

Side-effects: In 50% of cases, a moderate dilatation of the conjunctival vessels occurs immediately after instillation and ceases after 15–20 minutes. In about 10% of cases, a more acute congestion of the conjunctiva occurs, persisting sometimes for two to three days. Some patients complain of a more or less acute burning sensation in the eyes persisting for several minutes after instillation. Other patients suffer from pain persisting for one or two hours after the first installation localised or around the eye, and is probably due to ciliary muscle

spasm. The usual analgesics can be given to the treatment of this unpleasant side effect when it occurs.

Adverse reactions: Symptoms of muscarine-like character occurring as a result of hypersensitivity of overdosage, such as nausea, salivation, sweating, bradycardia, abdominal pain, bronchial constriction, etc., can be controlled by subcutaneous injection of 0.5–2 mg atropine sulphate, which may be repeated at intervals until the symptoms are controlled.

Precautions: The cholinesterase inhibition brought about by Tosmilen can sometimes be demonstrated in the blood and this must be taken into account if muscle-relaxing agents liable to decomposition by cholinesterase are administered systemically.

Long term treatment with Tosmilen, depending on strength of solution, age of patient, frequency of installation and duration of treatment, could possibly lead to cataract. Patients being so treated should be examined carefully for signs of this complication developing.

Pharmaceutical precautions Diluent (for immediate use) – saline.

Legal category POM.

Package quantities 5 ml dropper bottles of 0.25% or 0.5% solution.

Further information Nil.

Product licence number

0.25% 0622/5907

0.50% 0622/5908

VISCLAIR* TABLETS

Presentation Visclair is a yellow sugar coated tablet containing 100 mg methylcysteine hydrochloride. The core is enteric coated to ensure absorption in the small intestine.

Uses Visclair is a systemically acting mucolytic with protective and healing properties.

The clinical effects of Visclair, is to liquify viscous or infected sputum, and to produce secretions of a more normal viscosity and volume. Reduction of cough and sputum is evident in patients responding to treatment.

Mucolytic action: The mucolytic action is in two phases. Firstly, because the sulphhydryl groups in VISCLAIR are a readily assimilable supply of sulphur, it can intervene in the synthesis of mucoproteins to produce mucus of a more normal viscosity. Secondly, as the tissue becomes saturated with the drug, the disulphide bonds uniting glucoprotein molecules can be severed, breaking down the mucin gel responsible for sputum viscosity.

Protection: Visclair has been shown, experimentally, to prevent desquamation of respiratory mucosa exposed to irritant vapours such as sulphur dioxide and carbon tetrachloride. In man there is some evidence for a similar therapeutic effect in chronic bronchitis.

Healing: The healing properties of cysteines are well established in cutaneous ulcers. Methylcysteine, an active constituent of Visclair has a predilection for mucosal tissue and provides additional sulphhydryl groups needed to accelerate the repair of damaged membranes in the bronchitic patient.

Indications: Chronic Bronchitis. Viscid or excess mucus secretions in upper/lower respiratory tract disorders, e.g. tracheostomies-bronchiectasis. As an adjunct in the management of upper respiratory tract disorder and bronchitis, e.g. chronic sinusitis and secretory otitis media.

Dosage and administration *Dosage: Adults:* 1 tablet three to four times daily before meals with a little water.

A rapid clinical effect can be achieved by giving tablets 4 times daily for the first 2 days of therapy.

The standard dose, 2 tablets three times a day, is given for 6 weeks and thereafter the dose should be reduced to 2 tablets twice daily.

Children over 5 years: one tablet three times daily.

Prophylactic Use: Prophylactic therapy is of benefit in some bronchitics, i.e., particularly those who show satisfactory response to short term therapy. Prophylactic therapy is best achieved by employing intermittent treatment. The dose is 1–2 tablets 2–3 times daily alternate days throughout the winter months. Prolonged treatment is essential.

Contra-indications, warnings, etc Visclair is well tolerated and serious toxic effects have not been reported. It is important that the tablets, which are enteric coated, should be swallowed whole.

Overdosage may cause excessive production of bronchial secretions and hence result in respiratory embarrassment. In such cases postural drainage and suction would be advisable.

In patients with tuberculosis sputum cultures should be carried out up to three months after cessation of therapy before assuming a negative result.

Patients should naturally be encouraged to cease smoking.

Treatment of overdosage: No specific toxic effects attributable to Visclair have been reported. Treatment should be directed to general supportive measures with induction of vomiting in conscious patients and a forced diuresis should be considered.

Pharmaceutical precautions *Storage:* Visclair tablets should be stored in a dry cool place.

Legal category P.

Package quantities Packs of 100 tablets.

Further information Nil.

Product licence number 0622/5003.

*Trade Mark

**Smith & Nephew
Pharmaceuticals Ltd**
Hampton Road,
Harold Hill,
Bromford,
Essex RM3 8SL



EPHY

Presentation 1-adrenaline base 1% in an isotonic buffered ophthalmic solution.

Uses For the treatment of primary open-angle and secondary glaucoma. It may be used in conjunction withotic or carbonic anhydrase inhibitor therapy.

Dosage and administration *Adults:* One drop instilled into the eye once or twice a day.

Children: At the discretion of the physician.

When used with pilocarpine or other miotics, Ephy could be instilled 5 to 10 minutes afterwards.

Contra-indications, warnings, etc Ephy should not be used where diagnosis of open-angle glaucoma has not been verified. It is contra-indicated in patients with narrow-angle because pupillary dilation may precipitate angle-closure glaucoma. Occasionally patients may complain of orbital discomfort or red eye. Rarely headache, irritation and local skin reactions may occur. As with other adrenaline preparations, melanosis may occasionally occur, but this has no pathological significance. Systemic effects are rare but can include tachycardia, extrasystoles and elevation of blood pressure.

Pharmaceutical precautions Ephy should not be used or dispensed from any container other than the original bottle. It should be stored, in its carton, in a cool place away from strong light. Ephy should not be used if the solution has become dark amber. Ephy should be discarded one month after opening. Ephy is fully potent for two years unopened.

Legal category P.

Package quantities Ephy is supplied as a sterile ophthalmic solution in a 7.5 ml bottle, with a separate sterile dropper.

Further information An air-excluding filling process of strict control of sterilisation ensure the long shelf-life of Ephy.

In common with other sympathomimetic agents Ephy does not affect accommodation.

Product licence number 0033/5022.

FLAMAZINE

Presentation A white hydrophilic cream containing silver sulphadiazine 1% w/w. The cream is a semi-solid in water emulsion. The silver sulphadiazine is in a fine crionised form.

Uses Topical burn treatment, and for the treatment of infected leg ulcers and pressure sores. It is particularly

effective against Gram-negative organisms such as *Pseudomonas aeruginosa*.

Dosage and administration Flamazine should be applied by means of a sterile spatula or a hand covered with a sterile glove in a layer approximately 3-5 mm thick.

In leg ulcers Flamazine should be applied followed by an absorbent gauze dressing and a support bandage, e.g. 10 cm Elastocrepe. Care should be taken not to spread Flamazine on to non-ulcerated skin, and it should not be used on very wet ulcers. The dressing should be changed at least three times a week and desloughing and cleansing carried out at the same time.

In the treatment of burns Flamazine should be applied every 24 hours.

Contra-indications, warnings, etc Teratology tests have been carried out in rabbits (Dutch-belted strain) and no evidence of teratogenicity has been found. Nevertheless the use of this drug during the first three months of pregnancy must be at the clinician's discretion. Further, because sulphonamide therapy is known to increase the incidence of kernicterus, silver sulphadiazine cream should be used with caution in pregnant females at term, in premature infants or in newborn infants during the first months of life.

Although reports of leucopenia following the use of Flamazine in the treatment of burns have been published, these reports do not appear to have been fully substantiated. However, in view of the reports it is as well to be aware of the possibility of low white blood cell counts occurring.

Sensitivity has been shown to occur but the incidence is lower than with other sulphonamides.

Flamazine should be used with caution if hepatic and/or renal function become impaired.

Pharmaceutical precautions The container should be stored in a cool place away from light. One container of Flamazine should be reserved for one patient; any remaining cream should be discarded after the completion of treatment.

Legal category POM.

Package quantities The preparation is obtainable in jars containing 250 g or 500 g and also tubes of 50 g.

Further information As well as its prophylactic effect, Flamazine may also exert a therapeutic action in wounds which are already infected. Flamazine is painless on application, does not cause electrolyte disturbance, is easy to apply and remove and does not stain.

Product licence number 0033/0056.

FLUORETS*

Presentation Sterile, individually wrapped paper strips each impregnated with 1 mg Fluorescein Sodium BP.

Uses Fluorescein is a corneal stain and can be used in diagnostic examinations, including Goldman tonometry and contact lens fitting.

Dosage and administration Pull tabs apart at right-hand end of envelope and withdraw Fluoret. Moisten tip with tear fluid from lower fornix, sterile water or sterile ophthalmic solution. Then gently stroke the Fluoret across the conjunctiva. For the best result the patient should blink several times.

Contra-indications, warnings, etc The applicator should be used once and then discarded. Care should be taken to handle the strip by the non-impregnated end only.

Pharmaceutical precautions No special precautions.

Legal category P.

Package quantities Gravity-delivered cartons of 100 individually wrapped Fluorets.

Further information Nil.

Product licence number 0033/5095.

GANDA*

Presentation Ganda is a clear, viscous, colourless to almost colourless liquid, available in four strengths.

Ganda 1+0.2 (Guanethidine monosulfate PhEur 1% w/v + Adrenaline BP 0.2% w/v)

Ganda 3+0.5 (Guanethidine monosulfate PhEur 3% w/v + Adrenaline BP 0.5% w/v)

Ganda 5+0.5 (Guanethidine monosulfate PhEur 5% w/v + Adrenaline BP 0.5% w/v)

Ganda 5+1 (Guanethidine monosulfate PhEur 5% w/v + Adrenaline BP 1% w/v)

in a buffered solution. It is supplied in a plastic dropper bottle packed in a nitrogen-filled pouch.

Uses For the treatment of primary open angle or secondary glaucoma. It may be used in conjunction with miotics or carbonic anhydrase inhibitor therapy.

Dosage and administration *Adult:* One drop to be instilled into the eye once or twice daily or at the discretion of the physician.

Children: At the discretion of the physician.

When used in conjunction with miotics, Ganda should follow the miotic after an interval of 5–10 minutes.

Contra-indications, warnings, etc Ganda should not be used in the case of a narrow angle between the iris and cornea as pupillary dilation may precipitate angle closure.

Occasionally a patient may complain of orbital discomfort or red eye (hyperaemia). Rarely, headache, irritation and local skin reactions may occur. As with other adrenaline preparations, melanosis may occasionally occur, but this has no pathological significance. Systemic effects are rare but can include tachycardia, extrasystoles, and elevation of blood pressure.

One clinical investigator has reported that in two cases out of 21, a paradoxical increase of I.O.P. occurred for which no explanation was offered.

Some degree of ptosis may represent an adverse effect in glaucoma, but will usually respond to a reduction in dosage or in the frequency of administration.

At prolonged high dosage a tendency to superficial punctate keratitis has been reported, responding either to a reduction in dosage or termination of treatment.

Pharmaceutical precautions Ganda is supplied in plastic dropper bottle in a nitrogen-filled pouch, inside a carton. It should be stored in its carton in a cool place away from strong light. The carton only should be removed before supplying to the patient. Ganda should not be diluted, nor should it be dispensed from a container other than the original bottle. Ganda should not be used if the solution has become dark amber. The contents of the bottle should be discarded one month after removal from the pouch. Ganda is fully potent for two years providing the pouch remains unopened.

Legal category POM.

Package quantities Ganda is supplied as a sterile ophthalmic solution in a 7.5 ml plastic dropper bottle. Each bottle is enclosed in a nitrogen-filled seal nylon/aluminium foil pouch inside a carton.

Further information The use of the nitrogen-filled overwrap ensures the long shelf-life of Ganda.

Ganda is a unique combination of Adrenaline BP and Guanethidine monosulfate PhEur in a plastic dropper bottle which has been specially designed for patient convenience. Its special formulation gives improved stability, and includes a viscosifier to enhance comfort and effectiveness.

In common with other sympathomimetic agents Ganda does not affect accommodation.

Product licence numbers

Ganda 1+0.2 0033/0075

Ganda 3+0.5 0033/0071

Ganda 5+0.5 0033/0070

Ganda 5+1 0033/0069

MINIMS* AMETHOCAINE HYDROCHLORIDE

Presentation Single-use, clear, colourless, sterile eye drops. Two strengths are available: Amethocaine (Tetracaine) Hydrochloride PhEur 0.5% and 1% w/v solution.

Uses As a topical anaesthetic.

Dosage and administration One drop or as required.

Contra-indications, warnings, etc Amethocaine may give rise to dermatitis in hypersensitive patients. Amethocaine is hydrolysed in the body to p-aminobenzoic acid and should not therefore be used in patients being treated with sulfonamides. On instillation an initial burning sensation may be complained of but this passes off in less than half a minute. The anaesthetised eye should be protected from dust and bacterial contamination. The cornea may be damaged by prolonged application of anaesthetic eye drops.

Each Minims unit should be discarded after a single use.

Pharmaceutical precautions Minims should be stored in a cool place, and should not be exposed to strong light.

Legal category POM.

of 20 units, each con-

% 0033/5000
0033/5001

ATE

or colourless sterile eye
tion of Atropine Sulfate

ologic.

One drop as required.

is, etc The protracted
o reverse, may be a
iatric there is a risk that
angle glaucoma into an
is recommended that
tion can be reversed by

discarded after a single

Minims should be
uld not be exposed to

of 20 units, each unit

n of the pupil occurs
ication.

12.

XYBUPROCAINE)

r, colourless, sterile eye
solution of Benoxinate
USP.

One drop of benoxinate
d into the conjunctival
e of the eye to allow
further drop after 90
sthesia for the fitting of

rvals provides sufficient
or a foreign body to be
elium, or for incision of
onjunctiva.
again after about one

is, etc The anaesthe-
rom dust and bacterial
r be damaged by pro-
c eye drops.
discarded after a single

Pharmaceutical precautions Minims should be stored in a cool place, and should not be exposed to strong light.

Legal category POM.

Package quantities Cartons of 20 units, each unit containing approximately 0.5 ml.

Further information When applied to the conjunctiva benoxinate is less irritant than amethocaine in normal concentrations.

Product licence number 0033/5004.

MINIMS* CASTOR OIL

Presentation Single-use, clear, almost colourless or slightly yellow, viscous sterile eye drops.

Uses As a lubricant and emollient.

Dosage and administration One or two drops as required.

Contra-indications, warnings, etc Each Minims unit should be discarded after a single use.

Pharmaceutical precautions Minims should be stored in a cool place and should not be exposed to strong light.

Legal category P.

Package quantities Cartons of 20 units, each unit containing approximately 0.5 ml.

Further information Nil.

Product licence number 0033/5018.

MINIMS* CHLORAMPHENICOL

Presentation Single-use, clear, colourless, sterile eye drops, available as a 0.5% w/v solution of Chloramphenicol PhEur.

Uses As a topical antibacterial preparation. Chloramphenicol is a broad spectrum antibiotic with bacteriostatic activity and is effective against a wide range of Gram-negative and Gram-positive organisms.

Dosage and administration *Adult:* One or more drops as required.

Children: One drop as required.

Contra-indications, warnings, etc Treatment with chloramphenicol should be discontinued immediately on the appearance of toxic symptoms or allergic skin rashes.

Each Minims unit should be discarded after a single use.

Pharmaceutical precautions Chloramphenicol Minims should be stored at 5°C. Do not freeze.

Legal category POM.

Package quantities Cartons of 20 units, each unit containing approximately 0.5 ml.

Further information Nil.

Product licence number 0033/0055.

MINIMS* CYCLOPENTOLATE HYDROCHLORIDE

Presentation Single-use, clear, colourless, sterile eye drops. Two strengths are available: Cyclopentolate Hydrochloride BP 0.5% and 1% w/v solutions.

Uses As a mydriatic and cycloplegic.

Dosage and administration *Adult:* One or two drops as required. Maximum effect is induced 30–60 minutes after instillation. In iritis or iridocyclitis 1 or 2 drops of a 0.5% w/v solution are instilled every six to eight hours. One or two drops of a 0.5% w/v solution are also used for breaking down adhesions of the iris to the lens. For refraction the instillation of 1 drop of a 0.5% w/v solution repeated after five minutes is usually sufficient. Deeply pigmented eyes may require a 1% w/v solution.

Children: At the discretion of the physician.

Contra-indications, warnings, etc Recovery of accommodation occurs within 24 hours.

Use may precipitate a case of latent narrow angle glaucoma into an acute attack.

Each Minims unit should be discarded after a single use.

Pharmaceutical precautions Minims should be stored in a cool place, and should not be exposed to strong light.

Legal category POM.

Package quantities Cartons of 20 units, each unit containing approximately 0.5 ml.

Further information Nil.

Product licence numbers

Cyclopentolate Hydrochloride 0.5%	0033/5005
Cyclopentolate Hydrochloride 1%	0033/5006

MINIMS* FLUORESCEIN SODIUM

Presentation Single-use, clear, orange-red, sterile eye drops. Two strengths are available: Fluorescein Sodium BP 1% and 2% w/v solutions.

Uses As a diagnostic stain. Fluorescein does not stain a normal cornea, but corneal and conjunctival abrasions, or ulcers are stained a bright green and foreign bodies are surrounded by a green ring.

Dosage and administration Sufficient solution should be applied to stain the damaged areas. Excess may be washed away with sterile saline solution.

Contra-indications, warnings, etc Special care should be taken to avoid microbial contamination.

Each Minims unit should be discarded after a single use.

Pharmaceutical precautions Minims should be stored in a cool place, and should not be exposed to strong light.

Legal category P.

Package quantities Cartons of 20 units, each unit containing approximately 0.5 ml.

Further information *Pseudomonas aeruginosa* grows well in Fluorescein solutions, therefore a single use preparation is to be preferred.

Product licence numbers

Fluorescein Sodium 1% 0033/0079

Fluorescein Sodium 2% 0033/5008

MINIMS* GENTAMICIN SULFATE

Presentation Single-use, clear, colourless sterile eye drops containing Gentamicin Sulfate BP equivalent 0.3% w/v gentamicin base.

Uses As a broad-spectrum bactericidal antibiotic, the treatment of infections of the eye caused by both Gram-positive and Gram-negative organisms, including *Pseudomonas aeruginosa*.

Dosage and administration One drop or as required.

Contra-indications, warnings, etc Each Mini unit should be discarded after a single use.

Pharmaceutical precautions Minims should be stored in a cool place, and should not be exposed to strong light. Do not freeze.

Legal category POM.

Package quantities Cartons of 20 units, each unit containing approximately 0.5 ml.

Further information Nil.

Product licence number 0033/0094.

MINIMS* HOMATROPINE HYDROBROMIDE

Presentation Single-use, clear, colourless, sterile eye drops available as a 2% w/v solution of Homatropine Hydrobromide PhEur.

Uses As a mydriatic and cycloplegic.

Dosage and administration One drop or as required.

Contra-indications, warnings, etc As with atropine mydriatic there is a risk that it may precipitate latent narrow-angle glaucoma into an acute attack.

Each Minims unit should be discarded after a single use.

Pharmaceutical precautions Minims should be stored in a cool place, and should not be exposed to strong light.

Legal category POM.

Package quantities Cartons of 20 units, each unit containing approximately 0.5 ml.

Further information Homatropine Hydrobromide has properties similar to those of atropine and is often used in preference to the latter because its action is more rapid in onset and it has a less prolonged mydriatic action.

Product licence number

Homatropine Hydrobromide 2% 0033/5010

MINIMS* HYOSCINE HYDROBROMIDE

Presentation Single-use, clear, colourless, sterile eye drops, available as a 0.2% w/v solution of Hyoscine Hydrobromide PhEur.

Uses As a mydriatic and cycloplegic.

One drop or as required.
It produces maximal
high returns to normal

s, etc As with any
may precipitate latent
acute attack.
discarded after a single

Minims should be
It should not be exposed to

of 20 units, each unit

can be used in patients

1/5011.

FLUORESCCEIN

It is a yellow sterile eye
(Fluorescein) Hydrochloride
Sodium BP 0.25% w/v.
It is a topical anaesthetic
Fluorescein units are
to intra-ocular pressure by

Adult: One or more
physician.

s, etc Known hyper-
sensitivity to local anaesthetics.
It protects the anaesthe-
sized area, particularly
during operation of anaesthesia
as it may be damaged by
alkaline eye drops.
discarded after a single

Minims should be
It should not be exposed to

of 20 units, each unit

1/0073.

ATE

colourless, sterile eye
solution of Neomycin

Preparation. Neomycin
antibiotic activity, being
aphylococci and some
Gram-negative aeruginosa.
viruses.

Dosage and administration One or more drops as
required.

Contra-indications, warnings, etc It should not be
used in patients with known hypersensitivity to Neo-
mycin and other related drugs. Caution is necessary if it
is applied to patients with eczema.
Each Minims unit should be discarded after a single
use.

Pharmaceutical precautions Minims should be
stored in a cool place, and should not be exposed to
strong light.

Legal category POM.

Package quantities Cartons of 20 units, each unit
containing approximately 0.5 ml.

Further information Nil.

Product licence number 0033/5012.

MINIMS* PHENYLEPHRINE HYDROCHLORIDE

Presentation Single-use, clear, colourless, sterile eye
drops, available as a 10% w/v solution of Phenylephrine
(Metaxedrine) Hydrochloride BP.

Uses As a mydriatic agent.

Dosage and administration **Adult:** One drop as
required.

Children: The use of Minims phenylephrine in infants is
not recommended.

Contra-indications, warnings, etc As with any
mydriatic there is a risk that it may precipitate latent
narrow angle glaucoma into an acute attack.

Phenylephrine should not be used in patients with
thyrotoxicosis, hypertension, or cardiovascular problems
including tachycardia, and patients on β blockers.

Each Minims unit should be discarded after a single
use.

Pharmaceutical precautions Minims should be
stored in a cool place, and should not be exposed to
strong light.

Legal category P.

Package quantities Cartons of 20 units, each unit
containing approximately 0.5 ml.

Further information Nil.

Product licence number 0033/5021.

MINIMS* PILOCARPINE NITRATE

Presentation Single-use, clear, colourless, sterile eye
drops. Three strengths are available: Pilocarpine Nitrate
PhEur 1%, 2%, and 4% w/v solutions.

Uses As a miotic for reversing the action of the weaker
mydriatics and in emergency treatment of glaucoma.

Dosage and administration To induce miosis one or
two drops should be used. In cases of emergency
treatment of acute narrow angle glaucoma, one drop
should be used every five minutes until miosis is
achieved.

Contra-indications, warnings, etc Pilocarpine in-
duces spasm of the ciliary muscle which may last up to
two hours.

Each Minims unit should be discarded after a single use.

Pharmaceutical precautions Minims should be stored in a cool place, and should not be exposed to strong light.

Legal category POM.

Package quantities Cartons of 20 units, each unit containing approximately 0.5 ml.

Further information Nil.

Product licence numbers

Pilocarpine Nitrate 1% 0033/5013

Pilocarpine Nitrate 2% 0033/5014

Pilocarpine Nitrate 4% 0033/5016

MINIMS* PREDNISOLONE SODIUM PHOSPHATE

Presentation Single use clear colourless sterile eye drops, available as a 0.5% w/v solution of Prednisolone Sodium Phosphate BP.

Uses Non-infected inflammatory conditions of the eye.

Dosage and administration

Adult: One or two drops to be instilled as required.

Children: At the discretion of the physician.

Contra-indications, warnings, etc Use is contra-indicated in viral, fungal, tuberculous and other bacterial infections. Prolonged application to the eye of preparations containing corticosteroids has caused increased intra-ocular pressure and therefore the drops should not be used in patients with glaucoma. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development and although the relevance of this finding to human beings has not been established, topical steroids should not be used in large amounts or for prolonged periods during pregnancy.

In children, long-term continuous topical corticosteroid therapy should be avoided due to possible adrenal suppression.

Pharmaceutical precautions Minims should be stored in a cool place, and should not be exposed to strong light.

Legal category POM.

Package quantities Cartons of 20 units, each unit containing approximately 0.5 ml.

Further information Nil.

Product licence number 0033/0091.

MINIMS* ROSE BENGAL

Presentation Single-use, clear, dark-red, sterile eye drops, available as a 1% w/v solution of Rose Bengal.

Uses As a diagnostic stain. Rose Bengal solution stains degenerated conjunctival and corneal epithelial cells. It is particularly useful in demonstrating these changes in Sjogren's syndrome, where lack of tears has caused damage. Pressure marks from contact lenses are shown by Rose Bengal indicating that alteration of the lens may be necessary.

Dosage and administration One or two drops as required.

Contra-indications, warnings, etc Can produce severe stinging in dry eyes where it should be used with care.

Each Minims unit should be discarded after a single use.

Pharmaceutical precautions Minims should be stored in a cool place, and should not be exposed to strong light.

Legal category P.

Package quantities Cartons of 20 units, each unit containing approximately 0.5 ml.

Further information Nil.

Product licence number 0033/0048.

MINIMS* SODIUM CHLORIDE

Presentation Single-use, clear, colourless, sterile eye drops, available as a 0.9% w/v solution of Sodium Chloride PhEur.

Uses As an irrigating solution.

Dosage and administration Adequate solution should be used to irrigate the eye.

Contra-indications, warnings, etc Each Minims unit should be discarded after a single use.

Pharmaceutical precautions Minims should be stored in a cool place, and should not be exposed to strong light.

Legal category P.

Package quantities Cartons of 20 units, each unit containing approximately 0.5 ml.

Further information Nil.

Product licence number 0033/5017.

MINIMS* SULFACETAMIDE SODIUM

Presentation Single-use, clear, colourless, sterile eye drops, available as a 10% w/v solution of Sulfacetamide Sodium BP.

Uses For the treatment of conjunctivitis. Sulfacetamide sodium is active against both Gram-positive and Gram-negative organisms, and has a mucolytic effect.

Dosage and administration *Adult:* One drop or more as required.

Children: At the discretion of the physician.

Contra-indications, warnings, etc Local application to the eye may cause burning or stinging, but this is rarely severe enough to necessitate discontinuation of treatment. Sulfacetamide Sodium should not be used on persons who have shown hypersensitivity to sulfonamides.

Each Minims unit should be discarded after a single use.

Pharmaceutical precautions Minims should be stored in a cool place, and should not be exposed to strong light.

Legal category POM.

s of 20 units, each unit
il.

33/5019.

ar, colourless, sterile eye
le: Tropicamide BP 0.5%

plegic.

Adult: 2 drops at five
r 1 or 2 drops after 30

le physician.

gs, etc Minims Tropi-
patients with a narrow
ea.
discarded after a single

s Minims units should
ould not be exposed to

s of 20 units, each unit
il.

5% solution in particular
or no cycloplegia.

7
3

ilable as white, biconvex
SNP/2 on one side and
tablet contains 5 mg
(1973).

nalgesic for the relief of
occurs within 20 minutes
Narphen is indicated for
g pre- and postoperative
l. Narphen is particularly
actable pain such as that
imal sedation.
c pain constriction of the
le and the low spasmo-
e advantageous.

Adults: One tablet every
orally; up to 20 mg may
if necessary.
t established.

gs, etc Narphen is con-
sive disorders, delirium
m, respiratory depression
. Narphen should not be
imine oxidase inhibitors,
ontinuation of treatment

It is wise to reduce dosage in the elderly, and in
hypothyroidism or chronic hepatic disease. Administra-
tion in labour may cause respiratory depression in the
new-born infant.

Care is required in the presence of renal insufficiency
or concurrent administration of other narcotic analgesics,
sedatives/hypnotics or anaesthetics.

At the commencement of dosage some patients may
experience a feeling of light-headedness or dizziness
which soon passes.

Nausea and vomiting may be troublesome although
emetic symptoms and constipation are less than with
other narcotic analgesics. If nausea and vomiting occur
anti-emetics such as those of the phenothiazine type
may be effective.

Pruritus and occasionally dryness of the mouth and
sweating have occurred. Hypotension is rare. As with
other narcotics respiratory depression, tolerance and
dependence may occur.

There is no, or inadequate, evidence of safety in human
pregnancy but the drug has been widely used for many
years without apparent ill consequence and animal
studies have not shown any hazard.

Treatment of overdose: Naloxone may be used as an
antidote to overdose or to antagonise any respiratory
depression that may occur.

Pharmaceutical precautions Protect from light.

Legal category POM, MDA.

Package quantities Tablets of 5 mg in containers of
25 and 100.

Further information Nil.

Product licence number 0033/5047R.

PRIMALAN*

Presentation White bi-convex tablets embossed Pri-
malan on one side, unmarked on reverse. Each tablet
contains 5 mg mequitazine.

Uses Antihistamine for the symptomatic treatment of
allergic conditions such as hay fever, vasomotor rhinitis,
urticaria, pruritus of allergic origin and allergic reactions
associated with insect bites and stings.

Dosage and administration *Adults:* One 5 mg tablet
to be taken orally twice a day.

Children: At present Primalan is not recommended for
children under the age of 12.

Contra-indications, warnings, etc Primalan should
not be given to patients sensitive to phenothiazines, or
given concurrently with monoamine oxidase inhibitors.
Primalan should not be administered during pregnancy.

Although Primalan has been found to cause less
drowsiness than other antihistamines of comparable
efficacy, patients should be warned not to take charge of
vehicles or machinery until it has been established that
sedation has not occurred. Primalan may also potentiate
the sedative effects of alcohol.

Primalan may potentiate sympathomimetic amines.

Dryness of the mouth and disturbance of visual
accommodation may occasionally occur particularly in
the early days of treatment.

Treatment of overdose: Gastric lavage and supportive
therapy. Avoid sedation with other phenothiazine
derivatives.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Securitainers of 100 tablets.

Further information Primalan has a prolonged action, allowing adequate control with twice daily dosage.

Product licence number 0033/0090.

SIMPLENE®

Presentation Simplene is a clear, viscous, colourless to almost colourless liquid, containing Adrenaline BP in a buffered solution. It is supplied in a plastic dropper bottle packed in a nitrogen-filled pouch and is available in two strengths.

Simplene 0.5% (Adrenaline BP 0.5% w/v)

Simplene 1% (Adrenaline BP 1% w/v)

Uses For the treatment of primary open angle or secondary glaucoma. It may be used in conjunction with miotics or carbonic anhydrase inhibitor therapy.

Dosage and administration *Adult:* One drop to be instilled into the eye once or twice daily.

Children: At the discretion of the physician.

When used with pilocarpine or other miotics, Simplene should be instilled 5 to 10 minutes afterwards.

Contra-indications, warnings, etc Simplene should not be used when the diagnosis of open-angle glaucoma has not been verified. It is contra-indicated in patients with a narrow-angle because pupillary dilation may precipitate angle-closure. Occasionally patients may complain of orbital discomfort or red eye. Rarely, headache, irritation and local skin reactions occur. As with other adrenaline preparations, melanosis may occasionally occur, but this has no pathological significance. Systemic effects are rare but include tachycardia, extrasystoles, and elevation of blood pressure.

Pharmaceutical precautions Simplene is supplied in a plastic dropper bottle in a nitrogen-filled pouch, inside a carton. It should be stored in its carton in a cool place away from strong light. The carton only should be removed before supplying to the patient. Simplene should not be diluted, nor should it be dispensed from any container other than the original bottle. Simplene should not be used if the solution has become dark amber. The contents of the bottle should be discarded one month after removal from the pouch. Simplene is fully potent for 2 years providing the pouch remains unopened.

Legal category POM.

Package quantities Simplene is supplied as a sterile ophthalmic solution in a 7.5 ml plastic dropper bottle. Each bottle is enclosed in a nitrogen filled, double-sealed, nylon/aluminium foil pouch, inside a carton.

Further information The use of the nitrogen-filled overwrap ensures the long shelf-life of Simplene.

Simplene is a unique presentation of adrenaline in a plastic dropper bottle, which has been specially designed for patient convenience. Its special formulation gives improved stability, and includes a viscoliser to enhance comfort and effectiveness.

In common with other sympathomimetic agents Simplene does not affect accommodation.

Product licence numbers

Simplene 1.0% 0033/0057

Simplene 0.5% 0033/0072

SNO® PHENICOL

Presentation Multi-dose, colourless to pale straw coloured eye drops containing Chloramphenicol PhEu 0.5% w/v supplied in a plastic dropper bottle.

Uses As a topical antibacterial. Chloramphenicol is a broad spectrum antibiotic with bacteriostatic activity and is effective against a wide range of Gram-negative and Gram-positive organisms.

Dosage and administration *Adults:* One or more drops as required.

Children: One drop as required.

Contra-indications, warnings, etc This product is not intended as a long term treatment for dry eye syndromes.

Pharmaceutical precautions Sno phenicol should not be diluted or dispensed from any container other than the original bottle and should be stored at 5°C. Do not freeze.

Sno phenicol is fully potent for two years unopened.

Sno phenicol, like other eye drops, should be discarded one month after opening.

Legal category POM.

Package quantities Sno phenicol is supplied as a sterile ophthalmic solution in a 10 ml plastic dropper bottle.

Further information The solution is formulated with a viscoliser for patient comfort.

Product licence number 0033/0076.

SNO® PILO

Presentation Multi-dose, clear, colourless to pale yellow, eye drops supplied in a plastic dropper bottle. Five strengths are available: 0.5%, 1.0%, 2.0%, 3.0% and 4.0% w/v, Pilocarpine Hydrochloride BP.

Uses For the treatment of Glaucoma.

Dosage and administration *Adults:* One or two drops four times a day or as required.

Children: At the discretion of the physician.

Contra-indications, warnings, etc Sno pilo is contra-indicated where pupillary constriction is undesirable e.g. in cases of acute iritis.

Ciliary spasm with a temporary reduction of visual acuity occurs. Sensitivity is only rarely observed but if reaction occurs the use of the drops should be discontinued.

Pharmaceutical precautions Sno pilo should not be diluted or dispensed from any container other than the original bottle and should be stored in a cool place. Sno pilo is fully potent for three years unopened. Sno pilo like other eye drops, should be discarded one month after opening.

Legal category POM.

Package quantities Sno pilo is supplied as a sterile ophthalmic solution in a 10 ml plastic dropper bottle.

Further information The solution is formulated with viscoliser for patient comfort. Sno pilo is less acidic than most pilocarpine solutions.

Product licence numbers

no pilo 0.5% w/v 0033/0064
no pilo 1.0% w/v 0033/0065
no pilo 2.0% w/v 0033/0066
no pilo 3.0% w/v 0033/0067
no pilo 4.0% w/v 0033/0068

WELLDORM*

Presentation An elongated oval film-coated tablet. The coated tablet has a uniform smooth, film coat, of bluish-purple colour. Each tablet contains 650 mg of dichloralphenazone BP. The tablets are packed in blister strips.

Uses For the treatment of insomnia in all age groups; and for administration in the early stages of labour.

Dosage and administration *Adult dose:* The hypnotic dose is two or three 650 mg tablets to be taken with a drink 20 minutes before bedtime.

Paediatric dose: For children under the age of 12 Welldorm Elixir would provide an adequate dose range.

Contra-indications, warnings, etc Acute intermittent porphyria. An acute attack may be precipitated.

There have been occasional reports of skin rashes, nausea, vomiting, headache, hangover, anaphylaxis and occasional sensitivity reactions. Blood dyscrasias are extremely rare. Welldorm has been extensively used for over 20 years, during which time only one case of thrombocytopenia attributable to the drug has been reported.

A study has shown that withdrawal or omission of Welldorm therapy in patients receiving anticoagulant therapy with coumarin derivatives, e.g. warfarin, can lead to marked lengthening of the prothrombin time.

Treatment of overdosage: Gastric lavage and supportive therapy. In severe cases haemoperfusion should be used.

Pharmaceutical precautions The tablets should be stored in a cool dry place.

Legal category POM.

Package quantities The tablets are packed in blister strips of 15, two strips (30 tablets) per carton.

Further information Welldorm is a chloral hydrate derivative which induces a near natural sleep and does

not interfere with the paradoxical/orthodox (REM/Non-REM) ratio.

Product licence number 0033/0032.

WELLDORM* ELIXIR

Presentation Welldorm Elixir is a clear, red syrup, with a pleasant passion-fruit flavour. Welldorm Elixir contains 225 mg Dichloralphenazone BP in each 5 ml dose.

Uses Welldorm Elixir is for the treatment of insomnia in all age groups and for sedation in children.

Dosage and administration *Adult dose:* 15–45 ml as an hypnotic dose.

Children: Hypnotic:

Up to 1 year: 2.5–5 ml

1–5 years: 5–10 ml

6–12 years: 10–20 ml

Sedative: Sedative doses are half the above hypnotic dose (Syrup BP should be used as a diluent).

Contra-indications, warnings, etc Acute intermittent porphyria. An acute attack may be precipitated.

There have been occasional reports of skin rashes, nausea, vomiting, headache, hangover and occasional sensitivity reactions. Blood dyscrasias are extremely rare. Welldorm has been extensively used for over 20 years, during which time only one case of thrombocytopenia attributable to the drug has been reported.

A study has shown that withdrawal or omission of Welldorm therapy in patients receiving anticoagulant therapy with coumarin derivatives, e.g. warfarin, can lead to marked lengthening of the prothrombin time.

Treatment of overdosage: Gastric lavage and supportive therapy. In severe cases haemoperfusion should be used.

Pharmaceutical precautions Syrup BP should be used as a diluent. Welldorm Elixir should be stored in a well-stoppered bottle away from direct sunlight.

Legal category POM.

Package quantities Welldorm Elixir is supplied in bottles containing 150 ml and 500 ml.

Further information Welldorm Elixir is a chloral hydrate derivative which induces a near natural sleep and does not interfere with the paradoxical/orthodox (REM/Non-REM) ratio.

Product licence number 0033/5025.

* *Trade Mark*

Smith Kline & French Laboratories Limited

Mundells

Welwyn Garden City

Hertfordshire AL7 1EY



SK&F

CENDEVAX* **Rubella vaccine, live BP** **(Cendehill* strain)**

Presentation Cendevax rubella vaccine is a live attenuated vaccine prepared in rabbit kidney cells. It is available in glass vials containing a pink freeze-dried pellet; a clear, colourless, sterile diluent is provided in a separate ampoule (monodose) or vial (10-dose). Each 0.5 ml of reconstituted vaccine contains not less than 1,000 TCID₅₀ of live attenuated Cendehill strain of rubella virus, together with not more than 25 µg (17 i.u.) neomycin sulphate.

Uses Routine immunisation of pre-pubertal girls against rubella. Also indicated in seronegative women of child-bearing age *who are not pregnant* and in whom the possibility of pregnancy can be excluded for at least three months following vaccination, including post-partum mothers, and for immunisation of children and adults to prevent transmission of rubella to the at-risk pregnant woman.

Dosage and administration *Adults and children:* 0.5 ml of the reconstituted vaccine administered by the subcutaneous route only.

The vaccine should be reconstituted using only the sterile diluent supplied with each dose. With multi-dose vials, the whole of the sterile diluent (7 ml) should be transferred into the vial containing the vaccine, keeping the latter upright. It should then be shaken to ensure complete solution. The syringe should be dry sterilised; the vaccine is readily inactivated by alcohol and other chemical disinfectants and antiseptics, and care is needed to avoid contact with these substances when sterilising syringes and skin before vaccination.

Contra-indications, warnings, etc

Contra-indications: **Never give to pregnant women, or to women of child-bearing age not fully aware of the need to avoid pregnancy for three months after vaccination**, since the vaccine virus may have an effect on the foetus.

Do not use in the presence of acute febrile illness, or in states of altered immunity which may accompany conditions such as leukaemia, lymphoma or generalised malignancy or treatment with corticosteroids, alkylating drugs, antimetabolites or irradiation. Do not give to those known to be hypersensitive to rabbit protein or fur or neomycin.

Cautions: While there is no evidence to indicate that the vaccine virus is transmissible to susceptible contacts, the theoretical possibility remains.

The possibility of interference from passive antibodies following administration of gamma globulin or anti-D immunoglobulin or blood transfusion should be borne in mind. Serum antibodies may be checked after three months.

It is not usually recommended that live vaccines be given within three weeks of each other.

Adverse reactions: Mild rash, slight temperature elevation and slight enlargement of the posterior cervic glands have been reported. Arthralgia, and less commonly arthritis, have occurred even more rarely an almost exclusively in adult women. These reactions have been mild and transient. Rare cases of myelodysplastic neuritis have been reported with rubella vaccines.

Overdosage: Not a problem.

Pharmaceutical precautions Protect from light. Reconstitute only with the diluent supplied. Although the vaccine should be used promptly after reconstitution it may when necessary be kept at a temperature between 2°C and 8°C for not longer than one hour before use. Cendevax rubella vaccine should be stored between 2°C and 8°C and should not be frozen (low temperatures will not harm the vaccine but may damage the diluent ampoule or vial).

Legal category POM.

Package quantities Monodose vials and 10-dose vials, each with a separate ampoule or vial containing 0.5 ml or 7 ml sterile diluent respectively.

Further information Because of possible interference from persisting maternal antibodies, there is little value in giving the vaccine to infants under one year of age.

While there is no evidence that vaccination during the incubation period of natural rubella will prevent the disease, there is no contra-indication to the use of the vaccine in these circumstances.

Product licence number 0002/5004.

DEXEDRINE* TABLETS

Presentation Half-scored, yellow tablets, marked SK&F, each containing 5 mg dexamphetamine sulphate.

Uses Dexedrine is a sympathomimetic amine with central stimulant and anorectic activity.

It is indicated in narcolepsy and in children with hyperkinetic states associated with minimal brain damage.

Dosage and administration *Adults:* In narcolepsy the usual starting dosage is 10 mg Dexedrine a day given in divided doses. Dosage may be increased necessary by 10 mg a day at weekly intervals to suggested maximum of 60 mg a day.

Children: In hyperkinetic states, the usual starting dosage for children aged 3-5 years is 2.5 mg a day, increased necessary by 2.5 mg at weekly intervals; for children aged 6 years and over, the usual starting dosage is 5 mg a day, increasing if necessary by 5 mg at weekly intervals. The usual upper limit is 20 mg a day, though some older children have needed 40 mg or more for optimal response.

Contra-indications, warnings, etc

Contra-indications: Do not use in patients known to be

tic amines, during, or for 14 in MAO inhibitor, in those , with symptomatic cardio- rate or severe hypertensive ig from hyperthyroidism or

n patients on guanethidine, ig may be antagonised by

drugs acting on the CNS, ility to drive or operate

retamine has been thought ects in rodents, and retro- ain significance in man has ility. Dexedrine has been there has been no other lence to suggest any asso- Nevertheless, drugs should nless essential, especially

a (especially with dosage ness, irritability, euphoria, nd other symptoms of over- rted. Also dry mouth, un- yastro-intestinal symptoms, ects such as tachycardia, ses in blood pressure. consumption of increasing those recommended, may At such levels, a psychosis, istinguishable from schizo- nt should be stopped grad- ay produce extreme fatigue

overdosage include excite- lions leading to coma; rhythmic; and respiratory sistis of the induction of je, together with supportive . Excessive stimulation or with diazepam. Excretion of increased by forced acid

ons No special storage

IA.

ainers of 100 tablets.

0002/5008.

S

ay-red capsules, double- } 10 mg phenoxybenzamine vder.

competitive long-acting α - ist.

nagement of hypertensive aeo chromocytoma; and as ent of urinary retention due nign prostatic hypertrophy. laynaud's disease, and in

combination with other antihypertensive agents in the treatment of hypertension.

Dosage and administration *Adults:* The usual starting dose in all indications is 10 mg b.d.

In phaeochromocytoma this may be increased by 10 mg daily until control of hypertensive episodes is achieved, or postural hypotension occurs. Usually the dosage required is 1 to 2 mg/kg body weight daily in two doses. Concomitant β -adrenergic blockade may be necessary to control tachycardia and arrhythmias notably when tumours are secreting an appreciable amount of adrenaline as well as noradrenaline.

In urinary retention due to either neurogenic bladder or prostatic hypertrophy, 10 mg b.d. is usually sufficient. If no effect is seen after two to three weeks' treatment, alternative therapy should be used.

Children: There is little experience in children, but doses of 0.3 to 0.5 mg/kg body weight daily in neurogenic bladder, and 1 to 2 mg/kg daily in phaeochromocytoma have been used successfully.

Contra-indications, warnings, etc

Contra-indication: Do not use in patients with congestive heart failure.

Cautions: Use with great caution in patients in whom a fall in blood pressure and/or tachycardia may be undesirable, such as the elderly or those with severe heart disease, cerebrovascular disease or renal damage. The mode of action should be borne in mind if used concurrently with α -sympathomimetics or myocardial depressants.

Use in pregnancy: There is little evidence as to the safety of Dibenyline in pregnancy and it should not be used in pregnancy unless essential.

Adverse reactions: Side-effects are generally mild and transient, but may include postural hypotension with dizziness and compensatory tachycardia, nasal congestion, inhibition of ejaculation, miosis and lassitude. Gastro-intestinal upset has also been reported.

Overdosage: The main effect of overdosage is profound hypotension, which may last several hours, tachycardia and collapse. Treatment consists of the induction of vomiting and/or gastric lavage together with appropriate symptomatic and supportive measures. Treat hypotension with plasma expanders and the 'head down' position. Noradrenaline is of little value when α -adren- ergic receptors are blocked. Adrenaline should not be used since stimulation of β -adrenergic receptors will further decrease blood pressure.

Pharmaceutical precautions Store in a cool, dry place and dispense in moisture-proof containers.

Legal category POM.

Package quantities Containers of 100 and 500 capsules.

Further information In phaeochromocytoma treatment should be started as soon as possible after diagnosis, and time allowed for stabilisation of the condition before invasive investigations or operations are carried out. Operative cover with intravenous phenoxybenzamine may be given. In a few inoperable cases long-term treatment with Dibenyline has been used.

In urinary retention due to neurogenic bladder, response is more likely in patients with lower motor neurone lesions or who have shown a positive phentolamine test.

Product licence number 0002/5009.

DYAZIDE* TABLETS

Presentation Peach-coloured, half-scored, circular tablets bearing the mark SKF E93, each containing 50 mg triamterene and 25 mg hydrochlorothiazide.

Uses Dyazide is a potassium-conserving diuretic preparation with antihypertensive activity.

It is recommended for the control of oedema in cardiac failure, cirrhosis of the liver or the nephrotic syndrome, and in drug-induced and pre-menstrual oedema. It is also indicated in the treatment of mild to moderate hypertension, alone or in combination with other antihypertensive drugs.

Dosage and administration *Adults only: In oedema:* The usual starting dosage is 1 Dyazide tablet twice a day after meals. The optimal dosage may be 3 tablets a day, 2 after breakfast and 1 after lunch.

Maintenance dosage: Once a diuresis has been established, dosage should be reduced. Usually 1 tablet a day, or two tablets on alternate days will suffice.

In hypertension: Initially 1 tablet twice a day after meals, thereafter adjusted to the patient's needs. If Dyazide is added to already established therapy with another antihypertensive drug, the dosage of the latter should be reduced, and later adjusted if necessary. If another antihypertensive drug is added to Dyazide therapy, the dosage of the latter will not normally be reduced.

A dosage of 4 tablets a day should not be exceeded; at this level adverse reactions such as raised blood urea are more likely.

Contra-indications, warnings, etc

Contra-indications: Do not give Dyazide to patients with hyperkalaemia, progressive renal failure, or known hypersensitivity to either constituent of the product. Potassium supplements, or other potassium-conserving drugs, should not be given routinely with Dyazide.

Cautions: Use Dyazide with caution in patients with hepatic or renal insufficiency; in those predisposed to gout since both components can elevate uric acid levels; and in diabetic patients since thiazide diuretics can provoke hyperglycaemia and glycosuria.

After the first week, it is advisable to determine blood urea and serum potassium levels periodically, particularly in the elderly and those with renal insufficiency.

Thiazides reduce excretion of lithium and may thus precipitate intoxication.

Use in pregnancy and lactation: Dyazide has been in clinical use for a number of years, and there is no experimental or clinical evidence to suggest associated foetal abnormalities. Nevertheless, thiazides have been shown to pass through the placenta and also into breast milk. In rare instances, thrombocytopenia, pancreatitis or hypoglycaemia have been reported in newborn infants of mothers treated with thiazides. The use of Dyazide in pregnant or nursing mothers should therefore be avoided unless essential.

Adverse reactions: Nausea, vomiting, diarrhoea, muscle cramps, weakness, dizziness, headache, dry mouth and rash have been reported. Photosensitivity is rare.

Minor serum electrolyte changes have been observed infrequently, and marked fluctuations in serum potassium levels are uncommon. Metabolic acidosis occasionally occurs. Electrolyte imbalance may also indicate excessive dosage or be secondary to the condition under treatment.

In common with most diuretics, Dyazide may reduce glomerular filtration rate and cause a temporary increase

in blood urea levels; again this may also indicate excessive dosage or be secondary to the condition under treatment.

Acute interstitial nephritis, reversed on stopping treatment, has been reported very rarely.

Rare cases of thrombocytopenic purpura and megaloblastic anaemia have been reported with triamterene-thiazides alone have caused jaundice, acute pancreatitis and, rarely, blood dyscrasias including agranulocytosis, thrombocytopenia and leucopenia.

Overdosage: Symptoms of electrolyte imbalance, hypertension, gastro-intestinal disturbance and muscular weakness may occur. Treatment consists of the induction of vomiting and/or gastric lavage, correction of fluid depletion and electrolyte imbalance, and symptomatic and supportive therapy. If hypotension persists after adequate fluid replacement, dopamine may be used.

Pharmaceutical precautions No special storage precautions are required.

Legal category POM.

Package quantities Containers of 100 and 500 tablets.

Further information Triamterene may cause a blue fluorescence of the urine under certain light conditions.

Product licence number 0002/0050.

DYTAC* CAPSULES

Presentation Opaque, maroon-coloured capsule double-marked SKF, each containing 50 mg triamterene as a yellow, granular powder.

Uses Triamterene is a potassium-conserving diuretic thought to act by directly inhibiting the exchange of sodium for potassium and hydrogen in the distal renal tubule.

Dytac is recommended for the control of oedema in cardiac failure, cirrhosis of the liver or the nephrotic syndrome, and in drug-induced and pre-menstrual oedema. When Dytac is used as an adjuvant to potassium-depleting diuretics, such loss may be inhibited and diuresis enhanced.

Dosage and administration *Adults only:* When given alone, the usual dosage range is from 3 to a maximum of 5 Dytac capsules a day. The optimal daily dosage is capsules, given in divided doses after breakfast and at lunch. After the first week, treatment should preferably be given on alternate days to ensure satisfactory maintenance diuresis without an increase in blood urea levels. When given with another diuretic, lower dosages of both should be used initially.

Contra-indications, warnings, etc

Contra-indications: Do not give Dytac to patients with hyperkalaemia, progressive renal failure, or known hypersensitivity to the drug. Potassium supplements, or other potassium-conserving drugs, should not be given routinely with Dytac.

Cautions: Use Dytac with caution in patients with hepatic or renal insufficiency; in those predisposed to gout since Dytac has been shown in rare instances to elevate uric acid levels; and with hypotensive agents since an additive effect may result.

After the first week, it is advisable to determine blood urea and serum potassium levels periodically, particularly in the elderly and those with renal insufficiency.

been available since 1962, but no clinical evidence to date has been reported to the foetus. Nevertheless, it should be avoided in pregnancy unless it is clearly indicated in the first trimester.

Nausea, vomiting, diarrhoea, weakness, and minor decreases in blood urea have been reported. Photosensitivity

and hyponatraemia have been observed. Hypokalaemia has been observed in patients. Metabolic acidosis and electrolyte imbalance may also occur or be secondary to the

use of thiazides. Dytac may reduce the effect of thiazides and cause a temporary increase in blood urea. This may also indicate a secondary condition under

reversed on stopping treatment, rarely. Thrombocytopenic purpura and megalo-

cytopenia, electrolyte imbalance, especially. Gastro-intestinal disturbance and possibly hypotension may occur. Correction of the induction of

Store in a dry place, away from light.

Containers of 30 and 250

Triamterene may cause a blue fluorescence under certain light conditions. 0002/5014.

Each capsule with opaque, yellow, and red SKF, each containing 100 mg benzthiazide as a yellow,

Water-conserving diuretic preparation. It is used in cardiac failure, nephrotic syndrome, and in renal oedema.

Adults only: The optimal dose is 100 mg a day, 2 being taken after the first week, treatment on alternate days, to ensure response without an increase in blood urea. Dosage may be reduced to 50 mg a day, taken after breakfast

Indications, etc. Give Dytide to patients with renal failure, or known constituent of the product. Other potassium-conserving diuretics with Dytide.

Cautions: Use Dytide with caution in patients with hepatic or renal insufficiency; in those predisposed to gout since both components can elevate uric acid levels; with hypotensive agents, since an additive effect may result; and in diabetic patients since thiazides can provoke hyperglycaemia and glycosuria.

After the first week, it is advisable to determine blood urea and serum potassium levels periodically, particularly in the elderly and those with renal insufficiency.

Thiazides reduce excretion of lithium and may thus precipitate intoxication.

Use in pregnancy and lactation: Dytide has been available since 1963, and there is no experimental or clinical evidence to suggest associated foetal abnormalities. Nevertheless, thiazides have been shown to pass through the placenta and also into breast milk. In rare instances, thrombocytopenia, pancreatitis or hypoglycaemia have been reported in newborn infants of mothers treated with thiazides. The use of Dytide in pregnant or nursing mothers should therefore be avoided unless essential.

Adverse reactions: Nausea, vomiting, diarrhoea, muscle cramps, weakness, dizziness, headache, dry mouth, decreases in blood pressure, and rash have been reported. Photosensitivity is rare.

Minor serum electrolyte changes have been observed infrequently, and marked fluctuations in serum potassium levels are uncommon. Metabolic acidosis occasionally occurs. Electrolyte imbalance may also indicate excessive dosage or be secondary to the condition under treatment.

In common with most diuretics, Dytide may reduce glomerular filtration rate and cause a temporary increase in blood urea levels; again this may also indicate excessive dosage or be secondary to the condition under treatment.

Acute interstitial nephritis, reversed on stopping treatment, has been reported very rarely.

Rare cases of thrombocytopenic purpura and megalo-

Overdosage: Symptoms of electrolyte imbalance, hypotension, gastro-intestinal disturbance and muscular weakness may occur. Treatment consists of the induction of vomiting and/or gastric lavage, correction of fluid depletion and electrolyte imbalance and symptomatic and supportive therapy. If hypotension persists after adequate fluid replacement, dopamine may be used.

Pharmaceutical precautions Store in a dry place, and dispense in moisture-proof containers.

Legal category POM.

Package quantities Containers of 30 and 250 capsules.

Further information Triamterene may cause a blue fluorescence of the urine under certain light conditions.

Product licence number 0002/5015.

ESKAMEL* CREAM

Presentation A smooth, brown, non-greasy cream, which dries rapidly to a flesh colour when applied to the skin. It contains 2% w/w resorcinol and 8% w/w sulphur.

Uses Eskamel has mild antiseptic, keratolytic and exfoliative properties, and is indicated in the treatment of acne.

Dosage and administration *Adults and children:* Wash the affected areas with soap and water, and dry carefully. Apply Eskamel thinly to the skin with the fingers but do not rub in. Once a day is usually enough, but if the patient has a very oily skin, the cream may be applied more often. Eskamel may be used under make-up to mask the spots and lesions of acne.

Contra-indications, warnings, etc

Contra-indications: Do not use in patients who are sensitive to sulphur or resorcinol.

Cautions: Use with care on acutely inflamed areas or near the eyes.

Adverse reactions: Moderate erythema and scaling are the expected effects of Eskamel. If these are excessive or if inflammation occurs, stop treatment until the reaction has subsided, and then apply Eskamel less often.

Overdosage: If ingestion occurs, mild gastro-intestinal disturbance might occur. Treatment consists of rinsing out the mouth together with symptomatic measures if required.

Pharmaceutical precautions Store in a cool place. Keep in the original specially lined tubes to prevent evaporation.

Legal category P.

Package quantities Tubes containing 25 g.

Further information Nil.

Product licence number 0002/5000.

ESKORNADE* SPANSULE* CAPSULES
ESKORNADE* SYRUP

Presentation Clear, colourless capsules, grey-capped and filled with a mixture of red, grey and white pellets. Each Spansule sustained-release capsule contains 2.5 mg isopropamide present as the iodide, 50 mg phenylpropanolamine hydrochloride, and 5 mg diphenylpyraline hydrochloride. Two-thirds of the phenylpropanolamine and diphenylpyraline is formulated for sustained release over a period of six to eight hours.

A pale green syrup, greengage-flavoured, each 5 ml dose containing 0.75 mg isopropamide present as the iodide, 15 mg phenylpropanolamine hydrochloride, and 1.5 mg diphenylpyraline hydrochloride.

Uses Eskornade is a combination of an oral nasal decongestant, an antihistamine (H_1 -receptor antagonist) and an anticholinergic.

It is indicated in the relief of congestion and hypersecretion in the nasal cavity and paranasal sinuses, associated with the common cold, allergic rhinitis, acute and chronic rhinitis, sinusitis and influenza.

Dosage and administration *Adults:* One Eskornade Spansule capsule every 12 hours or two 5 ml doses of Eskornade syrup three times a day.

Children aged 2 to 6 years: One 2.5 ml dose of Eskornade syrup three times a day.

Children aged 7 years and over: One 5 ml dose three times a day.

Contra-indications, warnings, etc

Contra-indications: Do not use in patients with glaucoma, intestinal obstruction of organic origin or intestinal atony, severe ulcerative colitis, prostatic hypertrophy or incipient urinary retention from any cause, hypertensive

disease, severe heart disease, or hyperthyroidism; in those sensitive to iodine; or during, or for 14 days after treatment with an MAO inhibitor.

Cautions: Patients who drive or operate machinery should be warned of the possibility of drowsiness. Alcoholic drinks should be avoided. Administer with caution to patients with organic heart disease or angina of effort. The iodine present may interfere with some tests of thyroid function.

Use in pregnancy: Eskornade has been available since 1960, and there is no experimental or clinical evidence to suggest any associated hazard to the foetus. Nevertheless, drugs should be avoided in pregnancy unless essential, especially during the first trimester.

Adverse reactions: Blurred vision, dry mouth, urinary hesitancy or retention, constipation, palpitations, drowsiness or insomnia, and dizziness may occur.

Overdosage: Signs and symptoms may be related to any of the product's constituents and may include nausea and vomiting, irritability, convulsions, fever, tachycardia and arrhythmias. Absorption of phenylpropanolamine and diphenylpyraline from the sustained-release Spansule capsule is likely to be prolonged, and this should be borne in mind. Treatment consists of gastric lavage together with appropriate supportive and symptomatic measures. Central excitation or convulsions may require treatment with diazepam. Physostigmine salicylate 1–4 mg parenterally in an adult, repeated as necessary, has been reported to reverse the central and peripheral effects of anticholinergic poisoning. Excretion of phenylpropanolamine may be increased by forced acid diuresis.

Pharmaceutical precautions Store Spansule capsules in a cool, dry place, and dispense in moisture-proof containers. Store syrup in a cool place and dilute only with Syrup BP, after which it is stable for up to 14 days at room temperature.

Legal category P.

Package quantities Containers of 30 and 250 Spansule capsules. Bottles containing 150 ml syrup.

Further information Nil.

Product licence numbers

Eskornade Spansule capsules	0002/5019
Eskornade syrup	0002/5020

EXPANSYL* SPANSULE* CAPSULES

Presentation Clear, colourless capsules, black capped and filled with a mixture of blue, lime-green, and white pellets. Each Spansule sustained-release capsule contains 50 mg ephedrine sulphate, 2 mg trifluoperazine present as the hydrochloride and 5 mg diphenylpyraline hydrochloride. Two-thirds of the dose of ephedrine and diphenylpyraline is formulated for sustained release over a period of six to eight hours.

Uses Expansyl combines the properties of an adrenergic bronchodilator, a phenothiazine tranquilliser and an antihistamine (H_1 -receptor antagonist) for routine, prolonged protection against bronchospasm in chronic bronchitis and mild bronchial asthma; also for relief of mild asthmatic attacks.

Dosage and administration *Adults only:* 1 Expansyl Spansule capsule night and morning, increasing if necessary to a maximum of 3 capsules a day.

Indications, warnings, etc

Contra-indications: Do not use in patients with hyperactive disease, severe heart disease, or hyperthyroidism; or for 14 days after treatment with an MAO inhibitor; or in patients with existing blood dyscrasias or with liver damage.

Precautions: Use with caution in patients with organic heart disease or angina of effort, or with prostatic hypertrophy. Nausea and vomiting as a sign of organic disease may be masked by the anti-emetic action of trifluoperazine.

Common with other drugs acting on the CNS, amyl may affect ability to drive or operate machinery.

Use in pregnancy: Expansyl has been available since 1961, and there is no experimental or clinical evidence to suggest any associated hazard to the foetus. Nevertheless drugs should be avoided in pregnancy unless essential, especially during the first trimester.

Adverse reactions: Drowsiness, dizziness, restlessness, insomnia, dry mouth, blurred vision, palpitation, and constipation may occur.

Extrapyramidal symptoms due to trifluoperazine are very unlikely at the recommended dosage. Extremely rarely, long-term therapy with trifluoperazine in low dose has been associated with tardive dyskinesia, which can be long-lasting or even irreversible.

Overdosage: Signs and symptoms may be related to any of the product's constituents, but those of ephedrine would usually predominate. They may include nausea, vomiting, irritability, convulsions, fever, tachycardia, mydriasis, extrapyramidal symptoms and hypotension. Absorption of ephedrine and diphenylpyraline from the sustained-release Spansule capsule is likely to be prolonged and this should be borne in mind. Treatment consists of gastric lavage, together with appropriate supportive and symptomatic measures. Do not induce vomiting. Extrapyramidal symptoms may be treated with anticholinergic antiparkinsonism drugs. Treat hypotension with fluid replacement; if severe or persistent, adrenaline may be considered. Adrenaline is contraindicated. Excretion of ephedrine may be increased by acid diuresis.

Pharmaceutical precautions Store in a cool, dry place, protect from light, and dispense in moisture-proof containers.

Legal category POM.

Package quantities Containers of 30 and 250 Spansule capsules.

Further information Nil.

Product licence number 0002/5021.

FOL* SPANSULE* CAPSULES

Presentation Clear, colourless capsules, transparent, orange-capped and filled with a mixture of coral-red, pale yellow, and white pellets. Each Spansule sustained-release capsule contains 150 mg dried ferrous sulphate and 0.5 mg folic acid. Four-fifths of the dose of iron is specially formulated for sustained release over a period of several hours.

Uses Fefol is a haematinic preparation for prophylaxis of iron and folic-acid deficiency during pregnancy.

Dosage and administration *Adults only:* 1 Fefol Spansule capsule a day throughout pregnancy. Some pregnant patients may need a higher prophylactic dose of iron because of dietary or other factors.

Contra-indications, warnings, etc

Cautions and contra-indications: The folic acid content of one capsule a day is unlikely to mask pernicious anaemia should this condition be present; pregnancy during pernicious anaemia is very rare.

Iron chelates with tetracyclines, and absorption of both agents may be impaired.

Adverse reactions: Nausea and other gastro-intestinal symptoms sometimes encountered during iron therapy are unlikely to occur with Fefol Spansule capsules.

Overdosage: Symptoms of overdosage with iron salts include epigastric pain, nausea and vomiting, haematemesis and circulatory collapse. In severe cases, encephalopathy, acute hepatic necrosis and acute renal failure may develop after a latent period. The sustained-release Spansule capsule presentation of ferrous sulphate may delay excessive absorption of iron and allow more time for the initiation of appropriate counter-measures. Treatment consists of gastric lavage followed by the introduction of 5 g desferrioxamine into the stomach. Serum iron levels should be monitored and in severe cases intravenous desferrioxamine should be given together with supportive and symptomatic measures as required.

Pharmaceutical precautions Store in a cool, dry place, and dispense in moisture-proof containers.

Legal category POM.

Package quantities Pack containing 2 or 144 blister strips each of 14 Spansule capsules. Containers of 250 and 5,000 Spansule capsules.

Further information Fefol Spansule capsules are formulated to release most of the iron in the upper small intestine where absorption is greatest, and not in the stomach where gastric irritation may be caused.

Product licence number 0002/5022.

FEFOL-VIT* SPANSULE* CAPSULES

Presentation Clear, colourless capsules, opaque white-capped and filled with a mixture of coral-red, orange-yellow, pale yellow, and white pellets. Each Spansule sustained-release capsule contains 150 mg dried ferrous sulphate, 0.5 mg folic acid, 2 mg thiamine mononitrate, 2 mg riboflavin, 1 mg pyridoxine hydrochloride, 10 mg nicotinamide, 2.17 mg calcium pantothenate and 50 mg ascorbic acid. Four-fifths of the dose of iron is specially formulated for sustained release over a period of several hours.

Uses Fefol-Vit is a haematinic with added vitamins, for prophylaxis of iron and folic-acid deficiency during pregnancy, particularly when inadequate diet calls for supplementary vitamins B and C.

Dosage and administration *Adults only:* 1 Fefol-Vit Spansule capsule a day throughout pregnancy. Some pregnant patients may need a higher prophylactic dose of iron because of dietary and other factors.

Contra-indications, warnings, etc

Cautions and contra-indications: The folic acid content of one capsule a day is unlikely to mask pernicious anaemia should this condition be present; pregnancy during pernicious anaemia is very rare.

Iron chelates with tetracyclines, and absorption of both agents may be impaired.

Adverse reactions: Nausea and other gastro-intestinal symptoms sometimes encountered during iron therapy are unlikely to occur with Fefol-Vit Spansule capsules.

Overdosage: Symptoms of overdosage with iron salts include epigastric pain, nausea and vomiting, haematemesis and circulatory collapse. In severe cases, encephalopathy, acute hepatic necrosis and acute renal failure may develop after a latent period. The sustained-release Spansule capsule presentation of ferrous sulphate may delay excessive absorption of iron and allow more time for the initiation of appropriate counter-measures. Treatment consists of gastric lavage followed by the introduction of 5 g desferrioxamine into the stomach. Serum iron levels should be monitored and in severe cases intravenous desferrioxamine should be given together with supportive and symptomatic measures as required.

Pharmaceutical precautions Store in a cool, dry place, and dispense in moisture-proof containers.

Legal category POM.

Package quantities Containers of 30, 250 and 4,000 Spansule capsules.

Further information Fefol-Vit Spansule capsules are formulated to release most of the iron in the upper small intestine where absorption is greatest, and not in the stomach where gastric irritation may be caused.

Product licence number 0002/0049.

FEOSPAN* SPANSULE* CAPSULES

Presentation Clear, colourless capsules, ruby-red-capped and filled with a mixture of green and coral-red pellets. Each Spansule sustained-release capsule contains 150 mg dried ferrous sulphate. Four-fifths of the dose of iron is specially formulated for sustained release over a period of several hours.

Uses Feospan is a haematinic for the prevention and treatment of iron deficiency.

Dosage and administration *Adults:* 1 Feospan Spansule capsule a day. In more severe cases, 2 capsules a day may be required.

Children aged over 1 year: 1 capsule a day. The capsule may be opened and the pellets mixed with soft, cool food, but they must not be chewed.

Contra-indications, warnings, etc

Cautions and contra-indications: Iron chelates with tetracyclines, and absorption of both agents may be impaired.

Adverse reactions: Nausea and other gastro-intestinal symptoms sometimes encountered during iron therapy are unlikely to occur with Feospan Spansule capsules.

Overdosage: Symptoms of overdosage with iron salts include epigastric pain, nausea and vomiting, haematemesis and circulatory collapse. In severe cases, encephalopathy, acute hepatic necrosis and acute renal failure may develop after a latent period. The sustained-release Spansule capsule presentation of ferrous sulphate may delay excessive absorption of iron and allow more time for the initiation of appropriate counter-measures. Treatment consists of gastric lavage followed by the introduction of 5 g desferrioxamine into the stomach. Serum iron levels should be monitored and in severe cases intravenous desferrioxamine should be given together with supportive and symptomatic measures as required.

Pharmaceutical precautions Store in a cool, place, and dispense in moisture-proof containers.

Legal category P.

Package quantities Containers of 30, 250 and 5, Spansule capsules.

Further information Feospan Spansule capsules formulated to release most of the iron in the upper small intestine where absorption is greatest, and not in the stomach where gastric irritation may be caused.

Product licence number 0002/5023.

FESOVIT* SPANSULE* CAPSULES

Presentation Clear, colourless capsules, opaque low-capped and filled with a mixture of coral-orange-yellow, and white pellets. Each Spansule sustained-release capsule contains 150 mg dried ferrous sulphate, 2 mg thiamine mononitrate, 2 mg riboflavin, 1 mg pyridoxine hydrochloride, 10 mg nicotinic acid, 2.17 mg calcium pantothenate and 50 mg ascorbic acid. Four-fifths of the dose of iron is specially formulated for sustained release over a period of several hours.

Uses Fesovit is a haematinic with added vitamins, the prevention and treatment of iron deficiency, particularly in the elderly patient where inadequate diet calls for supplementary vitamins B and C.

Dosage and administration *Adults:* One Fesovit Spansule capsule a day. In more severe cases, 2 capsules a day may be required.

Children aged over 1 year: One Fesovit Spansule capsule a day. The capsule may be opened and the pellets mixed with soft, cool food, but they must not be chewed.

Contra-indications, warnings, etc

Cautions and contra-indications: Iron chelates with tetracyclines, and absorption of both agents may be impaired.

Adverse reactions: Nausea and other gastro-intestinal symptoms sometimes encountered during iron therapy are unlikely to occur with Fesovit Spansule capsules.

Overdosage: Symptoms of overdosage with iron salts include epigastric pain, nausea and vomiting, haematemesis and circulatory collapse. In severe cases, encephalopathy, acute hepatic necrosis and acute renal failure may develop after a latent period. The sustained-release Spansule capsule presentation of ferrous sulphate may delay excessive absorption of iron and allow more time for the initiation of appropriate counter-measures. Treatment consists of gastric lavage followed by the introduction of 5 g desferrioxamine into the stomach. Serum iron levels should be monitored and in severe cases intravenous desferrioxamine should be given together with supportive and symptomatic measures as required.

Pharmaceutical precautions Store in a cool, place, and dispense in moisture-proof containers.

Legal category P.

Package quantities Containers of 30, 250 and 5, Spansule capsules.

Further information Fesovit Spansule capsules formulated to release most of the iron in the upper small intestine where absorption is greatest, and not in the stomach where gastric irritation may be caused.

Product licence number 0002/0029.

HISTRYL* SPANSULE* CAPSULES HISTRYL* PAEDIATRIC SPANSULE* CAPSULES

Presentation Clear, colourless capsules, opaque pink-
ped and filled with a mixture of white and two shades
ink pellets in two strengths. Each Spansule sustained-
release capsule, size No. 2, contains 5 mg diphenylpy-
rine hydrochloride, and each paediatric Spansule
capsule, size No. 4, contains 2.5 mg diphenylpyraline
hydrochloride. Two-thirds of the dose of diphenylpyral-
ine is specially formulated for sustained release over a
period of six to eight hours.

Uses Histryl is an antihistamine (H_1 -receptor antag-
onist) for relief of allergic and vasomotor rhinitis, urticaria,
allergic oedema, allergic eczema, insect bites and
stings, food and drug allergy, and the urticarial and
dermatous lesions of serum sickness.

Dosage and administration *Adults:* 1 or 2 Histryl
capsules (5 mg) at night and morning. The higher
dose should be reserved for more severe conditions.

Children aged 7 years and over: 1 Histryl paediatric
capsule (2.5 mg) twice a day.

Contra-indications, warnings, etc

Precautions: Patients who drive or operate machinery
should be warned of the possibility of drowsiness.
Alcoholic drinks should be avoided.

Use in pregnancy: Histryl has been available since 1957,
but there is no experimental or clinical evidence to
suggest any associated hazard to the foetus. Neverthe-
less, drugs should be avoided in pregnancy unless
essential, especially during the first trimester.

Adverse reactions: Drowsiness, dryness of the mucous
membranes, dizziness and blurred vision may occasion-
ally occur.

Overdosage: Symptoms of overdosage may include
nausea and vomiting, and effects of CNS excitation
and/or depression including coma. Absorption of di-
phenylpyraline from the sustained-release Spansule
capsule is likely to be prolonged and this should be borne
in mind. Treatment consists of the induction of vomiting
and/or gastric lavage together with symptomatic and
supportive measures.

Pharmaceutical precautions Store in a cool, dry
place, and dispense in moisture-proof containers.

Legal category P.

Package quantities Both strengths in containers of
10 and 250 Spansule capsules.

Other information Nil.

Product licence numbers

Histryl Spansule capsules	0002/5031
Histryl paediatric Spansule capsules	0002/5032

KERECID* OPHTHALMIC OINTMENT KERECID* OPHTHALMIC SOLUTION

Presentation An off-white, translucent ophthalmic
ointment containing 0.5% w/w idoxuridine.

Uses Clear, colourless and odourless aqueous ophthalmic
solution containing 0.1% w/v idoxuridine, together with
0.2% w/v thiomersal.

Pharmacology Kerecid is an antiviral agent active against herpes
simplex virus and certain other DNA viruses. It is
indicated in herpes simplex keratitis, particularly in acute

dendritic ulcers; infections with stromal involvement
may respond less favourably.

Dosage and administration *Adults and children:*
Kerecid ophthalmic ointment: Apply approximately
every 4 hours, five times a day, with the last dose at
bedtime. The ointment should be placed inside the
conjunctival sac of the infected eye.

Kerecid ophthalmic solution: Initially 1 drop instilled into
the eye every hour during the day and every two hours
at night. Do not administer more often than hourly. When
a definite improvement is seen, shown by a loss of
corneal staining with fluorescein, reduce dosage to 1
drop every two hours during the day and every four
hours at night. For best results the dosage schedule must
be followed closely.

To minimise recurrences, continue treatment for three
to five days after healing appears to be complete, that is,
after complete loss of corneal staining with fluorescein.
Treatment should not usually be continued for more than
21 days.

Observe patients frequently during treatment. Im-
provement in dendritic keratitis and other superficial
infections is generally seen within a week, but may
occasionally occur much earlier. If superficial infections
show no sign of improvement after seven to eight days,
alternative treatment is indicated. A faint dendritic
pattern in the deeper epithelial layers that neither stains
nor produces symptoms may persist for two to four
weeks. This does not indicate failure of treatment or a
need for continued therapy.

Antibiotics may be used to control secondary infec-
tions; and atropine preparations may be given if needed.
Do not, however, mix Kerecid ophthalmic solution with
these adjuvant medications.

Contra-indications, warnings, etc

Contra-indications: Do not administer boric acid during
treatment as it may cause irritation in the presence of
Kerecid.

Cautions: Caution is required with concomitant use of
topical corticosteroids which may encourage the spread
of viral infection. They should not be used in the presence
of active corneal ulceration, but may be considered
when the stromal disease seriously affects vision, or
when oedema or uveitis is present. Kerecid should be
continued for several days after corticosteroid treatment
has been completed.

Use in pregnancy: One isolated study has indicated that
idoxuridine may have embryotoxic effects in rabbits, but
these effects were not confirmed in extensive repeat
studies. Other work has shown very high parenteral
doses to be embryotoxic in mice and rats. Kerecid has
been available since 1963 and no other experimental or
clinical evidence of any associated hazard to the foetus
has emerged. While local application to the eye is
unlikely to produce significant levels within the body,
Kerecid should not be administered in pregnancy unless
essential, especially during the first trimester.

Adverse reactions: Transient irritation and pain on
administration may occur; itching, inflammation, oedema
and, rarely, allergic reactions and occlusions of the
lacrimal puncta, have been reported.

Overdosage: Excessive use may damage the corneal
epithelium. Toxic effects are unlikely to follow ingestion.

Pharmaceutical precautions Store ophthalmic oint-
ment in a cool place. Store ophthalmic solution below
8°C but do not freeze. The contents are sterile until the

pack is opened; discard any unused contents one month after opening.

Legal category POM.

Package quantities Ophthalmic ointment in tubes of 5 g. Ophthalmic solution in polythene bottles with integral dropper, each containing 15 ml.

Further information Nil.

Product licence numbers

Kerecid ophthalmic ointment 0002/0047

Kerecid ophthalmic solution 0002/5035

LISSONUM*

Presentation White, oblong, film-coated tablets, with convex faces and a breakline on both sides, each containing 450 mg lithium carbonate (12.2 mmol Li^+) in controlled-release form.

Uses Lissinum is a controlled-release tablet, designed to reduce fluctuations in serum lithium levels and the likelihood of adverse reactions.

It is indicated for the treatment of acute episodes of mania or hypomania and for the prophylaxis of recurrent manic-depressive illness.

Dosage and administration *Adults only:* Lissinum should be given twice a day.

Treatment of acute mania or hypomania: Patients should be started on one or one and a half tablets twice a day. Dosage should then be adjusted to achieve a serum lithium level of 0.8 to a maximum of 1.5 mmol/l. Serum concentration of lithium should be measured after four to seven days' treatment and then at least once a week until dosage has remained constant for 4 weeks. When the acute symptoms have been controlled, recommendations for prophylaxis should be followed.

Prophylaxis: The usual starting dosage is one tablet twice a day. Dosage should then be adjusted until a serum level of 0.5 to 1.0 mmol/l is maintained. Serum concentration of lithium should be measured after four to seven days' treatment and then every week until dosage has remained constant for four weeks. Frequency of monitoring may then be gradually decreased to a minimum of once every two months.

Blood samples for measurement of serum lithium concentration should be taken just before a dose is due and not less than 12 hours after the previous dose.

Levels of more than 2 mmol/l must be avoided.

Tablets may be halved but should not be chewed or broken up.

The full prophylactic effect of lithium may not be evident for 6 to 12 months, and treatment should be continued through any recurrence of the illness.

Contra-indications, warnings, etc

Contra-indications: Do not use in patients with impaired renal function, cardiac disease, or untreated hypothyroidism. Lithium should not be given to patients with low body sodium levels, including, for example, dehydrated patients, those on low sodium diets, or those with Addison's disease.

Cautions: Vomiting, diarrhoea, intercurrent infection and drugs likely to upset electrolyte balance, such as diuretics, may all reduce lithium excretion and thereby precipitate intoxication; reduction of dosage may be required. In elderly patients, lithium excretion may also

be reduced. An anti-diuretic effect leading to water retention has been reported following the use of diuretics during treatment with lithium salts. There is a possibility of water intoxication and lithium intoxication with diuretics and lithium salts are co-prescribed. The possibility of hypothyroidism and of renal dysfunction arises during prolonged treatment should be borne in mind.

There have been reports of interaction between lithium and some neuroleptics, particularly haloperidol at high dosages.

Use in pregnancy and lactation: Lithium crosses placental barrier. In animal studies, lithium has been reported to interfere with fertility, gestation and foetal development. There is epidemiological evidence that drug may be harmful in human pregnancy. Lithium therapy should not be used during pregnancy, especially during the first trimester, unless the benefits are considered to outweigh the risks. If given, however, serum levels should be measured frequently because of changes in renal function associated with pregnancy and parturition.

Since lithium is secreted in breast milk, bottle feed is advisable.

Adverse reactions: At therapeutic serum levels, nausea and diarrhoea, fine tremor of the hands, muscle weakness, vertigo, giddiness, weight gain, oedema, and a dazed feeling may occur. Hypothyroidism has been reported. Rarely hyperthyroidism may occur. Mild polyuria and polydipsia are not infrequent and, occasionally nephrogenic diabetes insipidus may be present. Reactions have been observed on biopsy in some patients but the relationship between these lesions and renal function has not been established.

Skin reactions including acne or acneiform eruptions, papular skin disorders, rashes, and exacerbation of psoriasis have been reported.

Intoxication: Vomiting, diarrhoea, drowsiness, lack of co-ordination and/or a coarse tremor of the extremities and lower jaw may occur, especially with serum levels above the therapeutic range. Ataxia, blurred vision, dysarthria, tinnitus, muscle hyperirritability, choreoathetoid movements and toxic psychosis have also been described.

If any of the above symptoms appear, treatment should be stopped immediately and arrangements made for serum lithium measurement.

Overdosage: Symptoms are similar to those listed above under *Intoxication* but more marked, particularly the central nervous system origin. In severe cases seizures, coma and death may ensue.

Treatment consists of the induction of vomiting and gastric lavage together with supportive and symptomatic measures. Particular attention should be paid to maintenance of fluid and electrolyte balance and of adequate renal function. Where convulsions are present, diazepam may be used. Forced alkaline diuresis, peritoneal dialysis or haemodialysis may help eliminate the lithium ion. The latter method is preferable, particularly where serum lithium exceeds 4 mmol/l.

Pharmaceutical precautions Store in a dry place

Legal category POM.

Package quantities Boxes containing 60 tablets or blister packs. Securitainers containing 1,000 tablets.

Further information Nil.

Product licence number 0002/0083.

CRALAX* MICRO-ENEMA

Presentation A disposable plastic tube with a 2-inch ble plastic nozzle, which contains 5 ml of a colourless ous liquid incorporating 450 mg sodium citrate, mg sodium alkylsulphoacetate and 5 mg sorbic acid, ether with glycerin, sorbitol and purified water.

es Micralax combines the action of sodium citrate, 'septising' agent which can displace bound water sent in the faeces; sorbitol, which enhances this on; and sodium alkylsulphoacetate, a wetting agent. Micralax is indicated whenever an enema is necessary relieve constipation: in dyschezia, especially in lidden patients; in geriatrics, paediatrics and obstet-; and in preparation for X-ray examination, proctos-ry and sigmoidoscopy.

sage and administration *Adults and children d 3 years and over:* Administer the contents of one :ro-enema rectally, inserting the full length of the zle.

o lubricant is needed as a drop of the mixture is ficient.

ontra-indications, warnings, etc

ontra-indication: Do not use in patients with inflam- tory bowel disease.

verse reactions: No side-effects have been reported. ressive use may cause diarrhoea and fluid loss, which uld be treated symptomatically.

armaceutical precautions Store in a cool place.

gal category P.

ckage quantities Packs of 12 and 100.

rther information Nil.

oduct licence number 0002/5037.

URO PHOSPHATES* LIQUID

esentation A clear, green liquid with a weak oholic odour and a bitter taste, each 10 ml dose ntaining 179.3 mg calcium glycerophosphate, 1.4 mg sodium glycerophosphate, and 1.1 mg ychnine alkaloid (in acid solution), together with % w/w alcohol.

ies As a tonic during convalescence and in the lerly and debilitated patient.

sage and administration *Adults:* 10 ml Neuro osphates twice a day, taken in water preferably before als.

ildren aged 7 years and over: 5 ml twice a day, as ove.

ontra-indications, warnings, etc

utions: As Neuro Phosphates contains strychnine, discriminate use may be dangerous, especially in the lerly patient.

verse reactions: No side-effects are to be expected at e recommended dosage.

er dosage: Even in gross overdosage, symptoms are e. Treatment consists of the induction of vomiting d/or gastric lavage together with appropriate support- and symptomatic measures. If muscular spasms or er symptoms of excitability are present, give nothing mouth and do not induce vomiting. The patient should ept absolutely quiet and sedation with diazepam ay be indicated.

Pharmaceutical precautions Neuro Phosphates may be diluted if necessary with purified water. It is stable after dilution for up to 14 days at room temperature.

Legal category POM.

Package quantities Bottles of 300 ml and 2 litres.

Further information Nil.

Product licence number 0002/5039.

PARNATE* TABLETS

Presentation Geranium-red, sugar-coated tablets, marked SKF, each containing 10 mg tranlylcypromine present as the sulphate.

Uses Parnate is a non-hydrazone monoamine oxidase inhibitor for the treatment of depression. It is not recommended for mild depressive states resulting from temporary situational difficulties.

Dosage and administration *Adults only:* Initially, one tablet morning and afternoon. If the response is not adequate after the first week, add a further tablet at midday, and continue for at least a week. A dosage of 3 tablets a day should only be exceeded with caution. When a satisfactory response has been obtained, dosage may be reduced to a maintenance level, often of 1 tablet a day.

When given with a tranquilliser, the dosage of Parnate is not affected. When given concurrently with electro-convulsive therapy, the usual dosage is 1 tablet twice a day during the series and 1 tablet a day afterwards as maintenance therapy.

Contra-indications, warnings, etc

Contra-indications: Do not give Parnate less than a week after stopping treatment with any other anti-depressant drug including other MAO inhibitors, because of persisting effects, then give half the usual dosage for the first week. Similarly, after stopping Parnate, allow at least two weeks to elapse before starting treatment with any drug that may interact.

Do not give Parnate with indirectly-acting sympatho-mimetic amines such as amphetamine, fenfluramine or similar anti-obesity agents, ephedrine or phenylpropan-olamine (certain 'cold-cures' may contain such agents), or with levodopa or dopamine, as severe hypertensive reactions may result; with pethidine and closely related narcotic analgesics as potentiation may occur; or with other MAO inhibitors, as symptoms of overdosage are possible.

Reports of hyperactivity, hypertonicity, hyperpyrexia, coma and death have been associated with the use of Parnate in combination with tricyclic anti-depressants; tetracyclic antidepressants should also be avoided. The use of clomipramine in patients already on Parnate may be particularly hazardous.

Do not use Parnate in patients with actual or suspected cerebrovascular disease or severe cardiovascular disease; in those with actual or suspected pheochromocytoma, or with hyperthyroidism; or in those with known liver damage or blood dyscrasias.

Dietary precautions: High levels of tyramine in certain foods have been the cause of severe hypertensive reactions in patients on MAO inhibitor therapy (see *Adverse reactions*). Accordingly, patients must be warned to avoid the following: matured cheeses, hydro-lysed protein extracts such as Marmite or Bovril, alcoholic

drinks, particularly red wines such as Chianti, and protein foods that are not fresh or whose preparation involved hydrolysis, fermentation, pickling, or 'hanging'; also broad-bean pods, which contain levodopa, and banana skins.

Cautions: Caution should be exercised when giving Parnate with the following: guanethidine, as its action may be antagonised; reserpine, as hyperactivity may occur; methyl dopa, as central excitation may result; other hypotensive agents because of possible additive effects; oral hypoglycaemic agents or insulin, as their action may be potentiated; anticholinergic antiparkinsonism drugs, as potentiation has been reported; narcotic analgesics, except pethidine which is contra-indicated (see above), because of possible potentiation; and carbamazepine, which has similarities with tricyclic antidepressants. Although the effects of barbiturates may be enhanced, and this possibility should be borne in mind, they have frequently been given with Parnate, particularly at night. Metrizamide should be avoided in patients on MAO inhibitors since they may lower the seizure threshold.

Patients should be specifically asked if they are taking any other medication because of the possibility of drug interactions.

Use Parnate with great caution in elderly patients; in those with cardiovascular disease in whom physical activity should be regulated, as the drug may suppress anginal pain; and in epileptic patients, as tranylcypromine has a variable effect on the convulsive threshold in animals. Parnate may aggravate some co-existing symptoms in depression such as anxiety and agitation. Parnate should preferably be withdrawn at least two weeks before elective surgery because of possible drug interaction.

Caution should be exercised in prescribing Parnate for patients with a previous history of dependence on drugs or alcohol.

In common with other drugs acting on the CNS, Parnate may affect ability to drive or operate machinery.

Use in pregnancy and lactation: Do not use in pregnancy, especially during the first and last trimesters, unless there are compelling reasons. There is no evidence as to drug safety in human pregnancy nor is there evidence from animal work that it is free from hazard. Tranylcypromine passes into the milk of lactating dogs.

Adverse reactions: Severe hypertensive reactions may occur, notably in association with foods containing tyramine (see *Dietary precautions*). Such reactions may be presaged by palpitations and unusually frequent headaches; patients should be warned to discontinue the drug if such symptoms occur. As well as a rapid rise in blood pressure, severe occipital headache, which may radiate frontally, is virtually always present, and pain and stiffness in the neck are usual; other features include multiple extrasystoles, often with bradycardia though sometimes with tachycardia, other arrhythmias, substernal pain, nausea and vomiting, sweating, pallor, sometimes followed by flushing, mydriasis and photophobia. Rarely, hypotension may dominate the clinical picture. ECG changes may be seen. The symptoms can mimic subarachnoid haemorrhage or may actually be associated with intracranial bleeding. Exceptionally, hemiparesis, hemiplegia or death has resulted.

Severe hypertensive reactions should be treated at once by reducing the blood pressure; slow intravenous injection of 5 mg phentolamine mesylate should be effective. Injectable or oral chlorpromazine is suitable for

milder reactions. Acute symptoms generally subside within 24 hours.

Insomnia is the most frequent side-effect; it may usually be overcome by giving the last dose of the drug not later than 3 pm, by reducing dosage, or by prescribing a mild hypnotic.

Mild headache, drowsiness, weakness, dizziness, palpitation, transient restlessness, dry mouth, blurred vision, nausea, oedema, weight gain, increased appetite, a rash have been reported. Overstimulation, including anxiety and agitation, developing rarely into hypomania has also been observed; the dosage should be reduced. Hypotension, which may be postural, may occur; it is usually temporary, but if it persists the drug should be stopped.

Dependence on Parnate, with tolerance to very high doses, has been reported rarely. This should be distinguished from the return of features of the original illness on cessation of treatment.

Liver dysfunction has occurred very rarely, and isolated instances of purpura and blood dyscrasias have been reported.

Overdosage: Signs and symptoms are usually of the type already described as adverse reactions, but may be much more intense, may include hyperpyrexia, tremor and convulsions, and may follow a latent period. Treatment consists of the induction of vomiting and/or gastric lavage together with supportive and symptomatic measures. External cooling is recommended for hyperpyrexia. Treatment of hypotension with fluid replacement; if severe or persistent, noradrenaline may be considered. Hypertension, if it occurs, may be relieved by slow intravenous injection of phentolamine mesylate. Beta-adrenergic receptor blockade has been used successfully.

Pharmaceutical precautions Store in a cool, dry place, and dispense in moisture-proof containers.

Legal category POM.

Package quantities Containers of 50 and 500 tablets.

Further information It is generally considered that no particular hazard is attached to the use of local anaesthetics containing small amounts of adrenaline in patients receiving Parnate unless cardiovascular disease is present.

Product licence number 0002/5040.

PARSTELIN* TABLETS

Presentation Leaf-green, sugar-coated tablet marked SKF, each containing 10 mg tranylcypromine present as the sulphate and 1 mg trifluoperazine present as the hydrochloride.

Uses Parstelin is a combination of a non-hydrizir monoamine oxidase inhibitor and a phenothiazine tranquilliser, for the treatment of depression complicated by anxiety. It is not recommended for mild depressive states resulting from temporary situational difficulties.

Dosage and administration *Adults only:* Initially, tablet morning and afternoon. If the response is not adequate after the first week, add a further tablet at midday, and continue for at least a week. A dosage of tablets a day should only be exceeded with caution. When a satisfactory response has been obtained, dosage may be reduced to a maintenance level, often of 1 tablet a day.

Contra-indications, warnings, etc

Contra-indications: Do not give Parstelin less than a week after stopping treatment with any other antidepressant drug including other MAO inhibitors, because of persisting effects, then give half the usual dosage for the first week. Similarly, after stopping Parstelin, allow at least two weeks to elapse before starting treatment with any drug that may interact.

Do not give Parstelin with indirectly-acting sympathomimetic amines such as amphetamine, fenfluramine, or other anti-obesity agents, ephedrine or phenylpropanamine (certain 'cold-cures' may contain such agents), with levodopa or dopamine, as severe hypertensive reactions may result; with pethidine and closely related narcotic analgesics, as potentiation may occur; or with other MAO inhibitors, as symptoms of overdosage are possible.

Reports of hyperactivity, hypertonicity, hyperpyrexia, coma and death have been associated with the use of tricyclic antidepressants in combination with tricyclic antidepressants; tetracyclic antidepressants should also be avoided. The use of clomipramine in patients already on Parstelin may be particularly hazardous.

Do not use Parstelin in patients with actual or suspected cerebrovascular disease or severe cardiovascular disease; in those with actual or suspected pheochromocytoma, or with hyperthyroidism; or in those with existing blood dyscrasias or known liver damage.

Dietary precautions: High levels of tyramine in certain foods have been the cause of severe hypertensive reactions in patients on MAO inhibitor therapy (see *Adverse reactions*). Accordingly, patients must be warned to avoid the following: matured cheese, hydrolysed protein extracts such as Marmite or Bovril, alcoholic drinks, particularly red wines such as Chianti, and protein foods that are not fresh or whose preparation involved hydrolysis, fermentation, pickling, or 'hanging'; also ad-bean pods, which contain levodopa, and banana skins.

Precautions: Caution should be exercised when giving Parstelin with the following: guanethidine, as its action may be antagonised; reserpine, as hyperactivity may occur; methylodopa, as central excitation may result; other hypotensive agents because of possible additive effects; oral hypoglycaemic agents or insulin, as their action may be potentiated; anticholinergic antiparkinsonism drugs, as potentiation has been reported; narcotic analgesics, except pethidine which is contra-indicated (see above), because of possible potentiation; and imipramine, which has similarities with tricyclic antidepressants. Although the effects of barbiturates may be enhanced, and this possibility should be borne in mind, they have frequently been given with Parstelin, particularly at night. Metrizamide should be avoided in patients on MAO inhibitors since they may lower the seizure threshold.

Patients should be specifically asked if they are taking any other medication because of the possibility of drug interactions.

Use Parstelin with great caution in elderly patients; in those with cardiovascular disease in whom physical activity should be regulated, as tranylcypromine may suppress anginal pain; and in epileptic patients as tranylcypromine has a variable effect on the convulsive threshold in animals. Tranylcypromine may aggravate some co-existing symptoms in depression such as anxiety and agitation. Parstelin should preferably be

withdrawn at least two weeks before elective surgery because of possible drug interaction.

Nausea and vomiting as a sign of organic disease may be masked by the anti-emetic action of trifluoperazine.

Caution should be exercised in prescribing Parstelin for patients with a previous history of dependence on drugs or alcohol.

In common with other drugs acting on the CNS, Parstelin may affect ability to drive or operate machinery.

Use in pregnancy and lactation: Do not use in pregnancy, especially during the first and last trimesters, unless there are compelling reasons. There is no evidence as to drug safety in human pregnancy nor is there evidence from animal work that it is free from hazard. Both tranylcypromine and trifluoperazine pass into the milk of lactating dogs.

Adverse reactions: Severe hypertensive reactions may occur, notably in association with foods containing tyramine (see *Dietary precautions*). Such reactions may be presaged by palpitations and unusually frequent headaches; patients should be warned to discontinue the drug if such symptoms occur. As well as a rapid rise in blood pressure, severe occipital headache, which may radiate frontally, is virtually always present, and pain and stiffness in the neck are usual; other features include multiple extrasystoles, often with bradycardia though sometimes with tachycardia, other arrhythmias, substernal pain, nausea and vomiting, sweating, pallor, sometimes followed by flushing, mydriasis and photophobia. Rarely, hypotension may dominate the clinical picture. ECG changes may be seen. The symptoms can mimic subarachnoid haemorrhage or may actually be associated with intracranial bleeding. Exceptionally, hemiparesis, hemiplegia or death has resulted.

Severe hypertensive reactions should be treated at once by reducing the blood pressure; slow intravenous injection of 5 mg phentolamine mesylate should be effective. Injectable or oral chlorpromazine is suitable for milder reactions. Acute symptoms generally subside within 24 hours.

Insomnia is the most frequent side-effect; it may usually be overcome by giving the last dose of the day not later than 3 pm, by reducing dosage, or by prescribing a mild hypnotic.

Mild headache, drowsiness, weakness, dizziness, palpitation, transient restlessness, dry mouth, blurred vision, nausea, oedema, weight gain, increased appetite and rash have been reported. Overstimulation, including anxiety and agitation, developing rarely into hypomania, has also been observed; the dosage should be reduced. Hypotension, which may be postural, may occur; it is usually temporary, but if it persists the drug should be stopped.

Dependence on tranylcypromine, with tolerance to very high doses, has been reported rarely. This should be distinguished from the return of features of the original illness on cessation of treatment.

Extrapyramidal symptoms due to the trifluoperazine component are very unlikely at the recommended dosage. Extremely rarely, long-term therapy with trifluoperazine in low dosage has been associated with tardive dyskinesia, which can be long-lasting or even irreversible.

Liver dysfunction has occurred very rarely, and isolated instances of purpura and blood dyscrasias have been reported.

Overdosage: Signs and symptoms are usually of the type already described as adverse reactions to tranylcypromine.

ine, but may be more intense, may include hyperpyrexia, tremor and convulsions, and may follow a latent period. In the unlikely event of symptoms from the trifluoperazine component, these are extrapyramidal in type. Treatment consists of gastric lavage together with supportive and symptomatic measures. Do not induce vomiting. External cooling is recommended for hyperpyrexia. Treat hypotension with fluid replacement; if severe or persistent, noradrenaline may be considered; adrenaline is contraindicated. Hypertension, if it occurs, may be relieved by slow intravenous injection of phentolamine mesylate. Beta-adrenergic receptor blockade has been used successfully.

Pharmaceutical precautions Store in a cool, dry place, protect from light, and dispense in moisture-proof, light-resistant containers.

Legal category POM.

Package quantities Containers of 50 and 500 tablets.

Further information It is generally considered that no particular hazard is attached to the use of local anaesthetics containing small amounts of adrenaline in patients receiving tranylcypromine unless cardiovascular disease is present.

Product licence number 0002/5041.

PHENOBARBITONE SPANSULE* CAPSULES

Presentation Clear, colourless capsules, blue-capped and filled with a mixture of dark blue, pale blue, and white pellets, in two strengths. Each Spansule sustained-release capsule, size No. 3, contains 60 mg, and each size No. 2 capsule, 100 mg phenobarbitone. Two-thirds of the dose is formulated for sustained release over a period of six to eight hours.

Uses Anticonvulsant and sedative, Phenobarbitone Spansule capsules are indicated in the treatment of epilepsy.

Dosage and administration *Adults:* Dosage depends on the need of the individual patient, and may vary from one 60 mg capsule a day in the morning or at night, to three 100 mg capsules a day.

Children aged 6 years and over: As in adults, the dosage requirement may vary, the highest usual dosage being two 60 mg capsules a day. The capsules may be opened and the pellets mixed with soft, cool food, but they must not be chewed.

Contra-indications, warnings, etc

Contra-indications: Do not use in patients with porphyria, severe liver damage, or known hypersensitivity to barbiturates.

Cautions: Patients who drive or operate machinery should be warned of the possibility of drowsiness. Patients should also be warned that alcohol may potentiate the effects of phenobarbitone. The drug should be used with care in the elderly, and in those with kidney or liver damage.

Because phenobarbitone can induce liver microsomal enzymes, the rate of metabolism of certain drugs can be increased. Those drugs whose expected effect may be reduced in this way include coumarin-type anticoagulants and some steroid hormones.

Prolonged use may lead to dependence of the barbiturate-alcohol type, and particular care should be

taken in treating patients with a history of dependence on drugs or alcohol.

Use in pregnancy and lactation: It has been suggested that certain anticonvulsants, possibly including phenobarbitone, may produce embryotoxic effects in man. Although this drug has been available for very many years, it should be avoided in pregnancy unless essential, especially during the first trimester.

Barbiturates can pass into breast milk and should be avoided by nursing mothers.

Adverse reactions: Drowsiness, which may be marked, and allergic reactions including skin reactions, may occur. Paradoxically in children irritability may be observed.

Overdosage: Absorption of phenobarbitone from the sustained-release Spansule capsule is likely to be prolonged, and this should be borne in mind. Treatment consists of the induction of vomiting and/or gastric lavage, together with intensive supportive and symptomatic measures. In severe poisoning, forced alkaline diuresis, haemodialysis or charcoal haemoperfusion may help to eliminate the drug.

Pharmaceutical precautions Store in a cool, dry place, and dispense in moisture-proof containers.

Legal category POM.

Package quantities Both strengths in containers of 30 and 250 Spansule capsules.

Further information Nil.

Product licence numbers

Phenobarbitone Spansule capsules 60 mg	0002/504
Phenobarbitone Spansule capsules 100 mg	0002/504

POLIOMYELITIS VACCINE, LIVE (ORAL) BP (Sabin strains)

Presentation Poliomyelitis Vaccine, Live (Oral) BP as supplied by Smith Kline & French, is a light orange to pink liquid stabilised with molar magnesium chloride. Each dose (3 drops) provides at least 10^6 TCID₅₀ type (LS-c, 2ab), 10^5 TCID₅₀ type 2 (P712, Ch, 2ab) and $10^{5.5}$ TCID₅₀ type 3 (Leon 12a, b) live attenuated strain of poliomyelitis virus grown in monkey kidney cell cultures, and contains not more than 7 µg (5 i.u.) neomycin sulphate.

Uses Active immunisation against poliomyelitis.

Dosage and administration *Adults and children:* For oral use only: NOT FOR INJECTION. Three drops of the vaccine constitute one dose which may be given with syrup or on a lump of sugar to mask the bitter salty taste of the magnesium chloride.

For a complete schedule, three doses of the vaccine should be given at intervals of at least four weeks (see also *Further information*).

Other unvaccinated members of the same household (including adults) should be advised vaccination at the same time as the vaccinee.

Contra-indications, warnings, etc

Contra-indications: The vaccine should not be used in the presence of acute febrile illness or intercurrent infection, diarrhoea, vomiting or other gastro-intestinal disturbance, neither should it be given in the presence of

mpaired immune response including leukaemia, lymphoma, generalised malignancy or treatment with corticosteroids, cytotoxic drugs or irradiation. Do not give to those known to be hypersensitive to neomycin (see also *Cautions*).

Cautions: The vaccine may contain trace amounts of penicillin and streptomycin which should not contraindicate its use except in those with extreme hypersensitivity to either antibiotic.

It is not normally recommended that live vaccines are given within three weeks of each other.

Use in pregnancy: Pregnant women should not be given oral poliomyelitis vaccine unless they are at definite risk from poliomyelitis.

Adverse reactions: Paralysis temporally associated with vaccination has been reported very rarely in recipients or contacts.

Overdosage: Not applicable.

Pharmaceutical precautions Protect from light and store between 2°C and 6°C. Under these conditions there is no significant loss of virus titre for 12 months.

Once opened, the vaccine should be used within three hours or discarded. Any unopened vaccine should be returned to storage between 2°C and 6°C as soon as possible. Potency is maintained for two weeks at room temperature (20°C to 25°C).

Legal category POM.

Package quantities Ten-dose vial with dropper.

Further information Current policy recommends that the first dose of oral poliomyelitis vaccine should be given at three months of age. The first and second doses should be separated by six to eight weeks and the second and third doses by four to six months. For convenience the vaccine may be given at the same time as the three-dose basic course of diphtheria/tetanus/pertussis vaccine.

It is currently recommended that a reinforcing dose of poliomyelitis vaccine should be given at school entry and at 15 to 19 years of age. Adults need not be offered a reinforcing dose unless they are at special risk.

Product licence number 0002/0076.

PRAGMATAR* OINTMENT

Presentation A pale, buff-coloured, oil-in-water cream containing 4% w/w cetyl alcohol-coal tar distillate, 3% w/w precipitated sulphur, and 3% w/w salicylic acid.

Uses Pragmatar has mild antipruritic, antiseptic, and keratolytic properties. It is indicated in the treatment of dandruff, other seborrhoeic conditions, and common scaly skin disorders.

Dosage and administration *Adults and children:* For mild dandruff, apply the ointment once a week when the hair is washed. For more severe cases, treat the entire scalp daily at bedtime, applying lightly but thoroughly with the fingertips. The ointment can be washed out the next morning or left as a pleasant hair dressing. For other indicated subacute or chronic skin disorders, apply daily in small quantities to affected areas only.

For use in infants, the ointment may be diluted by mixing with a few drops of water in the palm of the hand.

Contra-indications, warnings, etc

Contra-indications: Do not use in patients who are sensitive to sulphur.

Caution: Use with care near the eyes, the groin, or on acutely inflamed areas. If any ointment should accidentally enter the eye, flush with normal saline solution.

Adverse reactions: No side-effects are to be expected if the ointment is used according to directions. Excessive use, however, may cause erythema and irritation.

Overdosage: If ingestion occurs, gastro-intestinal disturbances may follow. Treatment consists of rinsing out the mouth together with symptomatic measures if necessary. Even with massive ingestion, salicylate poisoning seems unlikely.

Pharmaceutical precautions Store in a cool place and protect from light.

Legal category P.

Package quantities Tubes containing 25 g.

Further information Nil.

Product licence number 0002/5044.

REDEPTIN* INJECTION

Presentation Each ampoule or vial of Redeptin contains an opalescent white aqueous suspension containing 2 mg fluspirilene in each 1 ml.

Uses Fluspirilene is a major tranquilliser of the diphenylbutylpiperidine group with a mildly alerting action. It is slowly absorbed after intramuscular injection. Detectable blood levels are reached within four hours of injection, and the antipsychotic action usually lasts for about a week, with a range of 5 to 15 days.

Redeptin is recommended for the treatment of schizophrenia, and has proved especially useful for maintenance therapy. It is of particular value in patients who are unreliable in taking oral medication.

Dosage and administration *Adults only:* The recommended starting dose is 2 mg a week by deep intramuscular injection; this may be increased by 2 mg a week according to response. The maintenance dosage for most patients is from 2 to 8 mg a week, but some may require up to 12 mg a week. Dosage should not exceed 20 mg a week.

Administration: Before administration the container should be shaken well. The 6 ml vial should be used on one occasion only.

Contra-indications, warnings, etc

Contra-indications: Do not use in patients who have suffered uncontrollable adverse effects during previous treatment with diphenylbutylpiperidine derivatives.

Cautions: Patients who drive or operate machinery should be warned of the possibility of drowsiness.

Patients with epilepsy should be treated with caution as attacks may be precipitated.

Use in pregnancy: Although there is no evidence from animal studies to suggest that Redeptin has embryotoxic effects, drug treatment should always be avoided during pregnancy unless essential, especially during the first trimester.

Adverse reactions: When side-effects occur, they are usually limited to the first two days after injection. Extrapyramidal reactions, especially dyskinesia and ak-

athisia but also tremor and salivation, may occur within 6 to 12 hours after injection and usually disappear within 48 hours; they can normally be controlled by reduction of dosage or by the use of anticholinergic antiparkinsonism drugs. The possibility of tardive dyskinesia should be borne in mind. Subcutaneous nodules at the site of injection have been reported, usually in patients on high doses for long periods. These nodules tend to disappear when treatment is stopped. They may be minimised by using as many different injection sites as possible. Other reactions reported include fatigue, upper gastro-intestinal symptoms such as nausea and vomiting, drowsiness, insomnia, restlessness, excitement, anxiety, headache and sweating. There have also been occasional reports of blurred vision, mild hypotension, dizziness, rash, and EEG and ECG changes. In a small number of patients side-effects may become progressively more marked over a period of weeks or months; these signs of accumulation can be eliminated by omitting one injection every four or five weeks.

Overdosage: In the unlikely event of accidental overdosage, signs and symptoms are likely to be predominantly extrapyramidal, possibly with some excitation. Treatment would consist of supportive and symptomatic measures. Extrapyramidal symptoms should be treated with an anticholinergic antiparkinsonism drug. The long-acting properties of the presentation should be borne in mind.

Pharmaceutical precautions Redeptin ampoules and vials should be stored upright at room temperature and protected from light.

Legal category POM.

Package quantities Redeptin ampoules, each containing either 2 mg fluspirilene in 1 ml or 6 mg fluspirilene in 3 ml, are available in boxes of 10. Redeptin vials, each containing 12 mg fluspirilene in 6 ml, are available in packs of 5.

Further information Nil.

Product licence number 0002/0056.

RIMEVAX*

Measles vaccine, live BP (Schwarz strain)

Presentation Rimevax Measles Vaccine, prepared in chicken embryo fibroblasts, is presented as a pink freeze-dried pellet in a glass vial with a separate ampoule of clear, colourless, sterile diluent. Each 0.5 ml dose of reconstituted vaccine contains not less than 1,000 TCID₅₀ of the highly attenuated live Schwarz strain measles virus and not more than 25 µg (17 i.u.) of neomycin sulphate.

Uses Rimevax is indicated for active immunisation against measles (rubeola).

If given to contacts within three days of exposure to measles, the full clinical disease may be suppressed.

Dosage and administration *Adults and children:* 0.5 ml of the reconstituted vaccine subcutaneously or intramuscularly. The vaccine should be reconstituted using the sterile diluent provided.

The vaccine is quickly inactivated by ether, alcohol and detergents and care should be taken to avoid contact with these substances when cleaning skin prior to vaccination. Syringes need to be dry sterilised.

Contra-indications, warnings, etc

Contra-indications: Do not use Rimevax in the presence of acute illness, whether active or expected following exposure to infection other than measles. This applies particularly to active tuberculosis and respiratory tract infection. It is also contra-indicated in states of altered immunity including those which may accompany conditions such as leukaemia, lymphoma, generalised malignancy or treatment with corticosteroids, cytotoxic drug or irradiation.

Rimevax may contain traces of chick embryo protein but this does not normally contra-indicate its use except in cases of severe hypersensitivity to eggs. Rimevax should not be given to those known to be hypersensitive to neomycin. A solution of 1:1000 adrenaline should be available for injection in rare cases of anaphylactic reaction.

Do not use during pregnancy.

Cautions: Measles vaccine should only be given to children with a history of convulsions with the simultaneous administration of human normal immunoglobulin [recommended dosage 1.3 mg protein/kg (0.6 mg protein/lb) body weight]. In such children or those with a family history of convulsions, consideration should be given to delaying immunisation until after the second birthday.

Because of the possibility of interference from passive antibodies, measles vaccine should not normally be given to infants below the age of one year, or to subjects who have received blood or human plasma transfusions or human immunoglobulin within the previous three months. If the vaccine is given in these circumstances serum antibodies should be checked at a later date.

Tuberculin testing should be delayed for about eight weeks after measles vaccination since false-negative results may be obtained during this period.

It is not usually recommended that live vaccines be given within three weeks of each other.

Adverse reactions: These are usually mild and are more likely around the eighth day after vaccination. They may include rash, malaise, cough, pharyngitis, coryza, pyrexia and headache. In a very few subjects convulsions may accompany the fever. Very rarely encephalitis has been reported in association with measles vaccination.

Pharmaceutical precautions Protect from light. Rimevax Measles Vaccine should be stored between 2°C and 8°C and should not be frozen (lower temperatures will not harm the vaccine but may damage the diluent ampoule). At room temperature (20°–25°C) Rimevax is stable for up to four weeks.

The vaccine should be reconstituted using the sterile diluent provided. Once reconstituted Rimevax should be used immediately and certainly within one hour.

Legal category POM.

Package quantities Single-dose vials, each with a separate ampoule containing sterile diluent, singly and in packs of 50.

Further information Current policy recommends routine vaccination against measles for children between 1 and 2 years of age. Rimevax may also be used for older children and adults known to be susceptible to measles.

The following groups of children at special risk may in particular benefit from vaccination: children from the age of one year upwards in residential care; those entering nursery school or other establishments accepting chil-

ren for day care; those with chronic conditions affecting physical development such as cystic fibrosis or congenital heart disease; and those with a history of convulsions provided the appropriate cautions (see *Cautions* above) are observed.

Maximum periods of stability of freeze-dried Rimevax:

2°-8°C	2 years
0°-25°C	4 weeks
7°C	14 days
1°C	7 days

It is recommended that the vaccine is stored at 2°-8°C (see *Pharmaceutical precautions*).

Product licence number 0002/0088.

KEFRON* AEROSOL FOR LOCAL APPLICATION

Presentation A volatile, non-inflammable liquid consisting of 15% w/w dichlorodifluoromethane and 5% w/w trichlorofluoromethane, in a pressurised canister.

Uses When applied to the skin as a jet. Skefron exerts local chilling effect. It is used for external treatment of painful conditions associated with muscle spasm, as in lumbago, fibrositis, torticollis and sprains.

Dosage and administration *Adults and children:* Hold container upright between 1 and 2 feet from the affected area, and press button firmly so that a jet and not a spray is produced. If the face is treated, screen the eyes, nostrils and mouth. Direct the jet horizontally at the area for three to five seconds, and repeat after half a minute. A third application may be given after a further half minute if necessary. This constitutes one treatment. Not more than three such treatments should be given in any one day. There may be a brief increase in pain before relief occurs.

Contra-indications, warnings, etc

Contra-indications: Do not use on inflamed or broken skin.

Adverse reactions: No side-effects are to be expected when Skefron is used according to directions.

Overdosage: Excessive use may damage the skin. Inhalation may cause choking and coughing but prevention of further inhalation and symptomatic treatment should be adequate.

Pharmaceutical precautions Store in a cool place. Do not puncture, break or incinerate containers even when apparently empty.

Legal category GSL.

Package quantities Canisters each containing 200 g.

Further information Nil.

Product licence number 0002/5071.

STELABID* TABLETS

STELABID* FORTE TABLETS

Presentation *Stelabid tablets:* Dull yellow, sugar-coated tablets, marked SKF in grey, each containing 5 mg isopropamide present as the iodide and 1 mg trifluoperazine present as the hydrochloride.

Stelabid Forte tablets: Dull yellow, sugar-coated tablets,

marked SKF and P92 in light grey, each containing 7.5 mg isopropamide present as the iodide and 2 mg trifluoperazine present as the hydrochloride.

Uses Stelabid is a combination of two long-acting compounds, an anticholinergic agent and a phenothiazine tranquilliser. It is indicated in the symptomatic treatment of peptic ulcer, and other gastro-intestinal disorders in which hypersecretion and/or painful spasms are a problem as, for example, in irritable or spastic colon and functional diarrhoea. Stelabid is especially indicated when such conditions are complicated by emotional factors such as tension and anxiety.

Dosage and administration *Adults only:* *Stelabid tablets:* 2 or 3 tablets a day, according to the severity of the condition. The dosage should be divided and taken in the morning and at bedtime. At the higher dosage, and particularly in patients troubled by night pain, 2 tablets may be taken at bedtime.

Stelabid Forte tablets: 1 tablet every 12 hours.

Contra-indications, warnings, etc

Contra-indications: Do not use in patients with glaucoma, intestinal obstruction of organic origin or intestinal atony, reflux oesophagitis, prostatic hypertrophy or incipient urinary retention from any cause, or ulcerative colitis; in those sensitive to iodine; or in patients with existing blood dyscrasias or known liver damage.

Cautions: Care should be exercised when treating elderly patients or those with cardiovascular disease.

Patients who drive or operate machinery should be warned of the possibility of drowsiness.

The iodine present may interfere with some tests of thyroid function.

Nausea and vomiting as a sign of organic disease may be masked by the anti-emetic action of trifluoperazine.

Use in pregnancy: Combinations of isopropamide and trifluoperazine have been available since 1960, and there is no experimental or clinical evidence to suggest any associated hazard to the foetus. Nevertheless, drugs should be avoided in pregnancy unless essential, especially during the first trimester.

Adverse reactions: Blurred vision, mydriasis, dry mouth, restlessness, insomnia, urinary hesitancy or retention, constipation, tachycardia, palpitations, and drowsiness may occur.

Extrapyramidal symptoms due to the trifluoperazine component are very unlikely at the recommended dosage. Extremely rarely, long-term therapy with trifluoperazine in low dosage has been associated with tardive dyskinesia, which can be long-lasting or even irreversible.

Overdosage: Signs and symptoms may be those of either isopropamide or trifluoperazine, or both, and may include extrapyramidal symptoms, CNS depression and hypotension. Treatment consists of gastric lavage, together with symptomatic and supportive measures. Do not induce vomiting. Central excitation may require a sedative such as diazepam. Physostigmine salicylate, 1-4 mg parenterally in an adult, repeated as necessary, has been reported to reverse the central and peripheral effects of anticholinergic poisoning. Extrapyramidal symptoms may be treated with an anticholinergic antiparkinsonism drug. Treat hypotension with fluid replacement; if severe or persistent, noradrenaline may be considered. Adrenaline is contra-indicated.

Pharmaceutical precautions Store in a cool, dry place, protect from light, and dispense in moisture-proof, light-resistant containers.

Legal category POM.

Package quantities *Stelabid tablets*: Containers of 100 and 500 tablets.

Stelabid Forte tablets: Containers of 100 tablets.

Further information Nil.

Product licence numbers

Stelabid tablets 0002/5073

Stelabid Forte tablets 0002/0040

STELAZINE* TABLETS

STELAZINE* SPANSULE* CAPSULES

STELAZINE* SYRUP

STELAZINE* CONCENTRATE

STELAZINE* INJECTION

Presentation Blue, sugar-coated tablets, marked SKF, containing either 1 mg or 5 mg trifluoperazine present as the hydrochloride.

Clear, colourless capsules, opaque yellow-capped and filled with a mixture of dark and light blue and white pellets. Each Spansule capsule, size No. 4, contains 2 mg, size No. 2, 10 mg, and size No. 1, 15 mg trifluoperazine present as the hydrochloride. Two-thirds of the dose of trifluoperazine is formulated for release over a period of six to eight hours.

A clear, pale yellow, peach-flavoured syrup, each 5 ml dose containing 1 mg trifluoperazine present as the hydrochloride.

A clear, pale yellow, peach-flavoured concentrate with a bitter numbing after-taste. Before dilution, each 1 ml of concentrate contains 10 mg trifluoperazine present as the hydrochloride.

Ampoules containing 1 mg trifluoperazine present as the hydrochloride in 1 ml.

Uses Stelazine is a piperazine phenothiazine tranquiliser with potent antipsychotic, anxiolytic, and anti-emetic activity.

Low dosage: Stelazine is indicated in anxiety states, depressive symptoms secondary to anxiety, and in senile agitation and confusion. It is also indicated in the symptomatic treatment of nausea and vomiting.

High dosage: Stelazine is indicated in acute and chronic schizophrenia of all types, psychosis due to organic brain damage, toxic psychosis, and behaviour disorders in mental subnormality.

Dosage and administration *Adults: Low dosage:* 2–4 mg a day as tablets or syrup, given in divided doses, or one or two 2 mg Spansule capsules a day, according to the severity of the patient's condition. If necessary, dosage may be increased to 6 mg a day, but above this level extrapyramidal symptoms are more likely to occur in some patients.

High dosage: The recommended starting dose for physically fit adults is 5 mg twice a day (or one 10 mg Spansule capsule a day); after a week this may be increased to 15 mg a day (which may be given as one 15 mg Spansule capsule). If necessary, further increases of 5 mg may be made at three-day intervals, but not more often. When satisfactory control has been achieved, dosage may be reduced gradually until an effective maintenance level has been established. Stelazine Span-

sule capsules are particularly useful for such maintenance therapy.

Intramuscular use: For a more rapid and intense effect or when oral administration presents difficulties, Stelazine may be given by deep intramuscular injection; the recommended dosage is 1–3 mg a day, given in divided doses. Higher dosages may sometimes be necessary up to a suggested maximum of 6 mg a day. Oral therapy should be substituted as soon as possible.

Children: Low dosage: For children aged 3–5 years, up to 1 mg a day as the syrup, given in divided doses. For children aged 6–12 years, the dosage may be increased to a maximum of 4 mg a day.

High dosage: For children aged under 12 years, the initial oral dosage should not exceed 5 mg a day, given in divided doses. Any subsequent increase should be made with caution, at intervals of not less than three days, and taking into account age, body weight and severity of symptoms.

Intramuscular use: There has been little experience in the use of intramuscular Stelazine in children. If required, a starting dose of 1 mg per 20 kg (44 lb) body weight a day, given in divided doses, is suggested.

Use of liquid presentations: Dilute Stelazine concentrate before use; one volume of the concentrate diluted preferably with Syrup BP or else purified water to produce 10 volumes gives a concentration of 5 mg trifluoperazine in each 5 ml dose. Both syrup and concentrate may be administered with a drink of water, milk, orange, tomato or other fruit juices, syrups or in carbonated beverages, or semi-solid foods such as soup, puddings or ice-cream.

Contra-indications, warnings, etc

Contra-indications: Do not use Stelazine in comatose patients, or in those with existing blood dyscrasias or known liver damage.

Cautions: Care should be exercised when treating elderly patients or those with cardiovascular disease, because of the occasional mild hypotensive effect of the drug; and when treating patients with angina pectoris, as Stelazine may increase activity.

Nausea and vomiting as a sign of organic disease may be masked by the anti-emetic action of Stelazine.

Metrizamide should be avoided in patients on phenothiazines since they may lower the seizure threshold.

Patients who drive or operate machinery should be warned of the possibility of drowsiness.

Use in pregnancy and lactation: Stelazine has been available since 1958, and there is no experimental or clinical evidence (including follow-up surveys in over 800 women who had taken low-dosage Stelazine during pregnancy) to suggest any associated hazard to the foetus. Nevertheless, drug treatment should be avoided in pregnancy unless essential, especially during the first trimester. Trifluoperazine passes into the milk of lactating dogs.

Adverse reactions: Lassitude, drowsiness, dizziness, transient restlessness, insomnia, dry mouth, blurred vision, muscular weakness, anorexia, mild hypotension and skin reactions may occasionally occur. Lactation and amenorrhoea are rare, tend to be dose-dependent, and may be related to increased secretion of prolactin.

Extrapyramidal symptoms are rare at daily dosages of 6 mg or less; they are considerably more common at higher dosage levels. These symptoms include parkinsonism; akathisia, with motor restlessness and difficulty

sitting still; and acute dystonia or dyskinesia, which may present with torticollis, facial grimacing, trismus, tongue protrusion and abnormal eye movements including oculogyric crises. Such reactions may often be controlled by reducing the dosage or by stopping medication. In more severe dystonic reactions, an anticholinergic antiparkinsonism drug should be given.

Tardive dyskinesia of the facial muscles, sometimes with involuntary movements of the extremities, has occurred in some patients on long-term high dosage and, more rarely, low-dosage phenothiazine therapy, including Stelazine. Symptoms may appear for the first time either during or after a course of treatment; they may become worse when treatment is stopped. The symptoms may persist for many months or even years, and while they gradually disappear in some patients, they appear to be permanent in others. Patients have most commonly been elderly, with organic brain damage. Particular caution should be observed in treating such patients. Gradual reduction of dosage to reveal persisting dyskinesia has been suggested, so that treatment may be topped if necessary. Anticholinergic antiparkinsonism agents have proved of little value in this syndrome.

Mild cholestatic jaundice, and blood dyscrasias such as agranulocytosis, pancytopenia, leucopenia and thrombocytopenia have been reported very rarely.

Very rare cases of skin pigmentation and lenticular opacities have been reported with Stelazine.

Overdosage: Signs and symptoms will be predominantly extrapyramidal; hypotension may occur. Absorption of trifluoperazine from the Spansule capsule is likely to be prolonged, and this should be borne in mind. Treatment consists of gastric lavage together with supportive and symptomatic measures. Do not induce vomiting. Extrapyramidal symptoms may be treated with an anticholinergic antiparkinsonism drug. Treat hypotension with fluid replacement; if severe or persistent, noradrenaline may be considered. Adrenaline is contra-indicated.

Pharmaceutical precautions Store tablets and spansule capsules in a cool, dry place, protect from light, and dispense in moisture-proof, light-resistant containers. Store Stelazine ampoules, syrup and concentrate in a cool place, and protect from light. When it is necessary to dilute the syrup, Syrup BP only should be used. The concentrate must be diluted before use, if possible with Syrup BP; this solution is stable for up to 2 weeks if kept in amber bottles in a cool place. Alternatively, dilute with water; this solution, however, is only stable for more than one week if a suitable preservative, such as 0.05% w/v sodium benzoate, is added. Diluents containing sodium salts of hydroxybenzoates should not be used as cloudiness may result.

Legal category POM.

Package quantities Tablets, 1 mg, in containers of 100 and 1,000. Tablets, 5 mg, in containers of 100, 500 and 5,000.

Spansule capsules, 2 mg, in containers of 30, 250 and 5,000. Spansule capsules, 10 mg and 15 mg, in containers of 100 and 5,000.

Syrup, in bottles containing 200 ml.

Concentrate, in bottles containing 100 ml and one litre.

Ampoules, each containing 1 ml, in boxes of 12.

Further information Nil.

Product licence numbers

Stelazine tablets, 1 mg

0002/5081

Stelazine tablets, 5 mg

0002/5082

Stelazine Spansule capsules, 2 mg

0002/5077

Stelazine Spansule capsules, 10 mg

0002/5078

Stelazine Spansule capsules, 15 mg

0002/5079

Stelazine syrup

0002/5080

Stelazine concentrate

0002/5076

Stelazine injection

0002/5075

TAGAMET* TABLETS

TAGAMET* SYRUP

TAGAMET* INJECTION

Presentation Pale green, circular, film-coated tablets, engraved TAGAMET on one side and SK&F 200 on reverse, containing 200 mg cimetidine.

Pale green, oblong, film-coated tablets, engraved TAGAMET on one side and SK&F 400 on reverse, containing 400 mg cimetidine.

A clear, orange-coloured, peach-flavoured syrup, each 5 ml dose containing 200 mg cimetidine.

Ampoules containing 200 mg cimetidine in 2 ml solution.

Uses Tagamet is a histamine H₂-receptor antagonist which inhibits both basal and stimulated gastric secretion of acid and reduces pepsin output.

Tagamet is indicated in the treatment of duodenal and benign gastric ulceration, recurrent and stomal ulceration, reflux oesophagitis and other conditions where reduction of gastric acid by Tagamet has been shown to be beneficial, i.e.: the prophylaxis of gastro-intestinal haemorrhage from stress ulceration in seriously ill patients; before general anaesthesia in patients thought to be at risk of acid aspiration (Mendelson's) syndrome, particularly obstetric patients during labour; and to reduce malabsorption and fluid loss in the short bowel syndrome. Tagamet is also recommended in the management of the Zollinger-Ellison syndrome.

Dosage and administration *Adults: Oral:* The usual dosage is 200 mg three times a day with meals and 400 mg at bedtime (1.0 g/day). In duodenal ulcer, 400 mg b.d., with breakfast and at bedtime, has also been shown to be effective.

If there is inadequate response, 400 mg four times a day (1.6 g/day) may be given, also with meals and at bedtime.

Treatment should be given initially for at least four weeks (six weeks in benign gastric ulcer) even if symptomatic relief has been achieved sooner.

Treatment may be continued for longer periods in those patients who may benefit from reduction of gastric secretion and the dosage may be reduced in those who have responded to treatment, for example to 400 mg at bedtime or 400 mg in the morning and at bedtime.

In patients with duodenal ulcer disease who have responded to the initial course, relapse may be prevented by continued treatment with 400 mg at bedtime or 400 mg in the morning and at bedtime for at least six months.

In reflux oesophagitis, 400 mg four times a day with meals and at bedtime for four to eight weeks is recommended.

In patients with very high gastric acid secretion (e.g. Zollinger-Ellison syndrome) it may be necessary to increase the dose to 400 mg four times a day, or in occasional cases to 2 g/day.

Antacids can be made available to all patients until symptoms disappear.

In the prophylaxis of haemorrhage from stress ulceration in seriously ill patients up to 2 g per day can be given in divided doses to maintain intragastric pH above 4.

In patients thought to be at risk of acid aspiration syndrome an oral dose of 400 mg can be given 90–120 minutes before induction of general anaesthesia. Up to this dose may be repeated (parenterally if appropriate) as required if operation is prolonged. Tagamet syrup should not be used. In obstetric patients during labour, an initial oral dose of 400 mg at the start of labour followed by 200 mg every two hours to a maximum of 1.6 g has been used. The usual precautions to avoid acid aspiration should be taken.

In the short bowel syndrome, e.g. following substantial resection for Crohn's disease, 1 g a day in divided doses, as above, can be used.

Parenteral: Tagamet may be given intramuscularly or intravenously.

The dose by intramuscular injection is normally 200 mg which may be repeated at four- to six-hourly intervals.

The dose by direct intravenous injection is normally 200 mg which should be given **slowly**, and may be repeated four- to six-hourly. If there is cardiovascular impairment, or if a larger dose is needed, the dose should be diluted and given over at least 10 minutes. In such cases infusion is preferable.

The dose by intermittent intravenous infusion is 100 mg/hour for two hours, repeated at four- to six-hourly intervals. The maximum infusion rate should not usually exceed 150 mg/hour (or 2 mg/kg body weight/hour). By continuous intravenous infusion an average rate of up to 75 mg/hour during 24 hours should suffice.

The total daily dose by any route should not normally exceed 2 g.

N.B. Dosage should be reduced in patients with impaired renal function (see *Cautions*).

Children: Experience with Tagamet in children is limited and it has not been evaluated in clinical studies (see **Further information**).

Contra-indications, warnings, etc No known contra-indications.

Cautions: Dosage should be reduced in patients with impaired renal function according to creatinine clearance. The following dosages are suggested: creatinine clearance of 0 to 15 ml per minute, 200 mg twice a day; 15 to 30 ml per minute, 200 mg three times a day; 30 to 50 ml per minute, 200 mg four times a day; over 50 ml per minute, normal dosage. Cimetidine is removed by haemodialysis.

Tagamet can prolong the elimination of drugs metabolised by oxidation in the liver. Pharmacological interactions with a number of drugs, e.g. diazepam, propranolol, have been demonstrated. Only those with oral anticoagulants and phenytoin appear, to date, to be of clinical significance. Close monitoring of patients on Tagamet receiving oral anticoagulants or phenytoin is recommended and a reduction in the dosage of these drugs may be necessary.

Clinical trials of over two year's continuous treatment and more than five years' widespread use have not revealed unexpected adverse reactions related to long-term therapy. The safety of prolonged use is not, however, established and care should be taken to observe periodically patients given prolonged treatment.

Before Tagamet treatment is commenced in gastric ulcer, malignancy should be excluded as treatment may alleviate symptoms and delay diagnosis.

In patients on drug treatment or with illnesses that could cause falls in blood cell count, the possibility that H_2 -receptor antagonism could potentiate this effect should be borne in mind.

Use in pregnancy and lactation: Although tests in animals have not revealed any hazards from the administration of Tagamet during pregnancy or lactation, both these and studies in women have shown that it does cross the placental barrier and is excreted in milk. As with most drugs, the use of Tagamet should be avoided during pregnancy and lactation unless essential.

Adverse reactions: Diarrhoea, dizziness or rash, usually mild and transient, and tiredness have been reported. Mild gynaecomastia appears to be a rare response. Biochemical or biopsy evidence of reversible liver damage has been reported occasionally. Reversible confusional states have also occurred, usually in elderly or already very ill patients (e.g. those with renal failure). Interstitial nephritis or acute pancreatitis, reversed or withdrawal of Tagamet, has been encountered very rarely. Isolated increases in plasma creatinine have been of no clinical significance.

Overdosage: Acute overdosage of up to 20 grams has been reported several times with no significant ill effects. Induction of vomiting and/or gastric lavage may be employed together with symptomatic and supportive therapy.

Pharmaceutical precautions Store syrup and ampoules in a cool place, and protect from light.

Legal category POM.

Package quantities Tablets, 200 mg, in containers of 500 and 5,000. Tablets, 400 mg, in calendar packs of 56 and in containers of 2,500. Syrup in bottles containing 200 ml. Ampoules in boxes of 10.

Further information Tagamet has been shown to be compatible with electrolyte and dextrose solutions commonly used for intravenous infusion.

Tagamet has not been evaluated in clinical trials in children. However, where inhibition of gastric acid secretion was considered essential, Tagamet in doses of 20 to 40 mg/kg/day was administered in divided doses by mouth or intravenously.

Product licence numbers

Tagamet injection	0002/0059
Tagamet tablets 200 mg	0002/0063
Tagamet tablets 400 mg	0002/0092
Tagamet syrup	0002/0073

VERTIGON* SPANSULE* CAPSULES

Presentation Clear, colourless capsules, opaque purple-capped and filled with a mixture of yellow-green and white pellets, in two strengths. Each Spansule sustained-release capsule, size No. 4, contains 10 mg, and each capsule, size No. 3, 15 mg prochlorperazine present as the maleate. Two-thirds of the dose is specially formulated for sustained release over a period of six to eight hours.

Uses Vertigon is a potent phenothiazine tranquilliser, anti-emetic, and vestibular sedative.

Vertigon Spansule capsules are indicated in the symptomatic treatment of vertigo due to Menière's

sease, labyrinthitis or other causes; nausea and vomiting associated with vertigo or other causes; and minor mental and emotional disturbances.

Dosage and administration *Adults and children aged 12 years and over:* Usually one 15 mg Vertigon spansule capsule once or twice a day. In less severe cases one 10 mg capsule once or twice a day may be adequate. When satisfactory control has been achieved, daily maintenance dosage of one 10 mg or 15 mg spansule may be given.

Contra-indications, warnings, etc

Contra-indications: Vertigon is contra-indicated in patients with existing blood dyscrasias or known liver damage.

Warnings: Caution should be exercised when treating elderly patients or those with cardiovascular disease because of the possibility of hypotension.

Nausea and vomiting as a sign of organic disease may be masked by the anti-emetic action of Vertigon.

Patients who drive or operate machinery should be warned of the possibility of drowsiness.

Use in pregnancy: Prochlorperazine has been available for many years, and there is no experimental or clinical evidence to suggest any associated hazard to the foetus. Nevertheless, drugs should be avoided in pregnancy unless essential, especially during the first trimester.

Adverse reactions: Drowsiness, dizziness, skin reactions, dry mouth and, rarely, hypotension may occur; effects such as amenorrhoea are extremely unusual at this dosage level.

Extrapyramidal reactions are very unlikely at the recommended dosage, but at the higher dosage levels used in psychiatry they are considerably more common. Prolonged, such dosage with phenothiazines may be

associated with skin pigmentation, and lenticular opacities. Tardive dyskinesia has occurred in some patients on long-term high-dosage and, more rarely, low-dosage phenothiazine therapy; this may be long-lasting or irreversible.

Rare cases of toxic hepatitis of a cholestatic type, and leucopenia and agranulocytosis have been reported with prochlorperazine.

Overdosage: Signs and symptoms will be predominantly extrapyramidal; hypotension may occur. Absorption of prochlorperazine from the sustained-release Spansule capsule is likely to be prolonged, and this should be borne in mind. Treatment consists of gastric lavage together with appropriate supportive and symptomatic measures. Do not induce vomiting. Extrapyramidal symptoms may be treated with an anticholinergic antiparkinsonism drug. Treat hypotension with fluid replacement; if severe or persistent, noradrenaline may be considered. Adrenaline is contra-indicated.

Pharmaceutical precautions Store in a cool, dry place, protect from light, and dispense in moisture-proof, light-resistant containers.

Legal category POM.

Package quantities Both strengths in containers of 100 Spansule capsules.

Further information Nil.

Product licence numbers

Vertigon Spansule capsules, 10 mg 0002/0036
Vertigon Spansule capsules, 15 mg 0002/0037

*Trade Mark

E. R. Squibb & Sons Limited
Squibb House
Staines Rd
Hounslow TW3 3JA



ADCORTYL* CREAM, OINTMENT, SPRAY AND ADCORTYL* IN ORABASE*

Presentation *Cream:* White cream containing triamcinolone acetonide 0.1% in an aqueous vanishing cream base.

Ointment: White, nearly translucent, containing triamcinolone acetonide 0.1% in Plastibase.*

Spray: Colourless, clear liquid containing triamcinolone acetonide 3.3 mg in 50 g vehicle.

Adcortyl in Orabase: White to light tan crystalline paste containing triamcinolone acetonide 0.1% in Orabase (gelatin, pectin and sodium carboxymethylcellulose in Plastibase*).

Uses *Actions:* Triamcinolone acetonide is a potent fluorinated corticosteroid with rapid anti-inflammatory, antipruritic and anti-allergic actions.

Indications: Adcortyl Cream, Ointment and Spray are recommended in steroid-responsive conditions which may include: atopic eczema, contact eczema, follicular eczema, infantile eczema, otitis externa, anogenital eczema (pruritus ani et vulvae), nummular eczema, seborrhoeic or flexural eczema, neurodermatitis, psoriasis, sunburn, insect bites.

Adcortyl in Orabase is indicated for aphthous ulcers, ulcerative stomatitis, denture stomatitis, desquamative gingivitis, erosive lichen planus and lesions of traumatic origin.

Dosage and administration *Adults and children:*

Cream: To be applied to moist weeping lesions two to four times daily.

Ointment: To be applied to dry scaly lesions two to four times daily.

Spray: To be applied two to four times daily. The canister should be shaken thoroughly and held 3 to 6 inches from the affected area.

Adcortyl in Orabase: To be applied to the lesion two to four times daily. Apply to the affected area; do not rub in.

Contra-indications, warnings, etc

Contra-indications: In tuberculous and most viral lesions of the skin, particularly herpes simplex, vaccinia, varicella. The products should not be used in fungal or bacterial skin infections without suitable concomitant anti-infective therapy.

Precautions: In infants, long-term continuous topical steroid therapy should be avoided. Adrenal suppression can occur, even without occlusion. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to humans has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

Side-effects: Triamcinolone acetonide is well tolerated. Signs of systemic toxicity such as oedema and electrolyte

imbalance have not been observed even when high topical dosage has been used.

Pharmaceutical precautions *Storage:*

Cream: At room temperature; avoid freezing.

Ointment: At room temperature.

Spray: In a cool place; normal aerosol precautions should be observed.

Adcortyl in Orabase: At room temperature.

Dilution: *Cream:* Cetomacrogol Cream (formula B) BPC Aqueous Cream BP is also suitable if the chlorocresol content is increased to 0.2%. Diluted creams should be stored below 25°C and should be discarded two weeks after dilution.

Ointment: White soft paraffin.

Adcortyl in Orabase: Should not be diluted. The manufacturer's advice should be sought before dilution with any other preparation.

Legal category POM.

Package quantities

Cream: Tubes of 30 g.

Ointment: Tubes of 30 g.

Aerosol Spray: Cans of 50 g.

Adcortyl in Orabase: Tubes of 10 g.

Further information Nil.

Product licence numbers

Adcortyl Cream 0034/5000

Adcortyl Ointment 0034/5004

Adcortyl Spray 0034/5007

Adcortyl in Orabase 0034/5006

**ADCORTYL*
INTRA-ARTICULAR/INTRADERMAL**

Presentation Sterile aqueous suspension containing triamcinolone acetonide 10 mg per ml.

Uses *Actions:* Triamcinolone acetonide is a synthetic glucocorticoid with marked anti-inflammatory and anti-allergic actions. Following local injection of Adcortyl relief of pain and swelling and greater freedom of movement are usually obtained within a few hours; such administration avoids the more severe systemic side-effects which may accompany parenteral or oral corticosteroid administration.

Indications: Intra-articular use: for alleviating the joint pain, swelling and stiffness associated with rheumatoid arthritis and osteoarthritis; also for acute and subacute bursitis, epicondylitis, tendinitis and acute, non-specific tenosynovitis.

Intradermal use: for localised hypertrophic inflammatory lesions which may include lichen simplex chronicus (neuro-dermatitis), psoriatic plaques, granuloma annulare, lichen planus, certain keloids and alopecia areata and alopecia totalis.

Dosage and administration Adcortyl injection is not for intra-venous use.

Adults: The dose of Adcortyl injection for intra-articular administration, and injection into tendon sheaths and bursae, is dependent on the size of the joint to be treated and on the severity of the condition. Doses of 2.5-5 mg (0.25-0.5 ml) for smaller joints and 5-15 mg (0.5-1.5 ml) for larger joints usually alleviate the symptoms. Intradermal dosage is usually 2-3 mg (0.2-0.3 ml), depending on the size of the lesion. No more than 5 mg (0.5 ml) should be injected at any one site. If several sites are injected the total dosage administered should not exceed 30 mg (3 ml). The injection may be repeated if necessary, at one or two week intervals.

B. Strict aseptic precautions should be observed.

Children: Adcortyl intra-articular/intradermal may be used in children in suitable adjusted dosages.

Contra-indications, warnings, etc

Contra-indications: In the presence of active infection or near joints or dermatological lesions to be treated. The preparation should not be used to alleviate joint pain arising from infectious states such as gonococcal or bacterial arthritis.

Precautions: Following intra-articular steroid therapy, patients should be specifically warned to avoid over use of joints in which symptomatic benefit has been obtained. Severe joint destruction with necrosis of bone may occur following repeated intra-articular injections are given over a long period of time. Care should be taken where injections are given into tendon sheaths to avoid injection into the tendon itself.

Due to the absence of a true tendon sheath, the chilles tendon should not be injected with depot corticosteroids.

In pregnant animals, systemic administration of corticosteroids can cause abnormalities of foetal development. The relevance to humans of this finding has not been established.

Side-effects: Reactions following intra-articular administration have been rare. In a few instances transient flushing and dizziness have occurred. Pain and other local symptoms may continue for a short time before effective relief is obtained, but an increase in joint discomfort has seldom occurred. Local atrophy sometimes occurs, but is temporary and disappears within a few weeks to months.

The possibility of the systemic effects which are associated with all steroid therapy should be considered.

Pharmaceutical precautions *Storage:* In an upright position at room temperature: avoid freezing.

Legal category POM.

Package quantities Multidose vials of 5 ml, 5 x 1 ml ampoules.

Further information Nil.

Product licence number 0034/5002.

ADCORTYL* TABLETS

Presentation White tablets containing 4 mg triamcinolone, scored one side and engraved Squibb and 512 in reverse.

Uses *Actions:* Triamcinolone is a potent corticosteroid with marked anti-inflammatory and anti-allergic actions.

Triamcinolone induces few of the gastro-intestinal disturbances of other glucocorticoids, causes little undesirable psychic stimulation, and does not normally give rise to sodium and water retention even with prolonged administration. Triamcinolone persists in the blood for a longer time than other related steroids.

Indications: Adcortyl tablets are indicated in steroid responsive conditions, and where anti-inflammatory and anti-allergic treatment is required.

Dosage and administration *Adult dosage:* The usual daily dose of Adcortyl tablets is 8-24 mg orally in divided doses. Once a satisfactory response is obtained, the dose is gradually reduced to 2-4 mg every two or three days until an optimum maintenance level is reached. In certain cases symptomatic relief may be maintained with the total dosage of the steroid given once daily or on alternate days. This regimen reduces the risk of adrenal suppression and has much to recommend it, where applicable. The dosages suggested here are merely intended as a guide to specific treatment and have been derived from clinical experience.

The table at the top of the next page gives detailed dosage recommendations.

Contra-indications, warnings, etc

Contra-indications: In latent or healed tuberculosis; in the presence of local or systemic viral infection; in acute psychoses and in patients with an active peptic ulcer; in acute glomerulonephritis and in active infections not controlled by antibiotics.

Corticosteroids are not indicated for patients with myasthenia gravis, diverticulitis, recent intestinal anastomoses, thrombophlebitis, psychotic tendencies, exanthematous disease, chronic nephritis, metastatic carcinoma, osteoporosis, and a history of peptic ulcer. In the presence of any of these conditions, the need for corticosteroid therapy must be carefully weighed against possible deleterious effects.

Precautions: The usual early unwanted corticosteroid effects, such as increase in weight, oedema and hypertension, generally do not occur with triamcinolone, but, as with other potent corticosteroids, clinical supervision is necessary.

During prolonged therapy a liberal protein intake is essential to counteract the tendency to gradual weight loss sometimes associated with negative nitrogen balance and wasting of skeletal muscle.

Corticosteroids are not recommended for pregnant patients, particularly in the first trimester, except when the disease for which they are indicated warrants their use. Hypo-adrenalism may occur in the newborn of mothers receiving corticosteroid therapy.

Diabetes may be aggravated, necessitating a higher insulin dosage. Latent diabetes mellitus may be precipitated.

Menstrual irregularities may occur, and this possibility should be mentioned to female patients.

Patients on long-term systemic therapy with triamcinolone may require supportive corticosteroid therapy in times of stress (such as trauma, surgery or severe illness) both during the treatment period and for a year afterwards.

Side-effects: Unwanted effects which may be associated with systemic corticosteroid therapy include: Cushingoid changes or other signs of fat deposition; weakness, bruising or purpura; striae; osteoporosis; spontaneous fractures; sweating or flushing of the face; thrombo-

<i>Condition</i>	<i>Initial daily dose</i>	<i>Maintenance daily dosage</i>
Rheumatoid arthritis	Adults [1] and children: 4-12 mg	Adults: lowest adequate dose Children: individualised
Rheumatic fever (acute)	In divided doses Adults: 16-20 mg Children: 8-10 mg	Adults and children: gradually reduce discontinue
Allergic disorders	Adults [2]: 8-16 mg Children: 4-8 mg	Adults: 4-16 mg Children: 2 mg or less
Bronchial asthma	Adults [2]: 8-16 mg Children: 8-12 mg	Adults: 2-8 mg Children: 1-4 mg
Dermatoses [3]	Adults [2]: 8-20 mg Children: 4-12 mg	Adults and children: 2 mg or less
Psoriasis [4] acute exacerbations	Adults: 4-32 mg (advocated for short-term control only)	Adults: 1-16 mg
Angioneurotic oedema	Adults: 8-16 mg	Adults gradually reduce
Nephrotic syndrome	Adults and children: 20-48 mg until diuresis (usually within 7- 10 days)	Adults and children: intermittent therapy 8-16 mg for three consecutive days per week
Pulmonary emphysema: pulmonary fibrosis [5]	Adults: 8-32 mg	Adults: 1-4 mg
Lymphomatous diseases; chronic leukaemia	Adults and children: 32-60 mg	Adults and children: 2-24 mg
Acute lymphatic leukaemia	Children: 1 mg/kg body weight	Same as initial dose
Systemic lupus erythematosus; other collagen diseases	Adults and children: 20-32 mg	Adults and children: 4-20 mg
Acute connective tissue diseases (acute bursitis, myositis, fibrositis, etc)	Adults [2]: 8-16 mg	Adults: 1-8 mg
Uveitis	Adults: 24-32 mg	Adults: gradually reduce
Sprue	Adults: 12-24 mg Children: 3 mg or more	Adults and children: gradually reduce
Urticaria	Adults [2] and children: 12-20 mg for five days	

Adcortyl tablets are suitable for administration to children; dosage should be adjusted according to total body area, body weight and severity of the condition.

1. A single daily dosage regimen may be tried. If response is unsatisfactory, daily dosage should be given in divided amounts.
2. Single daily doses have been effectively employed.
3. For some chronic dermatoses, an alternate-day dosage regimen, using doses equivalent to daily dosage, may be effective. Severe pemphigus requires high initial doses, even up to 100 mg daily in divided doses.
4. Potent systemic steroids are not recommended for mild, uncomplicated psoriasis. Psoriasis recurs when medication is discontinued and may be more severe due to a rebound phenomenon.
5. Appropriate antibiotic therapy must be given simultaneously.

embolism; necrotising angitis; acute pancreatitis; ulcerative oesophagitis; activation or aggravation of peptic ulcer or other gastro-intestinal upsets; oedema; hypertension; hirsutism; acneiform eruptions; vertigo; headache; or severe mental disturbances. Increased intracranial pressure, papilloedema and posterior subcapsular cataracts have also been associated with prolonged corticosteroid administration.

Where adverse reactions occur they are usually reversible following cessation of therapy.

Overdosage: Careful monitoring of serum electrolytes should be undertaken. Patients should be slowly weaned off the high dose by giving reducing quantities of Adcortyl tablets over a period of one to three weeks.

Pharmaceutical precautions *Storage:* At room temperature.

Legal category POM.

Package quantities Bottles of 100.

Further information Nil.

Product licence number 0034/5009

ADCORTYL[®] WITH GRANEODIN[®] CREAM, AND OINTMENT

Presentation *Cream:* White vanishing cream.

Ointment: Smooth, soft, translucent ointment.

Each gram of the cream and ointment contains:

Triamcinolone acetonide	0.1%
Neomycin (as sulphate)	0.25%
Gramicidin	0.025%

Uses *Actions:* Triamcinolone acetonide is a potent fluorinated corticosteroid with rapid anti-inflammatory antipruritic and anti-allergic actions.

The combined action of the antibiotics neomycin and gramicidin provides comprehensive antibacterial therapy against a wide range of Gram-positive and Gram

gative bacteria, including those micro-organisms responsible for most bacterial skin infections.

Indications: For the treatment of inflammatory dermatoses, which are complicated or threatened by secondary infection such as: atopic eczema, contact eczema, follicular eczema, infantile eczema, otitis externa, anogenital pruritus (pruritus ani et vulvae), psoriasis, nummular eczema, post-traumatic infective eczema, seborrheic or flexural eczema, neurodermatitis.

Dosage and administration *Adults and children:* Apply to the affected areas two to four times daily.

Intra-indications, warnings, etc

Intra-indications: In tuberculosis and most fungal and all lesions of the skin, particularly herpes simplex, eczema and varicella. Also in the treatment of deep-seated bacterial infections.

Precautions: The use of occlusive dressings should be avoided because of the increased risk of sensitivity reactions. In infants, long-term continuous topical steroid therapy should be avoided. Adrenal suppression can occur, even without occlusion. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to humans has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

Side-effects: Sensitivity reactions to neomycin may occur especially with prolonged use. Gramicidin sensitivity has occasionally been reported.

Pharmaceutical precautions *Storage: Cream:* At room temperature; avoid freezing.

Ointment: At room temperature.

Contraindication: Not recommended, as this would reduce the concentration of the antibiotics to below therapeutic levels.

Legal category POM.

Packaging quantities *Cream/Ointment:* 15 g tubes

Further information Nil.

Product licence numbers

Capoten with Graneodin Cream	0034/5015
Capoten with Graneodin Ointment	0034/5017

APOTEN* TABLETS ▼

Presentation *Capoten tablets 25 mg:* Slightly mottled, white, square biconvex tablets each containing captopril 25 mg. Engraved with 'Squibb' and '452' on one side and with quadrisection bars (for identification only) on the other.

Capoten tablets 50 mg: Slightly mottled, white, oval, convex tablets each containing captopril 50 mg. Engraved with 'Squibb' and '482' on one side with a section bar on the other.

Capoten tablets 100 mg: Slightly mottled, white, oval, convex tablets each containing captopril 100 mg. Engraved with 'Squibb' and '485' on one side with a section bar on the other.

Uses **Actions:** Captopril 1-[(2S)-3-mercapto-2-ethyl-propionyl]-L-proline is a highly specific competitive inhibitor of angiotensin I-converting enzyme, the enzyme responsible for the conversion of angiotensinogen to angiotensin II.

Its mechanism of action in hypertension has not yet been fully elucidated; however, it appears to lower blood pressure primarily through suppression of the renin-angiotensin-aldosterone system.

Until further experience has been obtained in the treatment of acute hypertensive crises, the use of Capoten should be avoided in these patients.

It has also been shown to be of benefit in the management of severe, treatment-refractory congestive heart failure.

Indications: *Hypertension:* The treatment of severe hypertension where standard therapy has failed.

Congestive heart failure: Captopril is indicated for the treatment of severe, treatment-refractory congestive heart failure. The drug should be used together with diuretics and digitalis, but only after these agents have failed to produce a satisfactory response.

Dosage and administration *Recommended dose and dosage schedule:* Capoten (captopril) should be taken one hour before meals.

Adults: Hypertension: The usual dose of Capoten is 25-50 mg t.i.d.

The initial daily dose of Capoten is 25 mg t.i.d. which should be increased to 50 mg t.i.d. if a satisfactory reduction of blood pressure has not been achieved in two weeks. If a patient is not receiving a diuretic and a satisfactory response has not been achieved after a further two weeks a modest dose of a thiazide diuretic (hydrochlorothiazide) or in patients with impaired renal function a loop diuretic (frusemide) should be added. The diuretic should be increased at one to two week intervals until a satisfactory response is obtained or its maximal antihypertensive dose is reached.

Should Capoten 50 mg t.i.d. together with the diuretic fail to give a satisfactory reduction in blood pressure, then Capoten should be increased to 100 mg t.i.d., and then, if necessary, 150 mg t.i.d. A maximum daily dose of 450 mg Capoten should not be exceeded.

For patients with accelerated or malignant hypertension who are unresponsive to conventional therapy, it may be necessary to increase the daily dose of Capoten (captopril) every 24 hours, until a satisfactory blood pressure response is obtained or the maximum dose of Capoten is reached.

When Capoten (captopril) is used alone, concomitant sodium restriction may be advantageous. Capoten may be used in conjunction with other antihypertensive agents, particularly thiazide diuretics and beta-blockers.

For some patients on multiple antihypertensive agents, there may be clinical reasons for which it would be impractical to discontinue all antihypertensive therapy prior to starting Capoten. Recognising that Capoten would usually be used in combination with a thiazide diuretic, the patient may have Capoten 25 mg t.i.d. initiated under close medical supervision while continuing diuretic therapy. Other currently administered antihypertensive agents should be discontinued according to the instructions of the manufacturer.

Heart failure: Capoten therapy must be started under close medical supervision. The usual starting dose is 25 mg t.i.d. A starting dose of 6.25 or 12.5 mg t.i.d. may minimise a transient hypotensive effect. After a dose of 50 mg t.i.d. is reached, further increases in dosage should be delayed where possible, for at least two weeks to determine if a satisfactory response occurs.

Capoten should be used in conjunction with a diuretic and where appropriate digitalis. A maximum daily dose of 450 mg should not be exceeded.

Patients with renal impairment: An average of about 75% of a given daily dose of captopril is usually excreted in the urine; captopril retention occurs in the presence of impaired renal function. After the desired therapeutic effect has been achieved, the total daily dose should be reduced or the dose intervals increased. The following maximum daily doses are suggested as a guide to minimise drug accumulation.

<i>Creatinine Clearance (ml/min/1.73m²)</i>	<i>Maximum Total Daily Dose (mg)</i>
> 80	450
80-41	300
40-21	150
20-11	75
< 10	37.5

When concomitant diuretic therapy is required, a loop diuretic (e.g. frusemide) is preferable to a thiazide diuretic.

Children: Safety and effectiveness in children have not been established. Capoten (captopril) should be used only if the potential benefit justifies the risk.

Starting dose should be 0.3 mg per Kg bodyweight up to a maximum of 6 mg per Kg bodyweight divided into three doses per day.

Contra-indications, warnings, etc

Contra-indications: A history of previous hypersensitivity to captopril.

Warnings: NEUTROPENIA/AGRANULOCYTOSIS and PROTEINURIA have been reported in patients receiving captopril.

Neutropenia/Agranulocytosis: Although neutropenia has occurred in patients receiving Capoten, it usually was found in those with impaired renal function, connective tissue disease, while under treatment with immuno-suppressant drugs, or combinations of these. Systemic lupus erythematosus (SLE) and other autoimmune/collagen disorders were present in one-third of these patients and almost all had renal impairment. In patients with normal renal function neutropenia rarely occurred. In patients with impaired renal function the incidence of neutropenia was approximately 1.1% and the daily dose of Capoten in these patients was relatively high. The median time of onset of neutropenia was approximately seven weeks after starting Capoten therapy (range 2½ to 13 weeks). The neutropenia sometimes was associated with significant alterations in red blood cell or platelet counts. Serious infections resulting from the neutropenia occurred only in patients with impaired renal function.

Bone marrow examinations of patients with neutropenia consistently showed myeloid hypoplasia, frequently accompanied by erythroid hypoplasia and decreased numbers of megakaryocytes.

Capoten should be used with caution in patients with impaired renal function or with connective tissue disease, particularly SLE, and in patients concurrently receiving drugs known to affect the white cells or immune response. White blood cell and differential counts should be performed on these patients before starting treatment and every two weeks during the first three months of therapy and periodically thereafter.

All patients treated with Capoten should be told to report any signs of infection (e.g. sore throat, fever). A complete white blood count should be done immediately when such a report is made and if this occurs during the

first three months of therapy, Capoten should be withdrawn until the results of the blood count are known.

Upon any sign of neutropenia (a neutrophil count 1,000/mm³) the physician should withdraw Capoten and other drugs, and follow the patient's course. Capoten is responsible for the neutropenia, the white count generally returns to normal within several weeks after discontinuing the drug.

Proteinuria: Proteinuria of greater than 1 g per day was seen in 1.2% of patients receiving captopril, and two-thirds of affected patients had evidence of prior renal disease. Nephrotic syndrome occurred in about one-quarter of these cases. Membranous glomerulopathy was found in some patients who had renal biopsy. It is not known whether this might have pre-existed and it is recognised that membranous glomerulopathy can occur in patients with hypertension. In most cases proteinuria occurred by the eighth month of therapy and subsided or cleared within six months whether or not captopril was continued, while some patients had persistent proteinuria. Parameters of renal function, such as BUN and creatinine, were seldom altered in the patients who developed proteinuria.

It is recommended that patients have urinary protein estimations (dip stick) prior to treatment, subsequent at monthly intervals during the first eight months, and periodically thereafter. For patients who develop persistent or increasing significant proteinuria, a 24-hour quantitative determination should be obtained, and this exceeds 1 g/day, the benefits and risks of continuing Capoten should be evaluated.

Hypotension: Although most patients tolerate Capoten well, those already on diuretic therapy may occasionally experience dizziness or lightheadedness, usually mild and indicative of hypotension, that may occur within one hour of the first dose. In most instances, symptoms are relieved simply by instructing the patient to lie down.

In patients who are receiving aggressive diuretic therapy, particularly those with either severe and renal dependent hypertension (e.g. renovascular hypertension) or severe congestive heart failure, exaggerated hypotensive responses have occurred, again usually within one hour of the initial dose of captopril. In these patients, by discontinuing diuretic therapy or significantly reducing the diuretic dose for four to seven days prior to initiating captopril the possibility of this occurrence is lessened. By commencing captopril therapy with small doses (6.25 or 12.5 mg) the duration of any hypotensive effect is reduced.

The exaggerated hypotensive response can be anticipated by medical supervision during the first hour after initial dosing; and if appropriate it can be reversed by intravenous infusion of normal saline.

The occurrence of first dose hypotension does not preclude subsequent dose titration with captopril.

Patients treated for severe congestive heart failure should be warned to increase their physical activity slowly.

Serum potassium: Since Capoten decreases aldosterone production, elevation of serum potassium may occur especially in patients with renal failure. Potassium sparing diuretics or potassium supplements, if needed, should be used with caution, since they may lead to a significant increase in serum potassium.

Changes in renal function: Some patients with renal disease, particularly those with renal artery stenosis, have developed increased concentrations of blood urea

tion of blood pressure
h a diuretic. Capoten
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is Store at room

Legal category POM.

Package quantities In bottles of 100.

Further information Capoten, as with any drug that reduces vascular resistance should not be used in patients with aortic stenosis because of the potentially harmful consequences of reduced coronary perfusion secondary to the reduced blood pressure.

Product licence numbers

Capoten tablets 25 mg 0034/0193.
Capoten tablets 50 mg 0034/0194.
Capoten tablets 100 mg 0034/0195.

CORGARD* TABLETS ▼

Presentation Mottled white, round, biconvex tablets. The 80 mg nadolol tablet is scored on one side and engraved Squibb with 241 while the 40 mg nadolol tablet is unscored with Squibb and 207 engraved on one side.

Uses *Actions:* Nadolol is a beta-adrenergic receptor blocking agent with a prolonged activity, permitting once-daily dosage in both angina and hypertension.

Nadolol is not metabolised. It has no membrane stabilising or intrinsic sympathomimetic activity, and its only effect on the autonomic nervous system is one of beta-adrenergic blockade.

Receptor blockade by nadolol results in protection from excessive or inappropriate sympathetic activity. Nadolol reduces the number and severity of attacks of angina pectoris by blocking response to catecholamine stimulation and thus lowers the oxygen requirement of the heart at any given level of effort.

Nadolol reduces both supine and erect blood pressure. The mechanisms by which beta-blockade lowers blood pressure have not been fully elucidated. Like other beta-blockers, nadolol exerts an antiarrhythmic action.

Indications: Corgard is indicated in the management of:

Angina pectoris: For the long-term management of patients with angina pectoris by continuous medication.

Hypertension: for the long-term management of essential hypertension, either alone or in combination with other antihypertensive agents.

Dosage and administration In both angina pectoris and hypertension the dosage should be titrated gradually with at least a week between increments to assess response. In elderly patients, particularly those with angina pectoris, a low initial dose should be used so that sensitivity to side-effects may be assessed; individuals show considerable variation in their response to beta-adrenergic blockade.

Angina pectoris: Initially 40 mg once daily. This may be increased at weekly intervals until an adequate response is obtained or excessive bradycardia occurs. Most patients respond to 160 mg or less daily. The value and safety of daily doses exceeding 240 mg have not been established.

If nadolol is to be discontinued, reduce dosage over a period of at least two weeks (*see Warnings*).

Hypertension: Initially 80 mg once daily. This may be increased by a weekly increment of 80 mg or less until an optimum response is obtained. Most patients respond to 240 mg or less, daily, but doses up to 640 mg have been required for a few patients. In some patients it is

necessary to administer a diuretic, peripheral vasodilator and/or other antihypertensive agents in conjunction with nadolol in order to achieve satisfactory response.

Treatment of hypertension associated with phaeochromocytoma may require the addition of an alpha-blocking agent.

Nadolol may be given in a once daily dosage without regard to meals.

The dosage interval should be increased when creatinine clearance is below 50 ml/min/1.73m².

Contra-indications, warnings, etc

Contra-indications: Like other drugs in this class, nadolol is contra-indicated in bronchial asthma; sinus bradycardia and 2nd and 3rd degree heart block; cardiogenic shock; right ventricular failure secondary to pulmonary hypertension; congestive heart failure.

Warnings: Exacerbation of angina and myocardial infarction have occurred after abrupt discontinuation of therapy with beta-adrenergic blocking agents in patients with angina pectoris or other evidence of coronary artery insufficiency. When discontinuing long-term treatment with nadolol, the dosage should be reduced gradually over a period of at least two weeks and the patient carefully monitored.

Beta-adrenergic blockade carries the potential hazard of precipitating cardiac failure. Should this occur and it is not controlled by digitalisation, nadolol should be withdrawn, consideration being given to the foregoing warning.

Beta-blockade impairs the ability of the heart to respond to stress. It has been the usual practice to recommend withdrawal of beta-blockers several days prior to surgery (except for phaeochromocytoma). However, this may render the patient's blood pressure unstable and difficult to control during anaesthesia and the anaesthetist may wish to advise on discontinuation of therapy. In the event of emergency surgery, the effects of nadolol may be reversed by isoprenaline or noradrenaline. However, such patients may be subject to protracted severe hypotension. General anaesthetics which can cause myocardial depression, such as cyclopropane, trichloroethylene, chloroform and ether, should be avoided if nadolol is continued during surgery.

Nadolol should be administered with caution to patients with chronic obstructive airways disease.

Care should be exercised in the administration of nadolol to diabetic patients since early signs of acute hypoglycaemia may be masked. It may also be necessary to adjust the dosage of hypoglycaemic drugs.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when the treatment was withdrawn. Discontinuance of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-adrenergic blocker should be gradual.

The safety of nadolol in pregnancy has not yet been established. Nadolol is excreted in human milk, therefore nursing mothers should only receive nadolol if deemed essential.

Precautions: Close observation of patients receiving catecholamine depleting drugs, such as reserpine, in combination with nadolol is advised, since an excessive reduction in sympathetic drive to the heart might occur.

Occasionally, beta-blockade with drugs such as nadolol may produce hypotension and/or marked brady-

cardia, resulting in vertigo, syncope or orthostatic hypotension.

As with any new drugs given for long period laboratory examinations should be carried out intervals.

Care should be taken in administering nadolol during and within two weeks of administration of adrenergic augmenting psychotropic drugs such as monoamine oxidase inhibitors.

Nadolol should be used with caution in patients with impaired renal or hepatic function.

Administration in renal failure: In patients with decreased renal function, dosage adjustment is necessary. The recommended dosage intervals are:

Creatinine Clearance (ml/min/1.73 m ²)	Dosage Interval (Hours)
< 10	40-60
10-30	24-48
31-50	24-36
> 50	24

Side-effects: Most patients tolerate nadolol well. Side effects resemble those reported with other beta-blocking drugs and rarely require withdrawal of treatment. Those reported infrequently include gastro-intestinal effects: bradycardia, fatigue, light-headedness, cold extremities, insomnia, paraesthesia and dryness of the mouth. Cardiac insufficiency, hypotension and AV block have occurred on rare occasions.

Overdosage or exaggerated response: Excessive bradycardia should be treated initially with atropine. If there is no response, isoprenaline may be administered with caution.

Cardiac failure should be managed by digitalisation and diuretics. Glucagon has also been reported to be useful.

Hypotension may be managed with vasopressors such as adrenaline.

Bronchospasm may be counteracted by isoprenaline and aminophylline.

Pharmaceutical precautions Store at room temperature, protected from excessive heat and moisture in tightly closed container.

Legal category POM.

Package quantities Bottles of 100 tablets.

Further information Nadolol has been reported to increase renal blood flow, especially through the cortical nephrons.

Nadolol has negligible lipid solubility.

Product licence numbers

80 mg 0034/0186

40 mg 0034/0185

CORGARETIC* TABLETS ▼

Presentation White, blue-speckled, round, biconvex tablets, in two strengths.

Corgaretic 40: nadolol 40 mg with bendrofluazide 5 n is engraved 'Squibb' and '283' on one side with a bisect bar on the other.

Corgaretic 80: nadolol 80 mg with bendrofluazide 5 n is engraved 'Squibb' and '284' on one side with a bisect bar on the other.

es Actions: Nadolol is a beta-adrenergic receptor blocking agent with a prolonged activity, permitting once-daily dosage.

Nadolol is not metabolised. It has no membrane blocking or intrinsic sympathomimetic activity, and its effect on the autonomic nervous system is one of alpha-adrenergic blockade.

Receptor blockade by nadolol results in protection from excessive or inappropriate sympathetic activity.

Nadolol reduces both supine and erect blood pressure. The mechanisms by which beta-blockade lowers blood pressure have not been fully elucidated.

Bendroflumazide is a thiazide diuretic which interferes with renal tubular electrolyte reabsorption, thereby increasing sodium and water excretion.

ications: For the treatment of hypertension. The combination of a diuretic and a beta-blocker may be of particular value in patients whose blood pressure has not been adequately controlled with either component given alone.

Usage and administration *Dose of Corgaretic:* One to two tablets once daily to a maximum of 160 mg nadolol and 10 mg bendroflumazide. For doses of nadolol in excess of 160 mg, the combination product may not be appropriate because an excessive dose of the thiazide component may be administered.

The dosage should be titrated gradually with at least one week between increments to assess response.

Bendroflumazide is usually given at a dose of 5 to 10 mg per day. The initial dose of nadolol is 40 to 80 mg daily; this may be increased by weekly increments of 40 to 80 mg until an optimum response is obtained.

Treatment of hypertension associated with pheochromocytoma may require the addition of an alpha-blocking agent.

Nadolol may be given in a once-daily dosage without regard to meals.

The dosage interval should be increased when creatinine clearance is below 50 ml/min/1.73 m²:

<i>Creatinine Clearance (ml/min/1.73 m²)</i>	<i>Dosage Interval (Hours)</i>
> 50	24
31-50	24-36
10-30	24-48
< 10	40-60

Contra-indications, warnings, etc *Corgaretic is*

contra-indicated: In bronchial asthma, sinus bradycardia, 2nd or 3rd degree heart block, cardiogenic shock, left ventricular failure secondary to pulmonary hypertension, congestive heart failure, anuria, past sensitivity to thiazide diuretics.

warnings: Abrupt withdrawal of beta-blockers from patients with ischaemic heart disease can exacerbate angina and myocardial infarctions. When discontinuing therapy, the dosage should be reduced gradually over at least two weeks and the patient carefully monitored.

Cardiac failure: Beta-blockers carry the risk of potentiating cardiac failure. Should this occur and is not controlled by digitalisation, nadolol should be withdrawn slowly (see above warning).

Anaesthesia: Beta-blockade impairs the ability of the heart to respond to stress. It has been the usual practice to recommend withdrawal of beta-blockers several days or to surgery (except for pheochromocytoma). However, this may render the patient's blood pressure stable and difficult to control during anaesthesia and

the anaesthetist may wish to advise on discontinuation of therapy. In the event of emergency surgery, the effects of nadolol may be reversed by isoprenaline or noradrenaline. However, such patients may be subject to protracted severe hypotension. General anaesthetics which can cause myocardial depression, such as cyclopropane, trichloroethylene, chloroform and ether, should be avoided if nadolol is continued during surgery.

Thiazides may decrease the arterial responsiveness to noradrenaline. In emergency surgery, pre-anaesthetic and anaesthetic agents should be administered in reduced dosage.

Chronic obstructive airways disease: Nadolol should be administered with caution.

Diabetes and hypoglycaemia: Diabetic patients should be monitored closely as nadolol may mask the early signs of acute hypoglycaemia, and thiazide diuretics can lower insulin tolerance. Therefore, dosages of hypoglycaemic drugs or insulin doses may need adjustment.

Skin rashes and dry eyes: There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when the treatment was withdrawn. Discontinuation of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-adrenergic blocker should be gradual.

Use in pregnancy: Both nadolol and bendroflumazide cross the placental barrier and are excreted in breast milk. Therefore, as safety in pregnancy or lactation has not been established, and animal studies have shown some foetotoxicity, Corgaretic is not considered suitable for pregnant patients or nursing mothers.

Precautions: Close observation of patients receiving catecholamine-depleting drugs, such as reserpine, in combination with nadolol is advised, since an excessive reduction in sympathetic drive to the heart might occur.

Occasionally, beta-blockade with drugs such as nadolol may produce hypotension and/or marked bradycardia, resulting in vertigo, syncope or orthostatic hypotension.

As with any new drugs given for long periods, laboratory examinations should be carried out at intervals.

Nadolol and bendroflumazide should be used with caution in patients with impaired renal or hepatic function.

Care should be taken in administering nadolol during and within two weeks of administration of adrenergic augmenting psychotropic drugs such as monoamine oxidase inhibitors.

Periodic determination of serum electrolytes to detect possible imbalance, e.g. hyponatraemia, hypochloric alkalosis and hypokalaemia, should be performed at regular intervals.

The possibility that thiazides may exacerbate or activate systemic lupus erythematosus has been reported.

Potassium depletion is a danger to digitalised patients or those with hepatic cirrhosis with ascites.

Thiazide diuretics may raise serum uric acid levels, thus exacerbating gout in susceptible patients.

Side-effects: Most patients tolerate nadolol well. Side-effects resemble those reported with other beta-blocking drugs and rarely require withdrawal of treatment. Those reported infrequently include gastro-intestinal effects,

bradycardia, fatigue, light-headedness, cold extremities, insomnia, paraesthesia and dryness of the mouth. Cardiac insufficiency, hypotension and AV block have occurred on rare occasions.

Adverse effects to bendrofluazide are uncommon at low dosage. Hypokalaemia may occur, particularly in patients with renal or hepatic impairment, and usually manifests as muscle weakness. Potassium depletion is particularly dangerous in digitalised patients. Coma may be precipitated in hepatic cirrhosis. Other reported adverse reactions include hyperuricaemia, hyperglycaemia, gastro-intestinal upset, jaundice, pancreatitis, blood dyscrasias and skin rashes associated with photosensitivity.

Overdosage or Exaggerated Response: Excessive bradycardia should be treated initially with atropine. If there is no response, isoprenaline may be administered with caution. Cardiac failure should be managed by digitalisation and diuretics. Hypotension may be managed with vasopressors such as adrenaline. Bronchospasm may be counteracted by isoprenaline and aminophylline.

Pharmaceutical precautions Store at room temperature, protected from excessive heat and moisture in a tightly closed container.

Legal category POM.

Package quantities Bottles of 100 tablets.

Further information Corgaretic tablets simplify the treatment of hypertension by increasing patient acceptability and dosage flexibility. The two available strengths allow increasing the dose of the beta-blocker nadolol, without necessarily increasing the bendrofluazide dosage.

Nadolol has been reported to increase renal blood flow especially through the cortical nephrons.

Nadolol has negligible lipid solubility.

Product licence numbers

Corgaretic 40 0034/0212

Corgaretic 80 0034/0213

FLORINEF* TABLETS

Presentation *Tablets 0.1 mg:* Round, pale pink tablets, scored on one side and engraved Squibb and 429 on reverse, containing 0.1 mg fludrocortisone acetate.

Tablets 1 mg: Round, pink tablets, scored on one side and engraved Squibb on the reverse, containing 1 mg fludrocortisone acetate.

Uses *Actions:* Qualitatively, the physiological action of fludrocortisone acetate is similar to hydrocortisone. In very small doses, fludrocortisone maintains life in adrenalectomised animals, enhances the deposition of liver glycogen and produces thymic involution, eosinopenia, retention of sodium and increased urinary excretion of potassium.

Indications: The treatment of Addison's disease and adrenal hyperplasia.

Dosage and administration *Adult dosage—Addison's disease:* A daily dosage range of 0.1–0.3 mg Florinef tablets orally produces satisfactory salt retention in patients with Addison's disease. Supplementary parenteral administration of sodium-retaining hormones is not

necessary. When an enhanced glucocorticoid effect is desirable, cortisone or hydrocortisone by mouth should be given concomitantly with Florinef tablets; the suggested daily oral dosage range for cortisone is 6.2–25 mg, and for hydrocortisone, 5–20 mg.

Adrenal hyperplasia: Satisfactory long-term inhibition of endogenous adrenal cortical secretion has been achieved with daily doses of 1 mg or 2 mg of Florinef tablets orally. This dosage range has been found to maintain the 17-ketosteroid excretion at or near normal levels. Since Florinef tablets may have an intense mineralocorticoid activity, it may be necessary to administer concomitantly potassium chloride. Restriction of dietary sodium intake may be required to prevent excessive salt and water retention.

Children: May be used adjusted to the age and weight of the child according to the severity of the condition.

Contra-indications, warnings, etc

Contra-indications: In latent or healed tuberculosis; the presence of local or systemic viral infection; in acute psychoses and in patients with an active peptic ulcer; acute glomerulonephritis and in active infections not controlled by antibiotics.

Corticosteroids are not indicated for patients with myasthenia gravis, diverticulitis, recent intestinal anastomoses, thrombophlebitis, psychotic tendencies, essential anthermatous disease, chronic nephritis, metastatic carcinoma, osteoporosis, and a history of peptic ulcer.

In the presence of any of these conditions, the need for corticosteroid therapy must be carefully weighed against possible deleterious effects.

Precautions and warnings: Due to its strong mineralocorticoid effect, the clinical use of Florinef is limited to such conditions as Addison's disease and adrenal hyperplasia.

Corticosteroids are not recommended for pregnant patients, particularly in the first trimester, except where the disease for which they are indicated warrants their use.

Side-effects: Arise from the glucocorticoid and mineralocorticoid actions of Florinef tablets. Cushingoid changes, or other signs of fat deposition; weakness; bruising or purpura; striae; osteoporosis; spontaneous fractures; sweating or flushing of the face; thromboembolism; necrotising angitis; acute pancreatitis; ulcerative oesophagitis; activation or aggravation of peptic ulcer or other gastro-intestinal upsets; oedema; hypertension; hirsutism; acneiform eruptions; vertigo; headache; severe mental disturbances. Increased intracranial pressure, papilloedema and posterior subcapsular cataracts have also been associated with prolonged corticosteroid administration.

Where adverse reactions do occur they are usually reversible following cessation of therapy.

Overdosage: A single large dose should be treated with plenty of water by mouth. Careful monitoring of serum electrolytes is essential, with particular consideration being given to the need for administration of potassium chloride and restriction of dietary sodium intake.

Pharmaceutical precautions *Storage:* At room temperature.

Legal category POM.

Package quantities *Florinef Tablets 0.1 mg:* Bottles of 100.

Florinef Tablets 1 mg: Bottles of 30.

Further information Nil.

Product licence numbers

Orinef Tablets 0.1 mg 0034/5027
Orinef Tablets 1 mg 0034/5028

**JINGILIN® CREAM AND OINTMENT
JINGILIN® IN ORABASE®**

Presentation *Cream*: Yellow containing amphotericin 100,000 units (30 mg) per gram.

Ointment: Yellow containing amphotericin 30,000 units (0 mg) per gram in Plastibase®.

Jingilin in Orabase: Yellow, crystalline paste containing amphotericin 20,000 units (20 mg) per gram Orabase® (gelatin, pectin and sodium carboxymethylcellulose in Plastibase®).

Uses *Actions*: Amphotericin is a polyene antifungal antibiotic active against a wide range of yeasts and yeast-like fungi including *Candida albicans*.

Indications: Cream and Ointment are indicated for cutaneous or mucocutaneous infections caused by susceptible fungi, particularly *C. albicans*.

Fungilin in Orabase is indicated for mycotic infections of the oral and perioral areas, including angular cheilitis, oral candidosis, dental trauma, ulcerative gingivitis and acute inflammatory gingivitis, glossitis and pericoronitis.

Dosage and administration *Cream and Ointment* could be applied two to four times daily.

Fungilin in Orabase should be applied two to four times daily, depending on the severity of the condition. Apply to the affected area; do not rub in.

Contra-indications, warnings, etc

Contra-indications: There are no known contra-indications.

Precautions: No special precautions apply.

Side-effects: No systemic or allergic reactions have been reported.

Pharmaceutical precautions *Storage: Cream*: At room temperature; avoid freezing.

Ointment: At room temperature.

Jingilin in Orabase: At room temperature.

Dilution: Fungilin topicals should not be diluted as this may reduce therapeutic efficacy.

Legal category POM.

Package quantities *Cream/Ointment*: 15 g tubes.

Jingilin in Orabase: Tubes of 10 g.

Further information Nil.

Product licence numbers

Jingilin Cream 0034/5032
Jingilin Ointment 0034/5035
Jingilin in Orabase 0034/5036

JINGILIN® LOZENGES, SUSPENSION AND TABLETS

Presentation *Lozenges*: Round, pale yellow, engraved 29 and Squibb, containing 10,000 units (10 mg) amphotericin.

Suspension: Orange-flavoured, viscous suspension containing 100,000 units (100 mg) amphotericin per ml.

Tablets: Yellow to tan, scored one side and engraved Squibb and 430 on reverse, containing 100,000 units (100 mg) amphotericin.

Uses *Actions*: Amphotericin is an antifungal antibiotic active against a wide range of yeasts and yeast-like fungi including *Candida albicans*. Absorption from the gastrointestinal tract is negligible even with very large doses. Extensive clinical experience has not shown problems of toxicity or sensitisation.

Indications: *Lozenges/Suspension*: For the treatment of candidal lesions (thrush) of the oral and perioral areas. The suspension may be used in the treatment of denture stomatitis.

Suspension/Tablets: For the suppression of the intestinal reservoir of *C. albicans* which may precipitate cutaneous or vaginal candidosis.

Dosage and administration *Adult dosage: Lozenges*: Dissolve 1 slowly in the mouth four times a day. Depending on the severity of infection, the dose may be increased to 8 lozenges daily.

To clear the condition fully may require 10-15 days' treatment.

Suspension: For denture stomatitis and oral infections caused by *C. albicans*, 1 ml should be placed in the mouth four times daily; it should be kept in contact with lesions for as long as possible.

For the treatment or suppression of intestinal candidosis, 2 ml four times daily.

Tablets: 1 or 2 tablets four times daily.

Administration of Fungilin for oral and intestinal candidosis should be continued for 48 hours after clinical cure to prevent relapse.

Infants and children: Suspension: For intestinal and oral candidosis, 1 ml should be dropped into the mouth four times daily. The suspension should be held in contact with oral lesions for as long as possible before swallowing.

For prophylaxis in the newborn, the suggested dose is 1 ml daily.

Contra-indications, warnings, etc

Contra-indications: There are no known contra-indications to the use of amphotericin.

Precautions: No special precautions apply.

Side-effects: Gastro-intestinal side-effects have occasionally been reported following continuous administration of amphotericin for several months in daily doses in excess of 3 g. These have been mild in nature and have readily cleared on cessation of treatment. No systemic toxic effects or allergic reactions have been associated with its oral use.

Overdosage: Since absorption of amphotericin from the gastro-intestinal tract is negligible, overdosage causes no systemic toxicity.

Pharmaceutical precautions *Storage: Lozenges/Tablets*: At room temperature.

Suspension: Cool place; protect from direct sunlight.

Dilution: Fungilin Suspension should not be diluted prior to use; it is formulated to coat and adhere to the oral lesions being treated.

Legal category POM.

Package quantities *Lozenges*: 20 in a tube.

Tablets: Bottles of 20.

Suspension: 12 ml bottles with graduated dropper.

Further information Nil.

Product licence numbers

Fungilin Lozenges	0034/5034
Fungilin Suspension	0034/5038
Fungilin Tablets	0034/5039

FUNGILIN* PESSARIES

Presentation Pale yellow, diamond-shaped, with Squibb logo engraved on one side, containing amphotericin 50,000 units (50 mg).

Uses *Actions:* Amphotericin is an antifungal antibiotic active against a wide range of yeasts and yeast-like fungi including *Candida albicans*.

Indications: Local treatment of vulvovaginal candidosis.

Dosage and administration *Adults:* 1 or 2 pessaries should be inserted high into the vagina for 14 consecutive nights or longer regardless of any intervening menstrual period.

Re-infection from the candidal content of the intestinal tract may be prevented by concomitant therapy with oral amphotericin.

Fungilin Cream or Ointment should be applied to the perineal region if necessary.

Children: Vulvovaginal candidosis is rarely a problem in children. Dosage should be as for adults together with concomitant oral amphotericin medication where necessary. Oral dosage should be 100 mg four times a day.

Contra-indications, warnings, etc

Contra-indications: There are no known contra-indications to the use of this product.

Precautions: No special precautions apply.

Side-effects: Fungilin is well tolerated and no systemic effects or allergic reactions have been reported.

Pharmaceutical precautions *Storage:* At room temperature.

Legal category POM.

Package quantities 15 in foil strips.

Further information Nil.

Product licence number 0034/5037.

FUNGIZONE* INTRAVENOUS

Presentation Each vial contains as a yellow, fluffy powder: amphotericin 50,000 units (50 mg), sodium desoxycholate approximately 41 mg, with sodium phosphate buffer.

Uses *Actions:* Amphotericin is a polyene antifungal antibiotic active against a wide range of yeasts and yeast-like fungi including *Candida albicans*. Crystalline amphotericin is insoluble in water; therefore, the antibiotic is solubilised by the addition of sodium desoxycholate to form a mixture which provides a colloidal dispersion for parenteral administration. Amphotericin is fungistatic rather than fungicidal in concentrations obtainable in body fluids. It probably acts by binding to sterols in the fungal cell membrane with a resultant change in membrane permeability which allows leakage of intracellular components. Amphotericin is slowly excreted by the kidneys. The cumulative urinary output

over a seven-day period amounts to approximately 40% of the amount of drug infused. No strains of *Candida* resistant to amphotericin have been reported in clinic use, and although *in vitro* testing does produce a small number of resistant isolates this occurs only following repeated subcultures.

Indications: Fungizone Intravenous should be administered primarily to patients with progressive, potential fatal infections. This potent drug should not be used to treat the common forms of fungal disease which show only positive skin or serological tests.

Fungizone Intravenous is specifically intended to treat cryptococcosis (torulosis); North American blastomycosis; the disseminated forms of candidosis, coccidioidomycosis and histoplasmosis; mucormycosis (phycomycosis) caused by species of the genera *Mucor*, *Rhizopus*, *Aspidium*, *Entomophthora*, and *Basidiobolus*; sporotrichosis (*Sporotrichum schenckii*), aspergillosis (*Aspergillus fumigatus*).

Amphotericin may be helpful in the treatment of American mucocutaneous leishmaniasis but is not the drug of choice in primary therapy.

Dosage and administration *Adults and children:* Fungizone should be administered by slow intravenous infusion over a period of six hours. Initial daily dose should be 0.25 mg/kg of body weight gradually increasing to a level of 1.0 mg/kg of body weight depending on individual response and tolerance. Within the range of 0.25-1.0 mg/kg the daily dose should be maintained at the highest level which is not accompanied by unacceptable toxicity.

In seriously ill patients the daily dose may be gradually increased up to a total of 1.5 mg/kg. Since amphotericin is excreted slowly, therapy may be given on alternate days in patients on the higher dosage schedule. Several months of therapy are usually necessary; a shorter period of therapy may produce an inadequate response and lead to relapse.

Caution: Under no circumstances should a total daily dose of 1.5 mg/kg be exceeded. The recommended concentration for intravenous infusion is 0.1 mg per ml (100 units per ml).

Contra-indications, warnings, etc

Contra-indications: Those patients who are hypersensitive to amphotericin, unless, in the opinion of the physician, the condition requiring treatment is life threatening and amenable only to such therapy.

Precautions: Prolonged therapy with amphotericin is usually necessary. Unpleasant reactions are quite common when the drug is given parenterally at therapeutic dosage levels. Some of these reactions are potentially dangerous. Hence amphotericin should be used parenterally only in hospitalised patients, or those under close clinical observation. If the BUN exceeds 40 mg per 100 ml, or the serum creatinine exceeds 3.0 mg per 100 ml the drug should be discontinued or the dosage markedly reduced until renal function is improved. Weekly blood counts and serum potassium determinations are also advisable. Low serum magnesium levels have also been noted during treatment with amphotericin. Therapy should be discontinued if liver function test results (elevated bromsulphalein, alkaline phosphatase and bilirubin) are abnormal.

Corticosteroids should not be administered concomitantly unless they are necessary to control drug reaction. Other nephrotoxic antibiotics and antineoplastic agents should not be given concomitantly except with great

sution. Whenever medication is interrupted for a period longer than seven days, therapy should be resumed by starting with the lowest dosage level, i.e. 0.25 mg/kg of body weight and increased gradually as outlined under 'dosage'.

Safety for use in pregnancy has not been established; therefore it should be used during pregnancy only if the possible benefits to be derived outweigh the potential risks involved.

Side-effects: While some patients may tolerate full intravenous doses of amphotericin without difficulty, most will exhibit some intolerance, often at less than the full therapeutic dosage. They may be made less severe by giving aspirin, antihistamines or antiemetics. Administration of the drug on alternate days may decrease nausea and phlebitis. Intravenous administration of small doses of adrenal corticosteroids just prior to or during the amphotericin infusion may decrease febrile reactions. The dosage and duration of such corticosteroid therapy should be kept to a minimum. Adding a small amount of heparin to the infusion may lessen the incidence of thrombophlebitis and coagulation problems. Extravasation may cause chemical irritation. The adverse reactions that are most commonly observed are: fever (sometimes with shaking chills), headache, anorexia, weight loss, nausea and vomiting, malaise, muscle and joint pains, dyspepsia, cramping epigastric pain, diarrhoea, local venous pain at the injection site with phlebitis and thrombophlebitis, normochromic normocytic anaemia and hypokalaemia. Abnormal renal function, which usually improves upon interruption of therapy, is also commonly observed; however, some permanent impairment often occurs, especially in those patients receiving large amounts (over 5 g) of amphotericin. The following adverse reactions occur less frequently or rarely: anuria (oliguria); cardiovascular toxicity including arrhythmias, ventricular fibrillation, cardiac arrest, hypotension; maculopapular rash; tinnitus; transient vertigo; blurred vision, or diplopia; convulsions and pruritus. Hepatotoxicity has been suggested.

Pharmaceutical precautions *Storage:* Vials of powder for reconstitution should be stored in a refrigerator. See package insert for storage after reconstitution and constitution directions.

Legal category POM.

Package quantities Vials of 50 mg.

Further information Nil.

Product licence number 0034/5041.

RANEODIN* OINTMENT AND OPHTHALMIC OINTMENT

Presentation Pale greenish yellow, containing neomycin sulphate 2.5 mg and gramicidin 0.25 mg per gram. Graneodin Ophthalmic Ointment is sterile.

Uses *Actions:* Neomycin is active against a wide range of Gram-positive and Gram-negative bacteria, including many of the organisms responsible for bacterial skin infections.

Gramicidin is active against Gram-positive bacteria and supplements the action of neomycin against the many common skin pathogens found in this group.

Indications—Topical: Superficial bacterial infections such

as impetigo; impetiginised eczema; infected eczema; furuncles; syphilis barbae; folliculitis; ecthyma; chronic ulcers of the skin; scratches or abrasions; bacterial infections of the ear.

For prophylaxis against infections following minor surgery.

Ophthalmic: Infections of the eyelids such as hordeolum, Meibomium cysts, blepharitis. Corneal or conjunctival infections.

Dosage and administration *Adults and children—*

Topical: To be applied two to four times a day. Any crusts should be removed and the ointment rubbed well in.

Ophthalmic: Half an inch of the ointment should be applied to the inside of the eyelid.

Contra-indications, warnings, etc

Contra-indications: Fungal or viral infections of the skin or for the treatment of deep-seated infections. These preparations are contra-indicated in persons with known sensitivity to neomycin.

Precautions: The possibility of sensitivity to neomycin should be taken into consideration especially in the treatment of patients suffering from leg ulcers. Since the use of occlusive dressings may increase the risk of sensitivity reactions such dressings should be avoided.

Side-effects: Sensitivity reactions to neomycin may occur especially with prolonged use. Gramicidin sensitivity has occasionally been reported.

Pharmaceutical precautions *Storage:* At room temperature.

Dilution: Not recommended.

Legal category POM.

Package quantities *Ointment:* Tubes of 15 g.

Ophthalmic Ointment: Tubes of 3.6 g.

Further information Nil.

Product licence numbers

Graneodin Ointment 0034/5042

Graneodin Ophthalmic Ointment 0034/5043

HALCIDERM* TOPICAL

Presentation A white topical preparation containing halcinonide 0.1% in a water-miscible base.

Uses *Actions:* Halcinonide is a potent corticosteroid with rapid anti-inflammatory, antipruritic and anti-allergic actions.

Halciderm is suitable for both wet and dry lesions.

Indications: Halciderm is indicated in acute and chronic corticosteroid-responsive conditions which may include: psoriasis, atopic eczema, contact eczema, follicular eczema, infantile eczema, neurodermatitis, anogenital eczema (pruritus ani et vulvae), nummular eczema, seborrhoeic or flexural eczema, otitis externa.

Dosage and administration *Adults and children:*

Halciderm should be applied to the affected area two, or occasionally three, times daily. In long-term therapy, or where lower strength preparations are required, do not dilute but use intermittently.

Contra-indications, warnings, etc

Contra-indications: Halciderm is contra-indicated in

tuberculous and most viral lesions of the skin, particularly herpes simplex, vaccinia and varicella. It should not be used in fungal or bacterial skin infections without suitable concomitant antimicrobial therapy. It is not intended for ophthalmic use, nor should it be applied in the external auditory canal of patients with perforated eardrums.

Precautions: In infants, long-term continuous topical steroid therapy should be avoided. Adrenal suppression may occur, even without occlusion. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to humans has not been established. However, topical corticosteroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

Side-effects: Halciderm is well tolerated. Local irritation is not common.

Pharmaceutical precautions *Storage:* Halciderm should be stored in a cool place.

Dilution: Due to special formulation of topical Halciderm, normal dermatological diluents should not be used. For further information consult the manufacturer.

Legal category POM.

Package quantities Tubes containing 15 g and 30 g.

Further information Halciderm contains halcinonide 0.1%, of which approximately half is present as microcrystals, while the remainder is dissolved in the non-aqueous phase. This formulation is designed to permit immediate utilisation of the steroid and to ensure that its activity is maintained for relatively prolonged periods.

Product licence number 0034/0160.

HYDREA* CAPSULES

Presentation Pink, opaque capsule body with green, opaque cap, both parts printed Squibb and 830 in black, containing hydroxyurea 500 mg.

Uses *Actions:* Hydroxyurea is an orally active antineoplastic agent. Although the mechanism of action has not yet been clearly defined, hydroxyurea appears to act by interfering with synthesis of DNA.

Indications: Active against a wide range of malignant lesions. Hydrea is particularly effective in the management of chronic myeloid leukaemia.

Hydrea is indicated for the treatment of malignant neoplastic disease, e.g. chronic leukaemias, acute leukaemias, Hodgkin's disease, multiple myeloma, lymphosarcoma, reticulum cell sarcoma, malignant melanoma, squamous cell carcinoma of the cervix, lung, pharynx, tongue, scalp and other sites, adenocarcinoma of the stomach and colon, breast sarcoma, hypernephroma, testicular tumours, ovarian neoplasms and astrocytoma.

In the treatment of tumours of the head and neck, lung, Hodgkin's disease, astrocytoma and sarcoma, best results have been obtained with concomitant radiotherapy.

Dosage and administration Treatment regimens can be continuous or intermittent. The continuous regimen is particularly suitable for chronic myeloid leukaemia, while the intermittent regimen, with its diminished effect on the bone marrow, is more satisfactory for the management of solid tumours.

Hydrea should be started 7 days before concurrent irradiation therapy.

Continuous therapy: Hydrea 20-30 mg/kg should be given daily in single doses. Dosage should be based on the patient's actual or ideal weight, whichever is the less. Therapy should be monitored by repeat blood count and discontinued if the WBC falls below 3,000 per mm³ or the platelet count below 100,000 per mm³. Hydrea should be resumed when the blood cells have returned to normal levels.

Intermittent therapy: Hydrea 80 mg/kg in single dose should be given every third day. Using the intermittent regimens the likelihood of WBC depression is diminished but if low counts are produced, 1 or more doses of Hydrea should be omitted.

Contra-indications, warnings, etc

Contra-indications: Marked leucopenia, thrombocytopenia, severe anaemia and those who have previously shown hypersensitivity to Hydrea.

Precautions: The myelosuppressive activity may be potentiated by previous or concomitant radiotherapy or cytotoxic therapy. Since Hydrea is a cytotoxic agent it has produced a teratogenic effect in some animal species. This product should not normally be administered to patients who are pregnant, or to mothers who are breastfeeding. Patients undergoing therapy with Hydrea should be monitored by repeat blood counts.

Side-effects: Bone-marrow suppression is the major toxic effect of Hydrea, while leucopenia, thrombocytopenia and anaemia may occur in that order. Other side effects are generally rare, but the following have been reported: anorexia, nausea, vomiting, headache, drowsiness, dizziness, stomatitis, alopecia, skin rash, melana abdominal pain, disorientations, pulmonary oedema, hallucinations, convulsions and potentiation of the erythema caused by irradiation.

Overdosage: Immediate treatment consists of gastric lavage, followed by supportive therapy for the cardio-respiratory systems if required. In the long term, careful monitoring of the haemopoietic system is essential and if necessary, blood should be transfused.

Pharmaceutical precautions *Storage:* At room temperature. Bottles should be kept tightly closed since hydroxyurea is hygroscopic.

Legal category POM.

Package quantities Bottles of 100.

Further information Nil.

Product licence number 0034/5044.

IPRAL* TABLETS

IPRAL* PAEDIATRIC SUSPENSION

Presentation *Tablets:* Round, white tablets engraved Squibb and 513, containing 100 mg trimethoprim.

Round, white tablets engraved Squibb and 514 containing 200 mg trimethoprim.

Paediatric Suspension: White, sugar-free suspensor containing 50 mg trimethoprim per 5 ml.

Uses *Actions:* Trimethoprim is active in-vitro against most pathogenic Gram-positive and Gram-negative bacteria. Exceptions are *Nocardia* species, *Treponem pallidum*, *Pseudomonas aeruginosa*, anaerobic bacteria.

and possibly *Mycobacterium* and *Neisseria* species and *M. rubeola abortus*.

Indications: *Urinary tract:* In the treatment of acute and chronic urinary tract infections and for prophylactic treatment of patients with a tendency to recurrent urinary infections.

Respiratory tract: In the treatment of acute and chronic bronchitis, bronchopneumonia and basal pneumonia.

Ipral is particularly useful for patients sensitive to ulphonamides.

Dosage and administration

Oral Tablets: *Adults and Children over 12 years:* For acute urinary tract and respiratory tract infections, 100 mg twice daily. For long-term and prophylactic therapy of urinary tract infections, 100 mg at night.

Oral Paediatric Suspension: *Children:* Acute treatment: based on a dose of approximately 8 mg/kg/day of trimethoprim:

Up to 12 years: 100 mg (10 ml suspension) twice daily

6 months to 6 years: 50 mg (5 ml suspension) twice daily

3 weeks to 6 months: 25 mg (2.5 ml suspension) twice daily

Ipral Paediatric Suspension may be diluted to half-strength with water, sorbitol or Syrup BP.

Contra-indications, warnings, etc

Contra-indications: Ipral should not be given to patients with severe renal insufficiency where blood levels cannot be monitored regularly. It should not be administered to pregnant women, premature infants nor during the first two months of life. Megaloblastic anaemia.

Precautions: Care is necessary in administration to patients with impaired renal function. Regular haematological examinations should be performed during long-term therapy. Special precautions should be exercised in patients with a predisposition to folate deficiency. Ipral is excreted in breast milk.

Side-effects: Ipral is well tolerated at therapeutic doses with few side-effects. Nausea, vomiting, gastro-intestinal upset and dermatological reactions such as pruritus and rash have been reported. Given over a prolonged period, Ipral may depress haemopoiesis due to an effect on folic acid metabolism. This effect may be reversed by intramuscular administration of 3-5 mg calcium folinate daily for five to seven days.

Treatment of overdose: Symptoms of overdose include diarrhoea and vomiting. Treatment is symptomatic and gastric lavage and forced diuresis may be used. Calcium folinate may be used to counteract any effect of Ipral on bone-marrow.

Pharmaceutical precautions *Storage:* Ipral tablets and suspension should be stored in closed containers at room temperature.

Legal category POM.

Package quantities

100 mg Tablets: Packs of 100 tablets.

200 mg tablets: Packs of 100 and 500 tablets.

Suspension: Bottles of 100 ml.

Further information Absorption from the oral route is rapid, and peak plasma levels are obtained between one and four hours. Ipral is well distributed throughout the tissues and is excreted, predominantly unchanged, in the urine.

Product licence numbers

Ipral Tablets 100 mg 0034/0190.

Ipral Tablets 200 mg 0034/0204.

Ipral Paediatric Suspension 0034/0196.

KENALOG* INTRA-ARTICULAR/INTRAMUSCULAR

Presentation Sterile, aqueous suspension of triamcinolone acetonide 40 mg per ml.

Uses Triamcinolone acetonide is a synthetic glucocorticoid with marked anti-inflammatory and anti-allergic actions.

Intra-articular injection: Following the local injection of Kenalog, relief of pain and swelling, with greater freedom of movement, is usually obtained within a few hours.

Intramuscular injection: Provides an extended duration of therapeutic effect and fewer side-effects of the kind associated with oral corticosteroid therapy, particularly gastro-intestinal reactions such as peptic ulceration. Studies indicate that, following a single intramuscular dose of 80 mg triamcinolone acetonide, adrenal suppression occurs within 24-48 hours and then gradually returns to normal, usually in approximately three weeks. This finding correlates closely with the extended duration of therapeutic action of triamcinolone acetonide.

Indications *Intra-articular injections of Kenalog* are indicated for alleviating the joint pain, swelling and stiffness associated with rheumatoid arthritis, osteoarthritis; also for acute and subacute bursitis, epicondylitis, tendinitis and acute, non-specific tenosynovitis.

Intramuscular injections of Kenalog are indicated where depot corticosteroid treatment is required, including certain allergic and dermatological conditions and connective tissue disorders. In seasonal allergies, remission of symptoms over the entire period may be achieved with a single intramuscular injection. It is not indicated in children under six years.

Dosage and administration

Kenalog intra-articular/intramuscular injection is not for intravenous use.

Intra-articular injection: For intra-articular administration or injection into tendon sheaths and bursae, the dose of Kenalog injection may vary from 5 mg to 10 mg (0.125-0.25 ml) for smaller joints and up to 40 mg (1 ml) for larger joints, depending on the specific disease entity being treated. Single injections into several sites for multiple joint involvement, up to a total of 80 mg, have been given without undue reactions.

It is recommended that, when injections are given into the sheaths of short tendons, Adcortyl injection (triamcinolone acetonide 10 mg/ml) should be used.

N.B. Strict aseptic precautions should be observed.

Intramuscular injection: *Adults and children over 12 years:* The suggested initial dose is 40 mg (1 ml) injected deeply into the upper, outer quadrant of the gluteal muscle. Subsequent dosage depends on the patient's response and period of relief. Patients with hay fever or pollen asthma who do not respond to conventional therapy may obtain a remission of symptoms lasting throughout the pollen season after a dose of 40-100 mg.

For children from 6-12 years of age: The suggested initial dose of 40 mg (1 ml) injected deeply into the gluteal muscle should be scaled according to the severity of symptoms and the age and weight of the child.

Since the duration of effect is variable, subsequent doses should be given when symptoms recur and not at set intervals.

Contra-indications, warnings, etc

Contra-indications: *Intra-articular injection* is contra-indicated in the presence of active infection in or near joints. The preparation should not be used to alleviate joint pain arising from infectious states such as gonococcal or tubercular arthritis.

Systemic corticosteroids are not indicated for patients with myasthenia gravis, diverticulitis, recent intestinal anastomoses, thrombophlebitis, psychotic tendencies, exanthematous disease, chronic nephritis, metastatic carcinoma, osteoporosis and a history of peptic ulcer.

In latent or healed tuberculosis; in the presence of local or systemic viral infection; in acute psychoses and in patients with an active peptic ulcer; in acute glomerulonephritis and in active infections not controlled by antibiotics.

Precautions *Intra-articular injection:* Patients should be specifically warned to avoid over-use of joints in which symptomatic benefit has been obtained. Severe joint destruction with necrosis of bone may occur if repeated intra-articular injections are given over a long period of time. Care should be taken if injections are given into tendon sheaths to avoid injection into the tendon itself.

Due to the absence of a true tendon sheath, the Achilles tendon should not be injected with depot corticosteroids.

Intramuscular injection: During prolonged therapy a liberal protein intake is essential to counteract the tendency to gradual weight loss sometimes associated with negative nitrogen balance and wasting of skeletal muscle.

Corticosteroids are not recommended for pregnant patients, particularly in the first trimester, except when the disease for which they are indicated warrants their use. Hypo-adrenalism may occur in the newborn of mothers receiving corticosteroid therapy.

Diabetes may be aggravated, necessitating a higher insulin dosage. Latent diabetes mellitus may be precipitated. Menstrual irregularities may occur, and this possibility should be mentioned to female patients.

Patients on long-term systemic therapy with Kenalog may require supportive corticosteroid therapy in times of stress (such as trauma, surgery or severe illness), both during the treatment period and for a year afterwards.

N.B. To avoid the danger of subcutaneous fat atrophy, it is important to ensure that *deep intramuscular injection is given into the gluteal site*. The deltoid should not be used. Alternate sides should be used for subsequent injections.

Side-effects *Intra-articular injection:* rarely gives rise to adverse reactions. Pain and other local symptoms may continue for a short time before effective relief is obtained. Local fat atrophy may occur if the injection is not given into the joint space.

Intramuscular injection: Local fat atrophy may occur (see under Precautions). Unwanted effects which may be associated with systemic corticosteroid therapy include: Cushingoid changes or other signs of fat deposition; weakness, bruising or purpura; striae; osteoporosis; spontaneous fractures; sweating or flushing of the face; thromboembolism; necrotising angitis; acute pancreatitis; ulcerative oesophagitis; activation or ag-

gravation of peptic ulcer or other gastro-intestinal upsets; hirsutism; acneiform eruptions; vertigo; headache; or severe mental disturbances. Increased intra-cranial pressure, papilloedema and posterior subcapsular cataracts have also been associated with prolonged corticosteroid administration.

Where adverse reactions occur they are usually reversible on cessation of therapy.

The usual early unwanted corticosteroid effects such as increase in weight, oedema and hypertension, generally do not occur with Kenalog, but, as with other potent corticosteroids, clinical supervision is necessary.

Pharmaceutical precautions *Storage:* At room temperature; avoid freezing.

Legal category POM.

Package quantities Ready filled syringes 1 ml and 2 ml (Intramuscular use only). 1 ml vials: pack of 1 (Intra-articular and intramuscular use).

Further information Nil.

Product licence number 0034/5045.

MODECATE* INJECTION

MODECATE* CONCENTRATE INJECTION

Presentation *Modecate injection:* Straw-coloured, viscous liquid containing fluphenazine decanoate 25 mg per ml in sesame oil.

Modecate Concentrate injection: Straw-coloured, viscous liquid containing fluphenazine decanoate 100 mg per ml in sesame oil. Ampoules are marked with a distinctive blue band.

Uses *Actions:* Fluphenazine decanoate is an ester of the potent neuroleptic fluphenazine, a phenothiazine derivative of the piperazine type. The ester is slowly absorbed from the intramuscular site of injection and is then hydrolysed in the plasma to the active therapeutic agent, fluphenazine.

Indications: For the treatment of psychotic disorders. Whilst Modecate injection has been shown to be effective in acute states, it is particularly useful in the maintenance treatment of chronic patients who are unreliable at taking their oral medication, and also of those who do not absorb their oral phenothiazines in adequate amounts.

Modecate Concentrate injection provides a high concentration of fluphenazine decanoate in a small volume which may be injected without discomfort to the patient and it is therefore particularly suitable for those patients who require higher doses for effective antipsychotic control.

Dosage and administration It is preferable that patients be stabilised on the injection in hospital.

Recommended dosage regimes

1. *Modecate injection 25 mg/ml*

- a) *Patients without previous exposure to a depot fluphenazine formulation:* Initially 0.5 ml (0.25 mg) for patients over 60 by deep intramuscular injection into the gluteal region.

Clinical response or side-effects may be observed within hours and further injections should be administered according to the initial response and severity of the condition.

It is desirable to maintain as much flexibility in the

dose as possible to achieve the best therapeutic response with the least side-effects; most patients are successfully maintained within the dose range 0.5 ml every five weeks to 4 ml every two weeks. In very disturbed patients, much higher doses of Modecate injection have been used in the first week with good results, but are seldom required for more than two months.

-) *Patients previously maintained on depot fluphenazines:* Patients who have suffered a relapse following cessation of depot fluphenazine therapy may be restarted on the same dose as they were receiving formerly, although the frequency of injections may need to be increased in the early weeks of treatment until satisfactory control is obtained.

Modecate Concentrate injection 100 mg/ml: Patients found to require the larger volumes of Modecate 5 mg/ml, for example in excess of 2 ml per injection, may be transferred directly to the equivalent dose of Modecate Concentrate on the basis that 1 ml Modecate Concentrate Injection is equivalent to 4 ml Modecate injection.

Contra-indications, warnings, etc

Contra-indications: Patients with marked cerebral atherosclerosis, phaeochromocytoma, renal or liver failure, or severe cardiac insufficiency. Modecate is not recommended for the treatment of anxiety and tension states, or geriatric confusion and agitation.

Precautions: Fluphenazine decanoate is not intended for use in children under 12 years of age. Caution over the dosage should be exercised in those patients, particularly the elderly, who have experienced marked extra-pyramidal reactions on oral phenothiazines or similar drugs.

Pregnancy: Although there is no clinical evidence to suggest that Modecate is teratogenic, the precise risk associated with its use in the first trimester of pregnancy remains unknown.

Lursing mothers: Breast feeding is not recommended in women receiving Modecate.

Side-effects: 1. *Extra-pyramidal. Acute dystonic reactions* occur infrequently but nearly always within the first 24-48 hours, and may include such dramatic manifestations as oculogyric crises and opisthotonos. They are rapidly relieved by intravenous administration of an antiparkinsonian agent such as procyclidine.

Parkinsonian-like states may occur particularly between the second and fifth days after each injection, but often decrease with subsequent injections. These reactions may be reduced by using smaller doses more frequently, or by the concomitant use of antiparkinsonian drugs such as benzhexol, bntropine or procyclidine.

With careful monitoring of the dose as few as 10% of patients may require antiparkinsonian drugs.

Adverse dyskinesia, similar to that associated with long-term oral neuroleptic therapy, has been reported in patients receiving Modecate injections. Bearing in mind that the movements may go unnoticed by the patient or be suppressed at the time of interview, periodic enquiry and observation are advised.

2. *Other:* As with other phenothiazines, drowsiness, atargy, blurred vision, dryness of mouth, constipation, mild hypotension, impairment of judgement and mental kills, epileptiform attacks, jaundice, abnormal lactation or menstruation and granulocytopenia are occasionally seen. Persistent oral dyskinesias, abnormal skin pigmentation and lens opacities, while sometimes seen following

long-term administration of phenothiazines, have not been reported following the use of Modecate alone. However, their possible occurrence should be considered.

While the injections produce some discomfort at the site of the injection, they seldom cause marked pain, and infections and abscesses are rare.

Overdosage: It should be treated symptomatically and supportively. Extrapyramidal reactions will respond to oral or parenteral antiparkinsonian drugs such as procyclidine or bntropine. In cases of severe hypotension, all procedures for the management of circulatory shock should be instituted, e.g. vasoconstrictors and/or intravenous fluids. However, only the vasoconstrictors metaraminol or noradrenaline should be used, as adrenaline may further lower the blood pressure through interaction with the phenothiazine.

Pharmaceutical precautions *Storage:* At room temperature. Do not store in a refrigerator, since this will cause precipitation of triglycerides from the sesame oil. If precipitation does occur, warming the product to 37°C will dissolve the precipitate without harming the active ingredient. Protect from direct sunlight.

Legal category POM.

Package quantities *Modecate Injection 25 mg/ml:* Ampoules 0.5 ml, 1 ml and 2 ml; Ready-filled syringes of 1 ml, 2 ml; Multidose vials of 10 ml.

Modecate Concentrate Injection 100 mg/ml: Ampoules 0.5 ml and 1 ml.

Further information Nil.

Product licence numbers

Modecate Injection 25 mg/ml	0034/5046
Modecate Concentrate Injection 100 mg/ml	0034/0189

MODITEN® ENANTHATE INJECTION

Presentation Straw-coloured, viscous liquid containing fluphenazine enanthate 25 mg per ml in sesame oil.

Uses *Actions:* Fluphenazine enanthate is an ester of the potent neuroleptic, fluphenazine, a phenothiazine derivative of the piperazine type. The ester is slowly absorbed from the intramuscular site of injection and is then hydrolysed in the plasma to the active therapeutic agent, fluphenazine.

Indications: For the treatment of psychotic disorders. Moditen Enanthate is particularly useful in the maintenance treatment of chronic patients who are unreliable at taking their oral medication, and those who absorb their oral phenothiazines in inadequate amounts.

Dosage and administration It is preferable that patients be stabilised on the injection in hospital.

Recommended dosage regimes: 1. *Patients without previous exposure to either of the depot fluphenazines:* Initially 0.5 ml (0.25 ml for patients over 60) by deep intramuscular injection in the gluteal region. Clinical or side-effects may be observed within hours and further injections may be administered according to the initial response and severity of the condition. It is desirable to maintain as much flexibility in the dose as possible to achieve the best therapeutic response with the least side-effects; most patients are successfully maintained

within the dose range 0.5 ml every three weeks to 4 ml every ten days. In very disturbed patients, much higher doses of Moditen enanthate have been used in the first week with good results, but are seldom required for more than two months.

2. Patients previously maintained on depot fluphenazines: Patients who have suffered a relapse following cessation of depot fluphenazine therapy may be restarted on the same dose as they were formerly receiving, although the frequency of injections may need to be increased in the early weeks of treatment until satisfactory control is obtained.

Contra-indications, warnings, etc

Contra-indications: Patients with marked cerebral atherosclerosis, phaeochromocytoma, renal or liver failure, or severe cardiac insufficiency. Moditen Enanthate is not recommended for the treatment of anxiety and tension states or geriatric confusion and agitation.

Precautions: Moditen Enanthate is not intended for use in children under 12 years of age. Caution should be exercised in those who have had marked extrapyramidal reactions on oral phenothiazines or similar drugs, particularly the elderly. Such patients should start on half the normal dose.

Pregnancy: Although there is no clinical evidence to suggest that Moditen Enanthate is teratogenic, the precise risk associated with its use in the first trimester of pregnancy remains unknown.

Nursing mothers: Breast feeding is not recommended in women receiving Moditen Enanthate.

Side-effects: Extrapyramidal: 1. *Acute dystonic reactions:* These occur infrequently but nearly always within the first 24-48 hours, and include such dramatic manifestations as oculogyric crises and opisthotonos. They are rapidly relieved by intravenous administration of an anti-Parkinsonian agent such as procyclidine.

2. *Parkinsonism:* Parkinsonian-like states may occur particularly between the second and fifth days after each injection but often decrease with subsequent injections. These reactions may be reduced by using smaller doses more frequently, or by the concomitant use of anti-Parkinsonian drugs such as benzhexol, benzotropine or procyclidine.

With careful monitoring of the dose as few as 10% of patients may require anti-Parkinsonian drugs.

3. *Tardive Dyskinesia:* Similar to that associated with long-term oral neuroleptic therapy, has been reported in patients receiving Moditen Enanthate injections. Bearing in mind that the movements may go unnoticed by the patient or be suppressed at the time of interview, periodic enquiry and observation are advised.

4. *Other:* As with other phenothiazines, drowsiness, lethargy, blurred vision, dryness of mouth, constipation, mild hypotension, impairment of judgement and mental skills, epileptiform attacks, jaundice, abnormal lactation or menstruation and granulocytopenia are occasionally seen. Persistent oral dyskinesias, abnormal skin pigmentation and lens opacities, while sometimes seen following long-term administration of phenothiazines, have not been reported following the use of Moditen Enanthate alone. However, their possible occurrence should be considered.

While the injections produce some discomfort at the site of injection, they seldom cause marked pain, and infections and abscesses are rare.

Overdosage: It should be treated symptomatically and

supportively. Extrapyramidal reactions will respond to oral or parenteral anti-Parkinsonian drugs such as procyclidine or benzotropine. In cases of severe hypotension all procedures for the management of circulatory shock should be instituted, e.g. vasoconstrictors and/or intravenous fluids. However, only the vasoconstrictor metaraminol or noradrenaline should be used as adrenaline will further lower the blood pressure through interaction with the phenothiazine.

Pharmaceutical precautions *Storage:* At room temperature. Do not store in a refrigerator, since this will cause precipitation of triglycerides from the sesame oil. If precipitation does occur, warming the product to 37°C will dissolve the precipitate, without harming the active ingredient. Protect from direct sunlight.

Legal category POM.

Package quantities Ampoules of 1 ml. Multidos vials of 10 ml.

Further information Nil.

Product licence number 0034/5048.

MODITEN* TABLETS

Presentation *Tablets 1 mg:* Round, pink, sugar coated tablets containing 1 mg fluphenazine hydrochloride.

Tablets 2.5 mg: Round, yellow, sugar-coated tablet containing 2.5 mg fluphenazine hydrochloride.

Tablets 5 mg: Round, white, sugar-coated tablets printed in green with Squibb and 877, containing 5 mg fluphenazine hydrochloride.

Uses *Actions:* Fluphenazine is a phenothiazine derivative of the piperazine type, its principal actions being those of tranquillisation and anti-emesis.

Indications: Moditen is indicated for the treatment of anxiety and tension, behaviour disorders in children, geriatric confusion and agitation, acute chronic psychoses, the management of psychomotor over-activity and hostility associated with schizophrenia, mania psychoses due to organic brain disease and senile psychoses.

Dosage and administration Because of its inherent length of activity only a single daily dose at breakfast is necessary. However, daily doses may be divided if so desired.

Anxiety and tension states (adults only): Initially 1-2 mg daily rising to 2-4 mg if necessary according to response. It is advised that 1 mg tablets be prescribed for this indication.

Geriatric confusion and agitation: Initially 1 mg daily adjusted according to response.

Behaviour disorders in children: Initially 0.25-0.5 mg daily, rising if necessary to 0.5 or 1 mg according to age and response.

Psychoses and severe behaviour disorders in children Initially 2.5-10 mg daily depending on the severity and duration of symptoms, rising to 20 mg daily as necessary. Doses exceeding 20 mg daily should be used with caution.

Contra-indications, warnings, etc

Contra-indications: Marked cerebral atherosclerosis

leochromocytoma, renal or liver failure and severe diastolic insufficiency.

cautions and side-effects: Extrapyramidal reactions may occur at daily doses of 3 mg or more and have been reported at lower doses on rare occasions, mostly in elderly patients with cerebral atherosclerosis. These reactions may be reduced by using a smaller dose or by concomitant use of anti-Parkinsonian drugs such as levodopa, benztropine or procyclidine. As with other phenothiazines drowsiness, lethargy, blurred vision, dryness of the mouth, constipation, mild hypotension, impairment of judgement and mental skills, epileptiform attacks, jaundice, lactation, abnormal menstruation and neutropenia are occasionally seen but extremely rarely in doses used for the treatment of anxiety and depression. Persistent oral dyskinesias, abnormal skin pigmentation and lens opacities, while sometimes seen following the long-term administration of high doses of phenothiazines, have not been reported following the use of Moditen alone. However, their possible occurrence should be considered.

overdosage: Overdosage should be treated symptomatically. Gastric lavage or stimulation of vomiting should be attempted in the conscious patient. Extrapyramidal reactions will respond to oral or parenteral anti-Parkinsonian drugs such as procyclidine or benztropine. In cases of severe hypotension all procedures for the management of circulatory shock should be instituted, i.e. vasoconstrictors and/or intravenous fluids. However, only the vasoconstrictors metaraminol or noradrenaline should be used as adrenaline will further lower the blood pressure through interaction with the phenothiazine.

pharmaceutical precautions *Storage:* At room temperature.

legal category POM.

package quantities Bottles of 100.

further information Nil.

product licence numbers

Moditen Tablets 1 mg	0034/5049
Moditen Tablets 2.5 mg	0034/5050
Moditen Tablets 5 mg	0034/5051

OTIPRESS* TABLETS OTIVAL* TABLETS

description *Motipress Tablets:* Each yellow, triangular-shaped, sugar-coated tablet contains nortriptyline hydrochloride, equivalent to 30 mg nortriptyline base and fluphenazine hydrochloride 1.5 mg.

Motival Tablets: Each pink, triangular-shaped, sugar-coated tablet contains nortriptyline hydrochloride, equivalent to 10 mg nortriptyline base and fluphenazine hydrochloride 0.5 mg.

uses *Actions:* Nortriptyline hydrochloride is a tricyclic antidepressant with more rapid activity and less sedation than the majority of drugs of its class. It possesses some opiate-like properties. It is not a mono-amine oxidase inhibitor.

Fluphenazine hydrochloride is a phenothiazine derivative of the piperazine type, its principal actions being those of tranquillisation and anti-emesis. In accordance with pharmacokinetic studies, nortriptyline and fluphen-

azine have been shown to be equally effective therapeutically whether taken together as a single daily dose, or in divided doses.

Indications: Motipress and Motival tablets are indicated for the treatment of patients suffering from mild to moderate anxiety, depression and mixed anxiety depressive states.

Motipress and Motival tablets are also useful in the treatment of phobic states and in conditions where a loss of concentration, interest and pleasure are a problem.

Dosage and administration *Motipress Tablets:* **Adults:** 1 tablet daily, preferably before retiring. This formulation is not indicated for the treatment of children.

Motival Tablets: **Adults:** The dose range is 1 tablet two to four times daily. Most patients respond to 1 tablet three times daily and very few patients require a dose in excess of this. This formulation is not indicated for the treatment of children.

Contra-indications, warnings, etc

Contra-indications: Motipress or Motival tablets should not be given to patients with a history of grand mal or organic brain damage. It is inadvisable to give mono-amine oxidase inhibitors (MAOIs) with Motipress or Motival tablets, nor should they be given within two weeks of cessation of treatment with a MAOI.

Precautions: Should be given with caution to patients with glaucoma and to those who have a propensity for urinary retention. Interactions with barbiturates, alcohol and narcotic drugs may occur, so central nervous depressants should be administered with caution. Motipress and Motival tablets may diminish the antihypertensive effect of adrenergic blocking agents and could potentiate the pressor response to locally injected sympathomimetic agents.

Although there has been no evidence of teratogenicity with fluphenazine or nortriptyline separately, or in combination, caution should be exercised with the use of Motival or Motipress in pregnancy.

Side-effects: Mild side-effects which include dryness of the mouth, drowsiness, faintness and constipation occur infrequently. Occasionally tachycardia, nasal congestion, blurred vision and excitement are seen.

Drowsiness is more likely to occur with Motipress tablets if taken on waking, e.g. in the morning.

Extrapyramidal reactions are unlikely to occur with this dose of fluphenazine alone, and it is probable that the anticholinergic activity of nortriptyline affords protection against such effects. This latter protection would be valuable in the event of overdosage.

Overdosage: Overdosage should be treated symptomatically and supportively. If the patient is conscious, prompt gastric lavage, dilution of the stomach contents to delay absorption, or stimulation of vomiting should be attempted. An open airway should be maintained. Extrapyramidal symptoms are amenable to anti-Parkinsonian drugs. In severe hypotension, all the standard procedures for the management of circulatory shock should be instituted, e.g. vasoconstrictors and/or intravenous fluids. If vasoconstrictors are required, metaraminol, or noradrenaline should be administered but not adrenaline, as this will further lower the blood pressure through interaction with the phenothiazine.

Pharmaceutical precautions *Storage:* At room temperature.

Legal category POM

Package quantities *Motipress Tablets*: 28 day calendar pack, bottles of 250.

Motival Tablets: Bottles of 100 and 500.

Further information Nil.

Product licence numbers

Motipress Tablets 0034/0174

Motival Tablets 0034/5052

MYSTECLIN* CAPSULES AND TABLETS

Presentation *Capsules*: Opaque, pink body with opaque, brown cap, both printed Squibb and 885 in white. Each capsule contains 250 mg tetracycline hydrochloride and 250,000 units nystatin.

Tablets: Orange, sugar-coated tablet with Squibb and 677 printed in black, containing tetracycline hydrochloride 250 mg and nystatin 250,000 units.

Uses *Actions*: Tetracycline hydrochloride has a broad antimicrobial activity against pathogenic organisms including many Gram-positive and Gram-negative bacteria, spirochaetes, certain rickettsiae, large viruses, *Mycoplasma pneumoniae* and *Entamoeba histolytica*. After oral administration therapeutically effective blood and urinary levels are obtained in a short period of time. It diffuses readily into most body tissues.

Nystatin is an antifungal antibiotic active against a wide range of yeasts and yeast-like fungi, including *Candida albicans*. Following wide use over many years, no clinical isolates resistant to this compound have emerged. Repeated subculture, *in vitro*, produces a small number of resistant isolates, but with reduced growth rate and pathogenicity. The possibility of these organisms causing disease in man is remote. Extensive clinical experience with nystatin has shown no problems of toxicity or sensitisation.

Indications: For infections caused by organisms sensitive to tetracycline, particularly in patients who may be susceptible to candidal overgrowth. These may include elderly or debilitated patients, diabetics, women taking hormonal contraceptive agents, patients with malignant disease especially if receiving cytotoxic drugs and those patients receiving high doses or prolonged courses of antibiotics or corticosteroids. Representative infections due to susceptible organisms including chronic bronchitis and other respiratory tract infections, urinary tract infections, brucellosis, acne and many mixed infections.

Dosage and administration *Adult dosage*: A minimum dose of 250 mg tetracycline four times daily. This dose may be doubled in severe infections.

Mysteclin should preferably be taken one hour before, or two hours after meals.

Contra-indications, warnings, etc

Contra-indications: The tetracycline group of antibiotics is normally contra-indicated during pregnancy except in certain severe infections where tetracycline may be the drug of choice, and the risk involved is justified.

Administration of tetracyclines in pregnant women may result in hepatic injury, particularly if used for the treatment of pyelonephritis. Tetracyclines are deposited in the skeleton of the human foetus and may result in the depression of bone growth and produce discolouration of the teeth in the child. As tetracycline passes into breast milk, breast feeding is not recommended during Mysteclin therapy. Mysteclin should not be used in patients

with a history of hypersensitivity to the tetracycline group of antibiotics. There are no known contra-indications to the use of nystatin.

Precautions: In treating patients with renal dysfunction since tetracycline may produce azotaemia, hyperphosphataemia, acidosis, weight loss or nausea and vomiting. Absorption of tetracycline from the gut is diminished by milk, salts of calcium, magnesium, aluminium and iron. Lowered absorption also results from alkalies, and concomitant administration of antacids should therefore be avoided.

The effects of anticoagulants are not usually altered by concurrent treatment with tetracycline, although few isolated cases of enhancement have been described. Therefore, occasionally, reduction in doses of concurrent anticoagulants may be required.

Tetracyclines may be deposited in areas of calcification in bones and teeth. The use of drugs of the tetracycline class during tooth development (last half of pregnancy, infancy and childhood to the age of eight years) may cause permanent discolouration of the teeth (yellow-grey-brown). This reaction is more common during long-term use of the drugs but has been observed following repeated short-term courses. Enamel hypoplasia has also been reported. Tetracycline drugs, therefore, should not be used in this age group unless other drugs are unlikely to be effective or are contra-indicated.

There are no special precautions for the oral use of nystatin.

Side-effects: Mysteclin is generally well tolerated but few patients may experience gastro-intestinal side-effects such as nausea, vomiting and diarrhoea.

A phototoxic reaction may be produced in some patients, although such reactions are less common with tetracycline than with other members of the group.

No systemic effects or allergic reactions have been associated with the oral use of nystatin.

Overdosage: The most common symptoms are nausea, vomiting and diarrhoea. The possibility of liver failure occurring should be borne in mind.

Pharmaceutical precautions *Storage*: *Capsule Tablets*: At room temperature.

Legal category POM.

Package quantities *Capsules*: Bottles of 100.
Tablets: Bottles of 100 and 500.

Further information By the inclusion of nystatin with tetracycline, the fungal overgrowth frequently associated with broad-spectrum antibiotic therapy is avoided.

Product licence numbers

Mysteclin Capsules 0034/5054

Mysteclin Tablets 0034/5056

MYSTECLIN* SYRUP

Presentation Deep orange, viscous liquid, with fruit flavour and containing per 5 ml tetracycline hydrochloride equivalent to tetracycline 125 mg and amphotericin 25 mg.

Uses *Actions*: Tetracycline has a broad antimicrobial activity against pathogenic organisms including many Gram-positive and Gram-negative bacteria, spirochaetes, certain rickettsiae, large viruses, *Mycoplasma pneumoniae* and *Entamoeba histolytica*. After oral a

istration therapeutically effective blood and urinary levels are obtained in a short period of time. It diffuses readily into most body tissues.

Amphotericin is an antifungal antibiotic active against a wide range of yeasts and yeast-like fungi, including *Candida albicans*. Following wide use over many years, clinical isolates resistant to this compound have emerged. Repeated subculture, *in vitro*, produces a small number of resistant isolates, but with reduced growth rate and pathogenicity. The possibility of these organisms causing disease in man is remote.

Indications: For infections caused by organisms sensitive to tetracycline, particularly in patients who may be susceptible to candidal overgrowth. These may include elderly or debilitated patients, diabetics, women taking hormonal contraceptive agents, patients with malignant disease especially if receiving cytotoxic drugs and those patients receiving high doses or prolonged courses of antibiotics or corticosteroids. Representative infections are due to susceptible organisms including chronic bronchitis and other respiratory tract infections, urinary tract infections, brucellosis, acne and many mixed infections.

Dosage and administration *Adult dosage:* A minimum dose of 250 mg tetracycline four times daily. This dose may be doubled in severe infections.

Pediatric dosage: A divided daily dose of 22-44 mg tetracycline per kg should be given according to the type and severity of the infection (see 'Precautions'). Mysteclin Syrup should preferably be taken one hour before, or two hours after meals.

Contra-indications, warnings, etc

Contra-indications: The tetracycline group of antibiotics is normally contra-indicated during pregnancy except in certain severe infections where tetracycline may be the drug of choice and the risk involved is justified. Administration of tetracyclines in pregnant women may result in hepatic injury, particularly if used for the treatment of pyelonephritis. Tetracyclines are deposited in the skeleton of the human foetus and may result in depression of bone growth and produce discolouration of the teeth in the child. As tetracycline passes into breast milk, breast feeding is not recommended during mysteclin therapy. Mysteclin should not be used in patients with a history of hypersensitivity to the tetracycline group of antibiotics. There are no known contra-indications to the use of amphotericin.

Precautions: In treating patients with renal dysfunction since tetracycline may produce azotaemia, hyperphosphataemia, acidosis, weight loss or nausea and vomiting. Absorption of tetracycline from the gut is diminished by milk, salts of calcium, magnesium, aluminium and iron. Impaired absorption also results from alkalis, and concomitant administration of antacids should therefore be avoided.

The effects of anticoagulants are not usually altered by concurrent treatment with tetracycline, although a few isolated cases of enhancement have been described. Therefore, occasionally, reduction in doses of concurrent anticoagulants may be required.

Tetracyclines may be deposited in areas of calcification of bones and teeth. The use of drugs of the tetracycline class during tooth development (last half of pregnancy, infancy and childhood to the age of eight years) may cause permanent discolouration of the teeth (yellow-brown). This reaction is more common during long-term use of the drugs but has been observed following repeated short-term courses. Enamel hypoplasia has also

been reported. Tetracycline drugs, therefore, should not be used in this age group unless other drugs are not likely to be effective or are contra-indicated.

There are no special precautions for the oral use of amphotericin.

Side-effects: Mysteclin is generally well tolerated, but a few patients may experience gastro-intestinal side-effects such as nausea, vomiting and diarrhoea.

A phototoxic reaction may be produced in some patients, although such reactions are less common with tetracycline than with other members of the group.

No systemic effects or allergic reactions have been associated with the oral use of amphotericin.

Overdosage: The most common symptoms are nausea, vomiting and diarrhoea. The possibility of liver failure should be borne in mind.

Pharmaceutical precautions *Storage:* At room temperature, protected from direct sunlight. Once the bottle is opened the contents should be used within two months.

Diluent: Syrup BP. The diluted syrup to be used within two months.

Legal category POM.

Package quantities *Syrup:* Bottles of 100 ml.

Further information By the inclusion of amphotericin with tetracycline, the fungal overgrowth frequently associated with broad-spectrum antibiotic therapy is avoided.

Product licence number 0034/5055.

NOCTEC* CAPSULES

Presentation Clear, orange-red gelatin capsules printed Squibb and 626 in white, each containing 500 mg chloral hydrate in solution.

Uses *Actions:* The hypnotic, chloral hydrate, in doses of 0.5-1 g, produces sedation in approximately 15 minutes followed by sleep in about half an hour. The action of the drug is confined to the cerebral hemispheres and the drug has virtually no effect on REM sleep.

Indications: For insomnia, particularly in geriatric patients who tolerate barbiturates poorly. It is a satisfactory pre-operative sedative and is useful as an hypnotic and sedative during the first stages of labour. In post-operative care and control of pain, Noctec is a valuable adjunct to opiates and analgesics.

Dosage and administration *Adults and children over 12 years of age:* 500 mg to 1 g taken 15 to 30 minutes before bedtime or one to two hours before surgery. Daily dose should not exceed 2 g. The capsules should be taken with water.

Contra-indications, warnings, etc

Contra-indications: In patients with marked hepatic or renal impairment. Large doses should not be used in patients with severe cardiac disease. In the presence of marked gastritis Noctec is best avoided.

Precautions: In patients taking coumarin anticoagulants, when Noctec is withdrawn from the drug regime, or its dosage changed, careful monitoring of the prothrombin time is required.

Noctec should be administered with caution to patients who have previously exhibited an idiosyncrasy or hypersensitivity to chloral hydrate. As with other hyp-

notics, alcohol potentiates the sedative effect. Similarly, there is a danger of misuse and the possibility that habituation may develop.

Side-effects: Few, except gastric irritation which may occur in some patients. Excitement, delirium and tolerance are rarely encountered.

Overdosage: Gastric lavage accompanied by supportive therapy for the cardiovascular and respiratory systems.

Pharmaceutical precautions *Storage:* In a cool place; avoid freezing.

Legal category POM.

Package quantities Bottles of 50 capsules.

Further information Nil.

Product licence number 0034/5057.

NYSTADERMAL* CREAM

Presentation A yellow to light buff cream containing in each gram nystatin 100,000 units and triamcinolone acetonide 0.1%.

Uses *Actions:* Nystatin is an antifungal antibiotic active against a wide range of yeasts and yeast-like fungi, including *Candida albicans*. Triamcinolone acetonide is a potent fluorinated corticosteroid with rapid anti-inflammatory, antipruritic and anti-allergic actions. The cream is formulated for use on moist weeping lesions.

Indications: Nystadermal cream is indicated for those cases of cutaneous candidosis where the addition of a corticosteroid to the antifungal antibiotic may be beneficial in controlling the commonly associated inflammation and pruritus.

Nystadermal cream will also be of benefit in those cases of eczema where *Candida* is either the precipitating cause or present as a secondary invader.

Dosage and administration *Adults and children:* To be applied to moist weeping lesions two to four times daily.

Contra-indications, warnings, etc

Contra-indications: Nystadermal Cream is contra-indicated in tuberculous and most viral lesions of the skin, particularly herpes simplex, vaccinia and varicella. It is also contra-indicated for fungal lesions not susceptible to nystatin and bacterial skin infections.

Precautions: In infants, long-term continuous topical steroid therapy should be avoided as adrenal suppression can occur, even without occlusion. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods. However, the unproven theoretical teratogenic hazard must be placed in perspective against the need for steroids to maintain the health of patients.

Side-effects: Side-effects have rarely been reported and have been only mild in nature.

Pharmaceutical precautions *Storage:* At room temperature; avoid freezing.

Dilution: Not recommended, as this may reduce therapeutic efficacy of nystatin.

If necessary, refer to the manufacturer.

Legal category POM.

Package quantities 15 g tubes.

Further information Nil.

Product licence number

Nystadermal Cream 0034/0131

NYSTAN* CREAM, OINTMENT, GEL AND DUSTING POWDER

Presentation *Gel:* Yellow to amber, opaque, containing 100,000 units nystatin per gram.

Cream: Pale buff, containing 100,000 units per gram nystatin in a vanishing-cream base.

Ointment: Yellow to amber containing 100,000 units nystatin per gram in Plastibase*.

Dusting Powder: White to pale yellow, containing 100,000 units nystatin per gram of powder.

Uses *Actions:* Nystatin is an antifungal antibiotic acting against a wide range of yeasts and yeast-like fungi including *Candida albicans*.

Indications: For the treatment of cutaneous and mucocutaneous mycoses, particularly those caused by *albicans*.

Dosage and administration *Adults and children:* be applied two to four times daily.

Contra-indications, warnings, etc

Contra-indications: There are no known contra-indications or special precautions for topical application nystatin.

Side-effects: There have been no substantiated reports of sensitivity associated with topical nystatin.

Pharmaceutical precautions *Storage:*

Gel: In a cool place; avoid freezing.

Cream: At room temperature; avoid freezing.

Ointment: At room temperature.

Dusting Powder: At room temperature, keep tightly closed.

Dilution: Nystan topicals should not be diluted as this may reduce therapeutic efficacy.

If necessary, refer to the manufacturer.

Legal category POM.

Package quantities *Cream/Ointment:* Tubes of 15 g and 30 g.

Gel: Tubes of 30 g.

Dusting Powder: Packs of 15 g.

Further information Nil.

Product licence numbers

Nystan Gel 0034/0142

Nystan Cream 0034/5058

Nystan Dusting Powder 0034/5059

Nystan Ointment 0034/0161

NYSTAN* ORAL SUSPENSION AND TABLETS

Presentation *Oral Suspension:* Yellow, cherry-m flavoured suspension providing 100,000 units nystatin per ml.

N.B. Suspension contains sugar.

Tablets: Sugar-coated, chocolate-brown tablets printed in white with Squibb and 580, containing 500,000 units nystatin.

es Actions: Nystatin is an antifungal antibiotic active against a wide range of yeasts and yeast-like fungi, including *Candida albicans*.

ications: Suspension for the prevention and treatment of candidal infections of the oral cavity, oesophagus and intestinal tract. It provides effective prophylaxis against intestinal candidosis in those born of mothers with vaginal candidosis.

Tablets for intestinal candidosis. They may be used for prophylaxis of candidal overgrowth during courses of broad-spectrum antibiotics.

Usage and administration Adults: *Suspension:* For treatment of denture sores, and oral infections in adults caused by *C. albicans*, 1 ml of the suspension could be dropped into the mouth four times daily; it could be kept in contact with the affected areas as long as possible.

Tablets: For the treatment of intestinal candidosis 1 tablet four times daily, but this dose may be doubled. For prophylaxis a total daily dosage of 1 million units has been found to suppress the overgrowth of *C. albicans* in infants receiving broad-spectrum antibiotic therapy. Older people with intestinal candidosis who are unable to swallow tablets should be given 5 ml of the suspension four times a day.

Administration should be continued for 48 hours after clinical cure to prevent relapse.

Children: *Suspension:* In intestinal and oral candidosis (thrush) in infants and children, 1 ml should be dropped into the mouth four times a day. The longer the suspension is kept in contact with the affected area in the mouth, before swallowing, the greater will be its effect.

For prophylaxis in the newborn the suggested dose is 1 ml once daily.

Contra-indications, warnings, etc

Contra-indications: There are no known contraindications to the use of nystatin.

Precautions: Nystan Oral Suspension contains sugar. In children with disaccharide intolerance a sugar-free formulation is available.

Side-effects: Nausea, vomiting and diarrhoea have occasionally been reported with doses of nystatin exceeding 4 to 5 million units daily. No systemic effects or allergic reactions have been associated with its oral use.

Overdosage: Since the absorption of nystatin from the gastro-intestinal tract is negligible, overdosage causes no systemic toxicity.

Pharmaceutical precautions Storage: *Suspension:* At room temperature; avoid freezing.

Tablets: At room temperature.

Dilution: Not recommended as this may reduce therapeutic efficacy.

If necessary, refer to the manufacturer.

Legal category POM.

Package quantities *Suspension:* Bottles of 30 ml with graduated dropper.

Tablets: Bottles of 28 and 100.

Further information Nil.

Product licence numbers

Nystan Oral Suspension 0034/0130
Nystan Tablets 0034/5063

NYSTAN* PESSARIES, VAGINAL CREAM AND TRIPLE PACK

Presentation *Pessaries:* Pale yellow to tan, diamond-shaped, with Squibb logo and 457 engraved on one side, containing 100,000 units nystatin.

Vaginal Cream: Pale buff containing in each 4 g application 100,000 units nystatin.

Triple Pack: 28 Nystavescent* pessaries (containing 100,000 units nystatin in an effervescent matrix). 42 oral tablets each containing nystatin 500,000 units and 30 g Nystan Gel (containing 100,000 units nystatin per gram).

Uses **Actions:** Nystatin is an antifungal antibiotic active against a wide range of yeasts and yeast-like fungi, including *Candida albicans*.

Indications: For the treatment of candidal vaginitis. In addition to local therapy the Triple Pack contains tablets for the eradication of *Candida* from the gut and the gel for topical application in the anogenital area, thereby preventing reinfection.

Dosage and administration *Pessaries:* **Adults:** 1 or 2 pessaries should be inserted high into the vagina for 14 consecutive nights or longer, regardless of any intervening menstrual period.

Vaginal Cream: **Adults:** Insert 1 or 2 applications (of 4 g each) high into the vagina for 14 consecutive nights, or longer, regardless of any intervening menstrual period. Reinfection from the candidal content of the intestinal tract may be prevented by concomitant therapy with oral nystatin.

Nystatin Cream, Gel, Ointment or Dusting Powder should be applied to the perineal region 2-4 times daily, if necessary.

Note: To prevent reinfection with *Candida*, the male consort should be treated concurrently with Nystan Gel, applied to the external genital area 2-4 times daily during the treatment period.

Children: Vulvovaginal candidosis is rarely a problem in children. It is suggested that the vaginal cream is the most acceptable formulation for children, together with concomitant oral medication where necessary.

Contra-indications, warnings, etc

Contra-indications: There are no known contraindications to the use of nystatin.

Precautions: In pregnancy, care should be taken while using an applicator to prevent the possibility of mechanical trauma.

Side-effects: Nystan is well tolerated and no substantiated sensitivity reactions have been associated with its use. Some transient local discomfort may be experienced.

Overdosage of Oral Tablets: Since the absorption of nystatin from the gastro-intestinal tract is negligible, overdosage causes no systemic toxicity.

Pharmaceutical precautions Storage: *Pessaries:* At room temperature.

Triple Pack: In a cool, dry place.

Vaginal Cream: At room temperature; avoid freezing.

Dilution: Not recommended for Vaginal Cream as this may reduce therapeutic efficacy.

Legal category POM.

Package quantities *Pessaries:* Foiled, in packs of 15 and 100 with applicators.

Vaginal Cream: Tubes of 60 g with applicator.

Triple Pack: 28 Nystavescent Pessaries in foil strip with applicator. 42 Nystan Oral Tablets. 30 g Nystan Gel. Patient treatment instructions are enclosed.

Further information Nil.

Product licence numbers

Nystan Gel	0034/0142
Nystan Pessaries	0034/5062
Nystan Vaginal Cream	0034/0137
Nystan Oral Tablets	0034/5063
Nystavescent Pessaries	0034/0111

NYSTAVESCENT* PESSARIES

Presentation Pale yellow, diamond-shaped pessaries engraved with Squibb, each containing nystatin 100,000 units in an effervescent matrix.

Uses Actions: Nystatin is an antifungal antibiotic active against a wide range of yeasts and yeast-like fungi, including *Candida albicans*.

Indications: Local treatment of vulvovaginal candidosis.

Dosage and administration One or two pessaries should be inserted high into the vagina for 14 consecutive nights or longer regardless of any intervening menstrual period.

Re-infection from the candidal content of the intestinal tract may be prevented by the concomitant therapy with oral nystatin (Nystan*).

Similarly, Nystan Cream, Ointment or Powder should be applied to the perineal region if necessary.

Contra-indications, warnings, etc

Contra-indications: There are no known contra-indications to the use of Nystavescent pessaries.

Side-effects: Occasionally some transient irritation and burning have been experienced.

Precautions: In pregnancy care should be taken in using an applicator to prevent the possibility of mechanical trauma.

Pharmaceutical precautions *Storage:* In a cool dry place.

Legal category POM.

Package quantities 15 Pessaries in foil strip with applicator. 100 Pessaries in foil strip with 6 applicators.

Further information Nil.

Product licence number 0034/0111.

OPHTHAINE* SOLUTION

Presentation Sterile, aqueous ophthalmic solution containing:

Proxymetacaine hydrochloride	0.5%
Chlorbutol	0.2%
Benzalkonium chloride	0.01%

Uses Actions: Proxymetacaine hydrochloride is a rapidly acting local anaesthetic. With a single drop the onset of anaesthesia occurs in an average of 13 seconds and will persist for an average of 15 minutes.

Indications: Topical anaesthesia in ophthalmic practice.

Dosage and administration *Adults and children:* Administered by topical instillation into the eye. The recommended doses are as follows:

Deep anaesthesia: Instil 1 drop every five to ten minutes for 5–7 doses.

Removal of sutures: Instil 1 or 2 drops two or three minutes before removal of stitches.

Removal of foreign bodies: Instil 1 or 2 drops prior to operating.

Tonometry: Instil 1 or 2 drops immediately before measurement.

Contra-indications, warnings, etc

Contra-indications: There are no known contra-indications with Ophthaine Solution.

Precautions: Ophthaine Solution is not miscible with fluorescein. However, the eye can be anaesthetised with Ophthaine Solution before fluorescein is administered. Regular and prolonged use of a topical ocular anaesthetic, e.g. in conjunction with contact lens insertion, may cause softening and erosion of the corneal epithelium which could produce corneal opacification with accompanying loss of vision.

Side-effects: Pupillary dilatation or cycloplegic effects have rarely been observed with Ophthaine Solution. Irritation of the conjunctiva or other toxic reactions attributable to the preparation have occurred only rarely.

Pharmaceutical precautions *Storage:* In a refrigerator. Discard any solution which is discoloured. The product should not be used one month after first opening the container.

Legal category POM.

Package quantities Bottles of 15 ml.

Further information Nil.

Product licence number 0034/5064.

PRONESTYL* TABLETS AND SOLUTION FOR INJECTION

Presentation *Tablets:* White, engraved Squibb at 754 on one side and scored on reverse, containing 250 mg procainamide hydrochloride.

Solution for Injection: A sterile, aqueous solution containing 100 mg/ml procainamide hydrochloride.

Uses Actions: Procainamide depresses the excitability of cardiac muscle to electrical stimulation and slows conduction in the atrium, the bundle of His and the ventricle, thereby reversing rhythmical abnormalities. In atrial arrhythmias procainamide slows atrial rate and may re-establish normal sinus rhythm.

The action of procainamide begins almost immediately after intramuscular or intravenous administration. Following oral administration, plasma levels are comparable to those obtained parenterally and therapeutic levels are usually obtained in 30 minutes.

Procainamide is less readily hydrolysed than procaine and plasma levels decline slowly – about 10–20% per hour.

The effects of Pronestyl are more beneficial in ventricular than in supraventricular, auricular and nodal arrhythmias.

Indications: Ventricular tachycardia, ventricular ectopic contractions, ventricular fibrillation, supraventricular auricular and nodal tachycardia. In the arrhythmias resulting from anaesthesia and cardiac surgery.

Dosage and administration *Adults – injection:* In most cases 25–50 mg per minute may be given intravenously under ECG control up to a total of 1 g. Where G control is not available 250 mg may be given ramucularly supplemented by oral dosage. In less severe cases and in maintenance therapy a dose of 100–200 mg may be given by intramuscular injection every 4 to 6 hours.

Oral: If used in conjunction with electrical defibrillation Pronestyl 250 mg every six hours will prevent recurrence in the majority of cases.

Following intravenous therapy or for less urgent cases 100 mg by mouth every four to six hours is an alternative route to parenteral administration.

Oral administration of Pronestyl is preferable. When parenteral therapy is necessary the intramuscular route of administration is the method of choice, the intravenous route being limited to emergencies and cases under ECG control.

Plasma concentrations correlate well with therapeutic and toxic effects: consequently plasma level assays could be carried out if facilities are available. The usual effective anti-arrhythmic concentration is 0.4–0.8 mg/100 ml. Toxic manifestations are rare in concentrations less than 1.2 mg/100 ml.

Pronestyl is not recommended for use in children.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to the drug is an absolute contra-indication. In this connection, cross sensitivity to procaine and related drugs must be borne in mind. Pronestyl is contra-indicated in patients with myasthenia gravis.

Procainamide should not be administered to patients with complete atrioventricular heart block. Procainamide is also contra-indicated in cases of high degree A-V block unless an electrical pacemaker is operative.

Precautions: Hypotension may occur when Pronestyl is administered intravenously and it should not be given to unconscious patients at a rate greater than 50 mg per minute up to a total of 1 g. Therefore, to initiate therapy, the intravenous dose should be diluted in 5% dextrose solution and BP prior to administration to facilitate control of dosage rate. Patients should be kept in a supine position and blood pressure readings made frequently. If hypotension occurs the rate of injection should be reduced and if necessary a vasopressor agent administered cautiously. ECG tracings should be made during an injection of Pronestyl so that administration may be stopped when the arrhythmia is interrupted or if evidence of extensive depression of conduction appears.

In patients with significant impairment of renal or hepatic function, accumulation of Pronestyl may occur, leading to drug toxicity.

Side-effects: Nausea, vomiting, diarrhoea, dizziness, headache, pruritis, chills, fever and allergic reactions are usually not sufficiently severe to discontinue treatment.

Agranulocytosis and a LE-like syndrome have been reported after prolonged courses of Pronestyl. The LE-like syndrome seldom appears in less than two months, but is very common after six months. It is virtually completely reversible and tests for antinuclear factors remain usually positive before clinical signs appear. If long-term treatment is considered desirable, it is advisable to undertake serological tests at no less than monthly intervals and to continue treatment for no longer than absolutely necessary.

Hypotension may occur particularly in conscious patients (see 'Precautions').

Overdosage: Severe hypotension may be treated by placing the patient in the supine position with the feet raised. If necessary an intravenous infusion of noradrenaline acid tartrate 8 mcg per ml in Sodium Chloride Injection BP may be started.

Pharmaceutical precautions *Storage:* Tablets/
Solution: At room temperature.

Legal category POM.

Package quantities *Tablets:* Bottles of 100.
Solution 100 mg/ml: 10 ml multidose vials.

Further information Nil.

Product licence numbers

Pronestyl Tablets 0034/5066
Pronestyl Solution 0034/5065

RAUDIXIN* TABLETS

Presentation *Tablets:* Orange, sugar-coated, printed Squibb and 713 in white, containing 50 mg *Rauwolfia serpentina* whole root.

Uses *Actions:* *Rauwolfia serpentina* is antihypertensive, tranquillising and bradycardic. The antihypertensive activity develops slowly over one to three weeks and may persist for a week after drug withdrawal.

Rauwolfia serpentina probably produces its antihypertensive effects through depletion of catecholamines from peripheral sites. In contrast, the sedative and tranquillising effects are thought to relate to brain 5-hydroxytryptamine depletion. It does not significantly affect normal blood pressure.

A complementary action is produced when combined with diuretics or other antihypertensive agents. Combined with other antihypertensive agents such as methyldopa or guanethidine, it permits a lower dosage of these to be given with a consequent reduction in their side-effects.

Indications: Raudixin is indicated in mild to moderate hypertension.

Dosage and administration *Adults:* Initially 4 tablets given daily in divided doses, morning and evening.

Maintenance therapy may vary from 1 to 6 tablets daily given as a single dose or as two divided doses.

Raudixin is not recommended for children.

Contra-indications, warnings, etc

Contra-indications: There are no known contra-indications.

Precautions: Patients with a past history of depression, suicidal tendencies, peptic ulcer or ulcerative colitis. Patients exhibiting signs of depression should be placed on a lower dosage or the drug should be discontinued. It should be administered with caution to patients with Parkinson's disease. *Rauwolfia* preparations cross the placental barrier and appear in cord-blood and breast milk. The safety of *Rauwolfia* in pregnancy has not been established.

Side-effects: Infrequent and mild in nature, which may be controlled by modifying dosage. These include nasal congestion, minor gastrointestinal disturbances, mild sedation and increased dreaming.

Overdosage: If conscious, emesis should be induced or the stomach emptied by aspiration or lavage. Atropine sulphate may be used to relieve para-symphathomimetic side-effects. Signs of motor dysfunction may be treated with benzhexol or other anti-Parkinsonian agents. Severe hypotension may respond to placing the patient in the supine position with the feet raised. Transfusion of plasma or suitable electrolyte solutions may be given slowly if necessary.

Pharmaceutical precautions *Storage:* At room temperature.

Legal category POM.

Package quantities Bottles of 100.

Further information Nil.

Product licence number 0034/5070.

RAUTRAX* TABLETS

Presentation Red, oblong, sugar-coated capsule-shaped, printed Squibb and 766 in black, containing *Rauwolfia serpentina* whole root 50 mg, hydroflumethiazide 50 mg and potassium chloride 625 mg.

Uses *Actions:* *Rauwolfia serpentina* is antihypertensive, tranquillising and bradycardic. The antihypertensive activity develops slowly over one to three weeks and may persist for a week after drug withdrawal. *Rauwolfia serpentina* probably produces its antihypertensive effects through depletion of the catecholamines from peripheral sites. In contrast, the sedative and tranquillising effects are thought to relate to brain 5-hydroxytryptamine depletion. It does not significantly affect normal blood pressure.

Hydroflumethiazide provides smooth reduction of elevated blood pressure but, where normal, has no appreciable effect.

Supplementary potassium provides protection against possible potassium depletion during long-term therapy.

When Rautrax is used in combination with other antihypertensives such as methyl dopa or guanethidine, it permits a lower dosage of these to be given, resulting in a reduction of the side-effects associated with these agents.

Indications: Mild to moderate hypertension.

Dosage and administration *Adults:* Initially 1-3 tablets preferably in divided doses morning and afternoon. After a period of two to three weeks a maintenance dose of as little as 1 tablet daily may suffice.

When used in combination with other antihypertensive agents it is recommended that the dosage of these should be reduced by at least one half.

Rautrax is not recommended for children.

Contra-indications, warnings, etc

Contra-indications: Severe renal failure.

Precautions: Any preparation containing *Rauwolfia* should be used with caution in patients with a history of depression, suicidal tendencies, peptic ulcer or ulcerative colitis, also in patients with Parkinson's disease. Care should be taken in treating patients with severely damaged kidneys and low urinary output. *Rauwolfia* preparations cross the placental barrier and appear in cord-blood and breast milk. The safety of *Rauwolfia* in pregnancy has not been established.

Side-effects: Infrequent and mild in nature, which may be controlled by modifying dosage. These include nasal congestion, minor gastro-intestinal disturbances, mild sedation and increased dreaming.

Warning: Symptoms and signs which might indicate ulceration or obstruction of the small bowel in patients taking tablets or capsules containing potassium salts; indications for stopping treatment immediately. The chance of this occurring with Rautrax is slight since the formulation is not enteric-coated.

Overdosage: If conscious, emesis should be induced the stomach emptied by aspiration or lavage. Atropine sulphate may be used to relieve parasympathomimetic side-effects. Signs of motor dysfunction may be treated with benzhexol or other anti-Parkinsonian agents. Severe hypotension may respond to placing the patient in the supine position with feet raised. Transfusions of plasma or suitable electrolyte solutions may be given slowly if necessary.

Pharmaceutical precautions *Storage:* At room temperature.

Legal category POM.

Package quantities Bottles of 100 and 500.

Further information Nil.

Product licence number 0034/5072.

REMIDERM* CREAM AND OINTMENT

Presentation *Cream:* white to pale buff vanishing cream containing triamcinolone acetonide 0.025% and halquinol 0.75%.

Ointment: white to pale buff, containing triamcinolone acetonide 0.025% and halquinol 0.75% in Plastibase*.

Uses *Actions:* Triamcinolone acetonide is a potent fluorinated corticosteroid with rapid anti-inflammatory antipruritic and anti-allergic actions.

Halquinol has a wide range of antimicrobial activity in contrast to the antibiotics, it is effective against most bacterial and fungal pathogens commonly found on the skin, also against antibiotic-resistant bacteria.

Indications: Inflammatory skin disorders, especially those complicated or threatened by secondary bacterial infection and/or fungal infection, including: atopic eczema, contact eczema, follicular eczema, infantile eczema, anogenital pruritus (pruritus ani et vulvae), nummular eczema, post-traumatic infective eczema, seborrhoeic or flexural eczema, neuro-dermatitis, psoriasis, otitis externa.

Dosage and administration *Adults and children:* To be applied two to four times daily.

Contra-indications, warnings, etc

Contra-indications: In tuberculous and most viral lesions of the skin, particularly herpes simplex, vaccinia or varicella.

Precautions: Care should be taken when applying Remiderm near the eyes. In infants long-term continuous topical corticosteroid therapy should be avoided. Adrenal suppression can occur, even without occlusion. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to humans has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

Side-effects: In acute weeping skin conditions transient stinging may be experienced. Sensitivity reactions to halquinol may occur.

Pharmaceutical precautions *Storage:* Cream: At room temperature; avoid freezing.

Intment: At room temperature.

Ilution: Not recommended. If dilution is necessary, the manufacturer should be consulted for advice. Halquinol incompatible with iron and certain other metals.

Legal category POM.

Package quantities Tubes of 15 g and 30 g.

Further information *Note:* Remiderm may cause slight staining on some clothing materials. Stains should disappear in laundering. Care should be taken to avoid contact with vinyl/plastic surfaces as these stains may be particularly resistant.

Product licence numbers

Remiderm Cream 0034/5076

Remiderm Ointment 0034/5077

REMIDERM* SPRAY

Presentation Aerosol preparation containing in each gram: 0.07 mg triamcinolone acetonide and 0.42 mg halquinol in a vehicle with propellant.

Uses *Actions:* Triamcinolone acetonide is a potent urinated corticosteroid with rapid anti-allergic actions. Halquinol has a wide range of antimicrobial activity; in contrast to the antibiotics, it is effective against most bacterial and fungal pathogens commonly found on the skin, also against antibiotic-resistant bacteria.

Indications: Inflammatory skin disorders, especially those complicated or threatened by secondary bacterial infection and/or fungal infection, including: atopic eczema, contact eczema, follicular eczema, infantile eczema, anogenital pruritis (pruritis ani et vulvae), nummular eczema, post-traumatic infective eczema, seborrhoeic or flexural eczema, neuro-dermatitis, psoriasis, otitis externa.

Dosage and administration *Adults and children:* To be applied two to four times daily.

Contra-indications, warnings, etc

Contra-indications: In tuberculous and most viral lesions of the skin, particularly herpes simplex, vaccinia and varicella.

Precautions: Care should be taken when applying Remiderm near the eyes. In infants, long-term continuous topical corticosteroid therapy should be avoided. Adrenal suppression can occur, even without occlusion. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to humans has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

Side-effects: In acute weeping skin conditions transient stinging may be experienced. Sensitivity reactions to halquinol may occur.

Pharmaceutical precautions *Storage:* At room temperature. Normal aerosol precautions should be observed.

Legal category POM.

Package quantities 50 g aerosol cans.

Further information *Note:* Remiderm may cause slight staining on some clothing materials. Stains should disappear in laundering. Care should be taken to avoid contact with vinyl/plastic surfaces as these stains may be particularly resistant.

Product licence number 0034/5078.

REMOTIC* EAR DROP CAPSULES

Presentation Each 0.3 ml opaque, yellow, nozzle soft gelatin capsule contains:

Triamcinolone acetonide	0.025%
Halquinol	0.75%

Uses *Actions:* Triamcinolone acetonide is a potent, fluorinated corticosteroid with rapid anti-inflammatory, antipruritic and anti-allergic actions.

Halquinol has a wide range of antimicrobial activity; in contrast to the antibiotics, it is effective against most bacterial and fungal pathogens commonly found on the skin, also against antibiotic-resistant bacteria.

Indications: For the treatment of inflammatory and infective conditions of the auditory meatus, including: otitis externa, chronic and acute otomycosis, otorrhoea, chronic suppurative otitis media, infected fenestration cavities, infected mastoid cavities.

†As an adjunct to systemic chemotherapy or other measures as indicated.

Dosage and administration *Adults and children:* The contents of 1 capsule should be squeezed into the ear two or three times daily.

Contra-indications, warnings, etc

Contra-indications: Tuberculous or viral skin disorders.

Precautions: Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to humans has not been established. However, topical steroids should not be used extensively in pregnancy i.e. in large amounts or for long periods. Not to be used near the eyes.

Side-effects: Transient stinging may occur in acute weeping lesions. Sensitivity reactions to halquinol may occur.

Pharmaceutical precautions *Storage:* In a cool place; avoid freezing.

Legal category POM.

Package quantities 15 capsules in foil strip.

Further information *Note:* Remotic may cause staining on some clothing materials. Stains should disappear in laundering. Care should be taken to avoid contact with vinyl/plastic surfaces as these stains may be particularly resistant.

Product licence number 0034/5079.

TRI-ADCORTYL* CREAM, OINTMENT AND OTIC OINTMENT

Presentation *Cream:* Pale buff.

Ointment: Yellow to amber.

Otic Ointment: Presentation for aural use.

Containing in each gram the following:

Triamcinolone acetoneide	0.1%
Neomycin (as sulphate)	0.25%
Gramicidin	0.025%
Nystatin	100,000 units

Uses Actions: Triamcinolone acetoneide is a potent fluorinated corticosteroid with rapid anti-inflammatory, antipruritic and anti-allergic actions.

The combined action of the antibiotics neomycin and gramicidin provides comprehensive antibacterial therapy against a wide range of Gram-positive and Gram-negative bacteria, including those micro-organisms responsible for most bacterial skin infections.

Nystatin is an antifungal antibiotic, active against a wide range of yeasts and yeast-like fungi, including *Candida albicans*.

Indications: The topical treatment of superficial bacterial infections, cutaneous candidosis and dermatological conditions known to respond to topical steroid therapy when threatened or complicated by bacterial or candidal superinfections. These include: atopic eczema, contact eczema, follicular eczema, infantile eczema, otitis externa, anogenital pruritus (pruritus ani et vulvae), nummular eczema, post-traumatic infective eczema, seborrhoeic or flexural eczema, neurodermatitis, psoriasis.

Dosage and administration Adults and children: *Cream, ointment:* Apply to the affected areas two to four times daily.

Otic Ointment: After cleaning, apply the nozzle to the aural canal and squeeze a small amount into the canal two to four times daily.

Contra-indications, warnings, etc

Contra-indications: In tuberculous and most viral lesions of the skin, particularly herpes simplex, vaccinia and varicella. Also in fungal lesions not susceptible to nystatin.

Precautions: Since the use of occlusive dressings may increase the risk of sensitivity, such dressings should be avoided. In infants, long-term continuous topical steroid therapy should be avoided. Adrenal suppression may occur, even without occlusion.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to humans has not been established. However topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

Otic Ointment: Care is necessary in applying this preparation if perforation of the eardrum is suspected.

Not for ophthalmic use.

Side-effects: Sensitivity reactions to neomycin may occur; gramicidin sensitivity has occasionally been reported.

Pharmaceutical precautions Storage: *Cream:* At room temperature; avoid freezing.

Ointment: At room temperature.

Dilution: Not recommended, as this would reduce the concentration of the antibiotics to below therapeutic levels.

Legal category POM.

Package quantities Tubes of 15 g and 30 g.

Otic Ointment: Tubes of 10 g.

Further information Tri-Adcortyl Ointment is preservative-free, and avoids the risk of allergic reactions to preservatives.

Product licence numbers

Tri-Adcortyl Cream	0034/5093
Tri-Adcortyl Ointment	0034/5094
Tri-Adcortyl Otic Ointment	0034/5095

TRICADERM* SOLUTION

Presentation Colourless alcoholic solution containing:

Triamcinolone acetoneide	0.2%
Salicylic acid	2.0%
Benzalkonium chloride	0.05%

Uses Actions: Triamcinolone acetoneide is a potent fluorinated corticosteroid with rapid anti-inflammatory antipruritic and anti-allergic actions.

Salicylic acid has bacteriostatic and fungicidal properties, it is also keratolytic.

Benzalkonium chloride is bactericidal in low concentration against a wide range of Gram-positive and Gram-negative bacteria.

Indications: Tricaderm Solution is indicated for steroid-responsive dermatoses of the scalp such as seborrhoea psoriasis, circumscribed chronic dermatoses and alopecia areata. Also chronic discoid lupus erythematosus and mycoses fungoides of the face.

Dosage and administration Adults: To be applied each evening before the patient retires. The solution should be applied drop by drop to cover the affected area. If a standard or occlusive dressing is to be used, it should be removed in the morning. As improvement occurs treatment need be repeated only every second or third night. Therapy should continue for not more than four weeks.

Tricaderm Solution is not recommended for children.

Contra-indications, warnings, etc

Contra-indications: Tuberculous and most viral lesions of the skin, particularly herpes simplex, vaccinia and varicella.

Systemic absorption could occur if occlusive dressings are used for an extensive area of the scalp.

Precautions: On acute lesions, transient stinging may be experienced. Caution should be exercised in dermatoses of the scalp where deep seated infections are suspected. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods. Tricaderm Solution must be kept away from the eyes. It is inflammable and, on scalp application, hair should not be dried in front of an open fire.

Side-effects: Tricaderm Solution is well tolerated. Local intolerance due to triamcinolone acetoneide or benzalkonium chloride is rare; however, salicylic acid may be mildly irritating.

Pharmaceutical precautions Storage: In a cool place.

Dilution: Not to be diluted.

Legal category POM.

Package quantities Bottles of 25 ml.

Further information Nil.

Product licence number 0034/5096.

'ELOSEF' CAPSULES 'ELOSEF' SYRUP

Presentation *Capsules* 250 mg: Opaque, orange body with opaque blue cap printed Squibb and 113 in white on each half. Each capsule contains 250 mg cephadrine.

Capsules 500 mg: Opaque blue printed in white with Squibb and 114 on each half. Each capsule contains 500 mg cephadrine.

Syrup 125 mg: When reconstituted contains 125 mg cephadrine per 5 ml.

Syrup 250 mg: When reconstituted contains 250 mg cephadrine per 5 ml.

Uses *Actions:* Cephadrine is a broad-spectrum, bactericidal antibiotic active against both Gram-positive and Gram-negative bacteria. It is also highly active against most strains of penicillinase-producing *Staphylococci*.

Microbiology: The following organisms have shown *in vitro* sensitivity to cephadrine:

Gram-positive – *Staphylococci* (both penicillin sensitive and resistant strains), *Streptococci*, both *Streptococcus pyogenes* (beta haemolytic) and Group D *Streptococcus* (enterococci) and *Diplococcus pneumoniae*.

Gram-negative – *E. coli*, *Klebsiella* and *Enterobacter* spp., *Proteus mirabilis* and other indole-negative *Proteus* spp., *Haemophilus influenzae*, *Shigella*, *Salmonella* and *Veissaria* spp.

Because cephadrine is unaffected by penicillinase, many strains of *E. coli* and *Staphylococcus aureus* which produce this enzyme are susceptible to cephadrine but resistant to ampicillin.

Indications: In the treatment of infections of the urinary, respiratory and gastro-intestinal tracts and of the skin and soft tissues. These include:

Upper respiratory infections – pharyngitis, sinusitis, otitis media, tonsillitis.

Lower respiratory infections – acute and chronic bronchitis, pneumonia.

Urinary tract infections – cystitis, urethritis, pyelonephritis.

Skin and soft tissue infections – abscess, cellulitis, furunculosis.

Gastro-intestinal tract – bacillary dysentery, enteritis.

Cephadrine has been shown to be effective in reducing the incidence of postoperative infections in patients undergoing surgical procedures associated with a high risk of infection. It is also of value where postoperative infections would be disastrous and where patients have a reduced host resistance to bacterial infection. Protection is best ensured by achieving adequate local tissue concentrations at the time contamination is likely to occur. Thus, cephadrine should be administered immediately prior to surgery and continued during the postoperative period.

Bacteriology studies to determine the causative organisms and their sensitivity to cephadrine should be performed. Therapy may be instituted prior to receiving the results of the sensitivity test.

Dosage and administration *Adults:* For urinary tract infections the usual dose is 500 mg four times daily or 1 g twice daily; severe or chronic infections may require

larger doses. Prolonged intensive therapy is needed for complications such as prostatitis and epididymitis. For respiratory tract infections and skin and soft tissue infections the usual dose is 250 mg or 500 mg four times daily or 500 mg or 1 g twice daily depending on the severity and site of infections. For gastro-intestinal tract infections, 500 mg three or four times daily may be employed.

Children: The usual dose is from 25 to 50 mg/kg/day total, given in two or four equally divided doses. For severe or chronic infections the dosage may be doubled, but the maximum dose should not exceed 4 g per day.

All patients, irrespective of age and weight: Larger doses (up to 1 g four times daily) may be given for severe or chronic infections. Therapy should be continued for a minimum of 48-72 hours after the patient becomes asymptomatic or evidence of bacterial eradication has been obtained. In infections caused by haemolytic strains of streptococci, a minimum of 10 days treatment is recommended to guard against the risk of rheumatic fever or glomerulonephritis.

Contra-indications, warnings, etc

Contra-indications: Patients with known hypersensitivity to the cephalosporin antibiotics.

Precautions: There is evidence of partial cross-allergenicity between the penicillins and the cephalosporins. Therefore cephadrine should be used with caution in those patients with known hypersensitivity to penicillins.

Patients with known or suspected renal impairment should receive careful clinical observation and appropriate laboratory studies since cephadrine may accumulate in the serum and tissues unless dosage is suitably reduced.

Although animal studies have not demonstrated any teratogenicity, as with all drugs caution should be exercised in pregnancy.

Cephadrine is excreted in breast milk and should be used with caution in lactating mothers.

After treatment with cephadrine, a false positive reaction for glucose in the urine may occur with Benedict's or Fehling's solution or with reagent tablets such as Clinistix[®], but not with enzyme-based tests such as Clinistix[®] or Diastix[®].

As with all antibiotics, prolonged use may result in overgrowth of non-susceptible organisms.

Pseudomonads are uniformly resistant to the cephalosporin class of antibiotics.

Side-effects: Limited essentially to gastro-intestinal disturbances and on occasion to hypersensitivity pneumonia. The latter are more likely to occur in individuals who have previously demonstrated hypersensitivity and those with a history of allergy, asthma, hay fever or urticaria. The majority of reported side-effects have been mild. Skin reactions have occasionally been reported.

Adverse reaction reports are rare, but include glossitis, heartburn, nausea, vomiting and diarrhoea. Hypersensitivity reactions include urticaria, skin rashes and joint pains.

As with other oral cephalosporins, mild transient eosinophilia and rarely positive direct Coombs tests have been reported.

Pharmaceutical precautions *Storage: Capsules:* In a cool place.

Powder for syrup: A cool place. After reconstitution; discard unused syrup after 14 days if stored in refrigerator, or seven days at room temperature.

Dilution: Velosef Syrup may be diluted with Syrup BP. The diluted syrup should be used within seven days.

Legal category POM.

Package quantities *Capsules:* Boxes of 20 in foil and bottles of 100.

Syrup: Bottles of 100 ml.

Further information Cephadrine has a high degree of stability to many beta-lactamases. It has a low degree of protein-binding and a large volume of distribution. Therefore, tissue levels are generally found to be high. Oral cephradine can be given twice or four times daily, and is well absorbed.

Product licence numbers

Velosef Capsules 250 mg	0034/0133
Velosef Capsules 500 mg	0034/0134
Velosef Syrup 125 mg/5 ml	0034/0135
Velosef Syrup 250 mg/5 ml	0034/0136

VELOSEF* FOR INJECTION

Presentation Velosef for Injection is a sterile powder blend of cephradine and L-arginine. After reconstitution, Velosef for Injection 500 mg, 1.0 g and 2.0 g vials provide 500 mg, 1.0 g and 2.0 g of cephradine activity, respectively.

Uses *Actions:* Cephradine is a broad-spectrum bactericidal antibiotic active against both Gram-positive and Gram-negative bacteria. It is also highly active against most strains of penicillinase-producing staphylococci.

Microbiology: The following organisms have shown in vitro sensitivity to cephradine:

Gram-positive – *Staphylococci* (both penicillin sensitive and resistant strains), *Streptococci*, both *Streptococcus pyogenes* (beta haemolytic) and Group D *Streptococci* (enterococci) and *Diplococcus pneumoniae*.

Gram-negative – *E. coli*, *Klebsiella* and *Enterobacter* spp.; *P. mirabilis* and other indole-negative *Proteus* spp., *Haemophilus influenzae*, *Shigella* spp., *Salmonella* spp. (including *Salmonella typhi*) and *Neisseria* spp.

Because cephradine is unaffected by penicillinase, many strains of *E. coli* and *Staphylococcus aureus* which produce this enzyme are susceptible to cephradine but resistant to ampicillin.

Indications: The treatment of infections of the urinary, respiratory and gastro-intestinal tracts and of the skin and soft tissues, bones and joints; also septicaemia and endocarditis. These include:

Upper respiratory infections – pharyngitis, sinusitis, otitis media, tonsillitis, laryngo-tracheo-bronchitis.

Lower respiratory infections – acute and chronic bronchitis, lobar and bronchopneumonia.

Urinary tract infections – cystitis, pyelonephritis.

Skin and soft tissue infections – abscess, cellulitis, furunculosis, impetigo.

Gastro-intestinal tract – bacillary dysentery, enteritis, peritonitis.

Cephradine has been shown to be effective in reducing the incidence of postoperative infections in patients undergoing surgical procedures associated with a high risk of infection. It is also of value where post-operative infection would be disastrous and where patients have a reduced host resistance to bacterial infection. Protection is best ensured by achieving adequate local tissue concentrations at the time contamination is likely to

occur. Thus, cephradine should be administered immediately prior to surgery and continued during the postoperative period.

Bacteriological studies to determine the causative organisms and their sensitivity to cephradine should be performed. Therapy may be instituted prior to receiving the results of the sensitivity test.

Sterile cephradine for injection is indicated primarily for those patients unable to tolerate oral medication. It is also indicated for intravenous use either by direct injection or by intravenous infusion for the treatment of serious and life-threatening infections.

Dosage and administration Intramuscular or intravenous injection and intravenous infusion.

Adults: The usual dose range of cephradine for injection is 2-4 g daily in four equally divided doses. This may be increased up to 8 g a day for severe infections, e.g. septicaemia and endocarditis. For the majority of infections, the usual dose is 500 mg q.i.d. in equally spaced doses; severe or chronic infections may require large doses. Prolonged intensive therapy is needed for complications such as prostatitis and epididymitis. Patients who are severely ill and who require high serum levels of cephradine for treating their infections should be started on intravenous therapy.

Limited experience indicates that intraperitoneal administration of cephradine may be effective after surgery in cases of peritonitis where a surgical drainage system has been established.

Children: The usual dose is 50-100 mg/kg/day total given in four equally divided doses. More serious illnesses (e.g. typhoid fever) may require 200-300 mg/kg/day.

All patients, regardless of age and weight: Therapy should be continued for a minimum of 48-72 hours after the patient becomes asymptomatic or evidence of bacterial eradication has been obtained. In infections caused by haemolytic strains of streptococci, a minimum of 10 days of treatment is recommended to guard against the risk of rheumatic fever or glomerulonephritis. In the treatment of chronic urinary tract infections, frequent bacteriological and clinical appraisal is necessary during therapy and may be necessary for several months afterwards. Persistent infections may require treatment for several weeks. Smaller doses than those indicated above should not be used. Doses for children should not exceed doses recommended for adults. As cephradine is available in both injectable and oral form, patients may be changed from cephradine injectable to cephradine oral at the same dosage level.

Reconstitution: For intramuscular use: Aseptically add sterile water for injection or 0.9% sodium chloride injection according to the following table:

Single dose* vial size	Volume of diluent to be added
500 mg	2.0 ml
1 g	4.0 ml
2 g	8.0 ml

* Preparation contains no bactericide and is not intended for multiple dose use.

Shake to effect solution and withdraw the entire contents. Intramuscular solutions should be used within 2 hours at room temperature; when stored in a refrigerator at 5°C, solutions retain full potency for 12 hours. Reconstituted solutions may vary in colour from light to straw yellow; however, this does not affect the potency.

or intravenous use: Cephadrine for injection may be administered by direct intravenous injection or by infusion. A 3 mcg/ml serum concentration can be maintained for each milligram of cephadrine per kg body weight per hour of infusion.

or direct intravenous administration: Suitable intravenous injection solutions are Sterile Water for Injection, 5% Dextrose Injection or 0.9% Sodium Chloride Injection.

Aseptically add 5 ml of diluent to the 500 mg vial, 10 ml to the 1 g vial or 20 ml to the 2 g vial. Shake to effect solution and withdraw the entire contents. The solution may be slowly injected directly into a vein over 3 to 5 minute period. The solution should be used within 2 hours when kept at room temperature; if stored at 5°C, solutions retain full potency for 12 hours.

or continuous or intermittent intravenous infusion: Suitable intravenous infusion solutions are Sterile Water for Injection (50 mg/ml cephadrine solutions are approximately isotonic); 5% or 10% Dextrose Injection, 0.9% Sodium Chloride Injection, Sodium Lactate Injection (M/6 sodium lactate); Dextrose and Sodium Chloride Injection; Lactated Ringer's Injection; Ringer's Injection; 5% Dextrose in Lactated Ringer's Injection; 5% Dextrose in Ringer's Injection.

V.B. Only cephadrine solubilised with arginine may be reconstituted with solutions containing calcium salts, such as Ringer's Solutions.

For further information on compatibilities consult the manufacturer.

Contra-indications, warnings, etc

Contra-indications: Patients with known hypersensitivity to the cephalosporin antibiotics.

Precautions: There is evidence of partial cross-allergenicity between the penicillins and the cephalosporins. Therefore cephadrine should be used with caution in those patients with known hypersensitivity to penicillins.

Patients with known or suspected renal impairment should receive careful clinical observation and appropriate laboratory studies, since cephadrine may accumulate in the serum and tissues unless the dosage is suitably reduced.

Although animal studies have not demonstrated any teratogenicity, safety in pregnancy has not been established.

Cephadrine is excreted in breast milk and should be used with caution in lactating mothers.

After treatment with cephadrine a false positive reaction for glucose in the urine may occur with Benedict's solution or Fehling's solution or with reagent tablets such as Clinistix*, but not with enzyme-based tests such as Clinistix* or Diastix*.

As with all antibiotics, prolonged use may result in overgrowth of non-susceptible organisms.

Pseudomonas are uniformly resistant to the cephalosporin class of antibiotics.

Side-effects: As with other cephalosporins untoward reactions will be limited essentially to gastro-intestinal disturbances and on occasion to hypersensitivity phenomena. The latter are more likely to occur in individuals who have previously demonstrated hypersensitivity and those with a history of allergy, asthma, hay fever or urticaria.

The majority of reported side-effects have been mild. Skin reactions have occasionally been reported.

Adverse reaction reports are rare but include glossitis, heartburn, nausea, vomiting and diarrhoea. Skin and

hypersensitivity reactions include urticaria, skin rashes and joint pains.

Although slight and transient elevations of BUN have been encountered, the serum creatinine measured in half the patients proved to be within normal limits, suggesting an extrarenal cause for the elevated readings.

As with other oral cephalosporins, mild transient eosinophilia and rarely positive direct Coombs tests have been reported.

Scattered and transient elevations in LDH's, serum transaminases and other liver function tests show no pattern suggestive of hepatic involvement but are more likely to be due to minor tissue damage at the site of injection, as has been reported with other injectable drugs.

As with other parenterally administered antibiotics, transient pain may be experienced at the injection site, but is seldom the cause for discontinuing treatment. Thrombophlebitis has been reported following intravenous injection.

No tooth pigmentation, photosensitivity or major blood dyscrasias have been reported.

Pharmaceutical precautions *Storage (before reconstitution):* At room temperature.

Legal category POM.

Package quantities 500 mg single-dose vials: Pack of 5.

1 g single-dose vials: Single-vial pack.

2 g single-dose vials: Single-vial pack.

Further information Nil.

Product licence numbers

Velosef Injection 500 mg 0034/0198

Velosef Injection 1 g 0034/0199

Velosef Injection 2 g 0034/0200

VERDIVITON* ELIXIR

Presentation Clear, green liquid containing in each 15 ml:

Thiamine mononitrate (vitamin B ₁)	2 mg
Riboflavin (vitamin B ₂)	1 mg
Pyridoxine hydrochloride (vitamin B ₆)	0.5 mg
Nicotinamide	15 mg
d-Panthenol	1 mg
Cyanocobalamin (vitamin B ₁₂)	15 mcg
Calcium glycerophosphate	110 mg
Sodium glycerophosphate	80 mg
Potassium glycerophosphate	20 mg
Manganese glycerophosphate	10 mg
Alcohol	17% by volume

Uses *Indications:* The maintenance of adequate levels of B vitamins particularly in those conditions where such levels may be thought to be lowered.

Dosage and administration *Adults:* Three 5 ml spoonfuls three times daily.

Children up to 12 years of age: One or two 5 ml spoonfuls in water three times daily.

Verdiviton should preferably be taken before meals.

Contra-indications, warnings, etc

Contra-indications: Where the use of alcohol is undesirable, hepatitis and alcoholism.

1250

E. R. SQUIBB & SONS LIMITED

Pharmaceutical precautions *Storage:* Cool place,
protected from light.

Further information Nil.

Legal category P.

Product licence number 0034/5097.

Package quantities Bottles of 240 ml.

**Trade Mark*

Stafford-Miller Limited

Stafford-Miller House

The Common

Hatfield, Herts AL10 0NZ

ALPHOSYL*

Representation *Lotion and Cream*: Containing allantoin 5% refined alcoholic extract of coal tar 5% in a greaseless vanishing-cream base.

Application PC: Refined alcoholic extract of coal tar 5% allantoin 0.2% in a foaming shampoo base.

The lotion is a light free-flowing emulsion and the cream is smooth and homogeneous, light tan in colour. The application is a light green/tan soft shampoo.

Uses Dermatological stimulant for the treatment of psoriasis, psoriasis of the scalp and dandruff.

Dosage and administration *Lotion and Cream*: Apply liberally two to four times daily, massage gently into the affected areas. Occlusive dressings are unnecessary.

Application PC: Wet scalp and hair, apply shampoo and vigorously massage to lather, rinse and repeat if necessary.

Contra-indications, warnings, etc For external use only. Discontinue if irritation occurs or in cases of sensitivity to coal tar.

Pharmaceutical precautions Do not refrigerate.

Legal category P.

Package quantities *Alphosyl Lotion*: Bottles of 50 ml.

Alphosyl Cream: Tube of 75 g.

Alphosyl Application PC: Tube of 60 g.

Further information Alphosyl Lotion is the basic treatment for psoriasis of the body and scalp.

Alphosyl Cream is designed especially for lubrication of the intertriginous areas.

Alphosyl Application PC is an adjunctive therapy for patients with psoriasis of the scalp, dandruff and other scalp disorders. It prevents irritation of the scalp and is used also in preparation for treatment with the Lotion.

Product licence numbers

Alphosyl Lotion 0036/5008

Alphosyl Cream 0036/5006

Alphosyl Application PC 0036/5005

ALPHOSYL* HC CREAM

Representation A cream containing refined alcoholic extract of coal tar 5% allantoin 2% and hydrocortisone PhEur 0.5% in a greaseless vanishing cream base. The cream is smooth, homogeneous, and is light tan in colour.

Uses Dermatological stimulant and local corticosteroid anti-inflammatory therapy for psoriasis.

Dosage and administration Apply two to four times daily, massaging gently into the affected areas.

Contra-indications, warnings, etc In infants, long-

term continuous therapy should be avoided. Adrenal suppression can occur even without occlusion.

Topical administration of corticosteroids to pregnant animals can cause abnormality of foetal development. The relevance of this finding to human beings has not been established. However, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for long periods.

Pharmaceutical precautions Store at room temperature.

Legal category POM.

Package quantities Tubes of 30 g and 45 g.

Further information Alphosyl HC Cream is intended for the treatment of the acute stages of psoriasis when the basic Alphosyl action is enhanced by the addition of hydrocortisone.

Product licence number 0036/0026.

COLIFOAM*

Representation White, odourless aerosol foam containing hydrocortisone acetate PhEur 10%. Other ingredients: propylene glycol, ethoxylated stearyl alcohol, polyoxyethylene-10-stearyl ether, cetyl alcohol, methyl and propyl parabens, triethanolamine and water. Inert propellants added.

Uses Anti-inflammatory corticosteroid therapy for the topical treatment of ulcerative colitis, proctosigmoiditis and granular proctitis.

Dosage and administration One applicatorful inserted into the rectum once or twice daily for two or three weeks and every second day thereafter. Shake can vigorously before use (illustrated instructions are enclosed in each pack).

Satisfactory response usually occurs within five to seven days.

Contra-indications, warnings, etc Local contra-indications to the use of intrarectal steroids include obstruction, abscess, perforation, peritonitis, fresh intestinal anastomoses and extensive fistulas.

General precautions common to all corticosteroid therapy should be observed during treatment with Colifoam. Treatment should be administered with caution in patients with severe ulcerative disease because of their predisposition to perforation of the bowel wall.

Safety during pregnancy has not been fully established.

Pharmaceutical precautions Do not refrigerate, incinerate or puncture the aerosol can. Shake vigorously before use. Keep out of reach of children.

Legal category POM.

Package quantities Aerosol canister containing 20 g

(14 applications) plus a plastic applicator and illustrated leaflet.

Further information One applicatorful of Colifoam provides a dose of approximately 90–100 mg of hydrocortisone acetate, similar to that used in a retention enema, for the treatment of ulcerative colitis, sigmoiditis and proctitis.

Product licence number 0036/0021.

EPIFOAM*

Presentation Muco-adherent, white, odourless aerosol foam containing:

Hydrocortisone acetate PhEur 1%

Pramoxine hydrochloride USP XX 1%

Other ingredients: propylene glycol, ethoxylated stearyl alcohol, polyoxyethylene-10-stearyl ether, cetyl alcohol, methyl *p*-hydroxybenzoate, propyl *p*-hydroxybenzoate, triethanolamine, deionised water, in aerosol canisters containing 10 g.

Uses For the treatment of post-episiotomy pain and discomfort. Also for the relief of steroid responsive dermatoses.

Dosage and administration A suitable quantity of foam should be dispensed onto a pad, preferably sterile, and applied to the site or affected areas 3–4 times daily.

Contra-indications, warnings, etc Do not use on infected lesions unless accompanied by appropriate anti-infective agents. Should not be used extensively in pregnancy. Avoid long term therapy in infants.

Pharmaceutical precautions Do not refrigerate, incinerate or puncture the aerosol can.

Shake well before use. Use at room temperature. Keep out of the reach of children.

For external use only.

Legal category POM.

Package quantities Aerosol canister containing 10 g of foam, (will deliver 25 applications of 5 ml).

Further information An illustrated instruction leaflet is enclosed with each pack.

Product licence number 0036/5002.

PHAZYME*

Presentation Pink, sugar-coated, two-phase tablet, each tablet containing:

In the outer layer,

Specially activated simethicone 20 mg

In the core, protected for release in the small intestine,

Pancreatin enzymes USNF XIV

Protease 3,000 NF units

Lipase 240 NF units

Amylase 2,000 NF units

Specially activated simethicone 40 mg

Uses Deflatulent action for the relief of pain and distention due to gastro-intestinal gas. Enzymatic action for the improvement of the digestive processes.

Dosage and administration One or two tablets to be swallowed with meals and upon retiring or as required.

Contra-indications, warnings, etc Specially acti-

vated simethicone is physiologically inert and is not absorbed and therefore has no side-effects or contra-indications.

Likewise the pancreatic enzymes have no side-effects or contra-indications.

Pharmaceutical precautions No special precautions.

Legal category P.

Package quantities Bottles of 100 tablets.

Further information Phazyme Tablets are compatible with any other therapy which may be prescribed concurrently.

Product licence number 0036/0025.

PROCTOFOAM HC*

Presentation Muco-adherent, white, odourless aerosol foam containing:

Hydrocortisone acetate PhEur 1%

Pramoxine hydrochloride USP XX 1%

Other ingredients: propylene glycol, ethoxylated stearyl alcohol, polyoxyethylene-10-stearyl ether, cetyl alcohol, methyl *p*-hydroxybenzoate, propyl *p*-hydroxybenzoate, triethanolamine, deionised water, in aerosol canister containing 20 g, with a plastic applicator.

Uses Anti-inflammatory, antipruritic anaesthetic. For the temporary relief of inflammation, pruritus, pain and swelling associated with haemorrhoids, proctitis, cryptitis, fissures, post-operative pain and pruritus ani. For treatment of post-episiotomy pain and discomfort.

Dosage and administration One applicatorful per rectum two or three times daily and after each bowel evacuation. Perianally or for post-episiotomy use – apply as needed. Not indicated in infants and young children.

Contra-indications, warnings, etc A complete rectal examination to rule out serious pathology should be completed before instituting therapy. Do not use on infected lesions unless accompanied by appropriate anti-infective agents. Discontinue use if sensitivity develops. Steroids should not be used unnecessarily during pregnancy since safety during pregnancy has not been fully established.

Pharmaceutical precautions Do not refrigerate, incinerate or puncture the aerosol can.

Shake well before use. Use at room temperature.

Legal category POM.

Package quantities Aerosol canister containing 20 g of foam (approximately 40 doses), plus a plastic applicator.

Further information One applicatorful of Proctofoam HC provides a dose of approximately 3–5 mg of both hydrocortisone acetate and pramoxine hydrochloride.

An illustrated instruction leaflet is enclosed with each pack.

Product licence number 0036/5002.

QUELLADA*

Presentation *Quellada Lotion*: Gamma benzene hexachloride 1% in a pleasantly perfumed lotion base, pearly white in colour.

Quellada Application PC: Gamma benzene hexachloride 1% in a specially formulated foaming shampoo base. Quellada Application PC is a yellow, clear liquid.

Uses Antiparasitic – ovacidal.

For the treatment of mite and lice infestations, e.g. scabies, head lice, pubic lice and body lice.

Dosage and administration *Lotion (scabies):* After hot bath or shower apply a thin layer to the whole body surface except face and scalp. Leave for 24 hours, then wash thoroughly.

Application PC (pediculosis): For use on the hairy areas of the scalp and body. Apply to wet hair, rub vigorously for four minutes, rinse and comb with a fine tooth comb.

Contra-indications, warnings, etc *Lotion:* External use only. Avoid contact with eyes and other mucous membrane.

Application PC: Avoid contact with the eyes. Should they accidentally get into the eyes immediately flush with water. Do not use more than twice in any one infestation nor in any one week. Do not use on broken or infected skin.

Pharmaceutical precautions Do not refrigerate.

Legal category P.

Package quantities Both Quellada Lotion and Quellada Application PC are available in bottles of 100 ml and 500 ml.

Further information As Gamma benzene hexachloride 1% is effective against both adult and egg stage of the sarcoptes scabiei and pediculus, one application is usually sufficient to clear infestation, provided that instructions are carried out correctly. Printed instructions are issued with each pack.

Irritation and sensitivity are rare.

Product licence numbers

Quellada Lotion 0036/5000
Quellada Application PC 0036/5001

TARCORTIN*

Presentation Hydrocortisone PhEur 0.5% and refined alcoholic extract of coal tar 5% in a vanishing cream base. It is a light tan, homogeneous cream.

Uses Stimulating, antipruritic. For all simple or refractory subacute and chronic skin affections, including chronic eczema, infantile eczema, localised neurodermatitis, seborrhoea, dermatitis venenata, pruritus ani and psoriasis.

Dosage and administration Apply twice daily or more frequently to the affected area by gentle massage until the cream has vanished into the skin. No dressing is needed.

Contra-indications, warnings, etc Contra-indicated in the presence of viral or fungal infections, tubercular or syphilitic lesions, and in bacterial infections unless used in conjunction with appropriate chemotherapy. Do not apply in large amounts or for prolonged periods during pregnancy.

In infants long-term continuous topical steroid therapy should be avoided. Adrenal suppression can occur, even without occlusion.

Pharmaceutical precautions No special precautions.

Legal category POM.

Package quantities Tubes of 30 g and 45 g.

Further information Clinical studies carried out in the United States, to determine the efficacy of the combination of hydrocortisone and coal-tar extract in comparison with hydrocortisone alone in the topical treatment of psoriasis and atopic dermatitis, suggest that the combination of hydrocortisone and coal-tar extract is superior to hydrocortisone alone in the majority of the conditions treated.

Product licence number 0036/5007.

*Trade Mark

STD Pharmaceutical Products Ltd

6 and 7 Broad Street

Hereford HR4 9AE

STD* INJECTION

Sodium Tetradecyl Sulphate Injection 3%

Presentation STD Injection is a sterile aqueous 3% solution of Sodium Tetradecyl Sulphate containing 2% Benzyl Alcohol and buffered to pH 7.6.

Uses The solution is designed for intravenous use and is used primarily as a sclerosant in the treatment of varicose veins of the leg by compression sclerotherapy.

The action of sodium tetradecyl sulphate in this technique is considered to be that of irritation to the intima of the vein wall, so that on compression of the vein fibrosis takes place and the vein is thus permanently occluded by a short fibrous cord therein.

Dosage and administration 0.5–1 ml at each of four sites (maximum 4 ml).

A dose of 0.5–1 ml is introduced into the superficial vein over the site of an incompetent perforating vein. It is never necessary or desirable to inject more than 1 ml at any one site and often half this volume will produce the desired effect. Three or four such injections can be given at the same visit into one limb.

The treatment of varicose veins by compression sclerotherapy is directed towards the restoration of the efficiency of the synchronised pumping systems within the leg by permanently destroying the leaking points rather than by the eradication of the superficial tortuous veins which may, in many cases, be capable of reverting to normal appearance and function after the restoration of the normal pattern of pressure within the veins of the limb.

Localisation of the perforating veins containing the injured valves is the supremely important object of diagnosis.

Treatment comprises the permanent blocking of the offending leak by producing a short fibrotic segment of vein involving the area of the junction of the perforating and superficial veins. This can be achieved by carrying out the following procedure:

1. Introducing the sclerosant into this vein after it has been emptied.

2. Maintaining the sclerosant in the empty and isolated segment for 30 seconds.

3. Applying compression immediately to the site of injection, maintaining it for a period of about six weeks, until one is quite sure that, when the patient stands erect, the internal pressure of the blood in the adjacent unobliterated vein cannot reopen the segment.

4. Application of compression is most suitably obtained by firm bandaging with a number of strong cotton crêpe bandages and by incorporating therein shaped rubber pads over the sites of injection.

An elastic stocking applied over the bandage aids compression and the retention of the bandages in position.

Contra-indications, warnings, etc The use of STD Injection of Sodium Tetradecyl Sulphate is not recommended for the treatment of varicose veins by compression

sclerotherapy when any of the following factors are present:

1. *Oral contraceptives*: Until such time as the ex-thromboplastic effect of the oral contraceptive tablet has been established, it is advisable not to use sclerotherapy on patients who are currently taking oral contraceptive.
2. *Inability to walk*: As the recommended treatment involves daily periods of walking by the patient it is not advisable to embark upon treatment if for any reason the patient cannot walk at least three miles each day.
3. *Obese legs*: It is recommended that patients with obese legs should not receive treatment. In many cases the obesity may be corrected by dieting, after which time treatment may be commenced.
4. *Any known allergy to sodium tetradecyl sulphate*: Treatment by injection of STD should not be continued if an allergic reaction has been experienced after previous injection of sodium tetradecyl sulphate.

Side-effects

1. (a) Allergy and Anaphylaxis – Rarely – see Precautions below.
(b) Allergy–Urticaria – see Precautions below.
2. Extravascular injection will give rise to pain, and may produce necrosis and ulceration (if close to surface).

Precautions

1. Allergy and Anaphylaxis:

- (a) History of allergy should be taken from all patient prior to treatment. In particular allergic reactions to previous injections of sodium tetradecyl sulphate should be noted (see contra-indication 4, above).
- (b) A higher incidence of allergic reaction is thought to result from repeated treatment involving Sodium Tetradecyl Sulphate Injection and may involve intervals of several years between courses of injection.

2. *Equipment of clinic*: The treatment of anaphylaxis may require, depending on severity of attack, some or all of the following: injection of adrenaline, injection of hydrocortisone, antihistamine injection, endotracheal tube, laryngoscope, mucus extraction pump. The treatment of varicose veins by STD injection should not be undertaken in clinics where these items are not readily available.

Pharmaceutical precautions Store in a cool place away from direct sunlight.

Legal category POM

Package quantities STD injection.

30 ml multidose containers.

100 × 1 ml single-dose ampoules.

Further information The use of a small dose, the isolation of the injection within the vein segment and the application of immediate, adequate and lasting compression are of supreme importance in obtaining a good result.

Product licence number 0398/5000.

***Trade Mark**

Sterling Health
urbiton
urrey KT6 4PH



DOXALIN*

Description Flat, round, white, uncoated tablets with bevelled edges, 16 mm in diameter, marked 'Droxalin' on both faces, containing:

polyhydroxyaluminium sodium carbonate	162 mg
magnesium Trisilicate BP	162 mg

Uses Droxalin is an antacid. It is recommended for the relief of gastric hyperacidity, dyspepsia, and symptoms of peptic ulcer.

Dosage and administration For oral administration only.

Adults: For hyperacidity: 1 or 2 tablets as required.

Peptic ulcer: 2 or more tablets, chewed every two or four hours, or when required for relief of symptoms.

Contra-indications, warnings, etc There are no known contra-indications or adverse reactions, and no cases of overdosage have been reported.

As the ingredients of Droxalin are not significantly

absorbed, systemic effects such as alkalosis due to changes in acid-base metabolism are not encountered.

The combination of aluminium and magnesium salts minimises constipating and laxative side-effects, which are rare and mild.

Pharmaceutical precautions None applicable.

Legal category GSL.

Package quantities Droxalin Tablets are available in packs of 30 and 180.

Further information The aluminium complex is rapidly activated by chewing to form a colloidal aluminium hydroxide gel, giving rapid relief of gastric hyperacidity and buffering gastric pH at an ideal non-alkaline level for long periods.

Each Droxalin tablet contains 7 to 9 mg sodium.

Product licence number 0071/5009.

*Trade Mark

Sterling Research Laboratories
St. Mark's Hill
Surbiton-upon-Thames
Surrey KT6 4PH



ACIDOL* PEPSIN

Presentation Near-white, bi-convex tablets, 11 mm in diameter, plain on both sides with a characteristic odour. Each tablet contains 97 mg pepsin and 388 mg betaine hydrochloride.

Uses Acidol-Pepsin Tablets provide a source of hydrochloric acid and pepsin for patients with achlorhydria.

Dosage and administration For oral administration only.

The usual adult dose is 1-3 tablets crushed and dissolved in a tumbler of water three times a day, preferably after meals.

Contra-indications, warnings, etc There are no known contra-indications or side-effects.

If Acidol-Pepsin Tablets are swallowed whole they are likely to cause irritation and symptoms of indigestion: they should therefore always be taken dissolved in water.

Because hydrochloric acid can dissolve dental enamel, the solution is best taken through a straw or a glass tube to protect the teeth.

Overdosage has not been reported. Although the ingestion of large amounts of hydrochloric acid may raise the chloride and lower the bicarbonate content of the blood it is most unlikely that metabolic acidosis would occur as a result of taking Acidol-Pepsin.

Pharmaceutical precautions Store in well-closed containers. Protect from damp.

Legal category P.

Package quantities Acidol-Pepsin is supplied in bottles of 50 tablets.

Further information In solution, betaine hydrochloride forms free hydrochloric acid. Each Acidol-Pepsin Tablet is approximately equivalent to 1 ml of Dilute Hydrochloric Acid BP.

Product licence number 0071/5017.

AT10*

Presentation A clear, deep straw-coloured, oily solution with a faint nut-like odour containing 0.25 mg/ml Dihydroxyacetone BP.

Uses AT10 is recommended for use in the acute, chronic and latent forms of hypocalcaemic tetany due to hypoparathyroidism where its action is to increase the rate of absorption and utilisation of calcium. It may also be used to treat those skin lesions such as pemphigus and impetigo herpetiformis which are associated with hypoparathyroidism.

Dosage and administration AT10 is for oral administration only.

Adults: In acute cases 3-10 ml may be given on each of the first three days of treatment, followed two to three days later by blood and urinary calcium estimations. The maintenance dose of AT10 is usually within the range 1-7 ml each week, but the precise amount depends on the results of serum and urinary calcium determination.

In chronic cases an initial dose of 2 ml of AT10 daily or on alternate days, may be sufficient to maintain normocalcaemia in moderate cases. The dose of AT10 usually has to be increased during menstruation, pregnancy and periods of unusual activity.

Contra-indications, warnings, etc As with calciferol, uncontrolled, prolonged administration of AT10 can result in hypercalcaemia which may lead to nephrocalcinosis. Therefore accurate blood calcium determinations must be made at the beginning of treatment and then periodically until the required maintenance dose has been established. The serum calcium level should subsequently be kept between 2.25-2.5 mmol/litre.

The Sulkowitch test (for urinary calcium) is a convenient supplement to blood calcium determinations, but it should not be regarded as a substitute, because hypoparathyroid patients treated with AT10 hypercalcaemia can occur in the presence of hypocalcaemia.

Overdosage will result in hypercalcaemia. The symptoms (described below) usually respond to withdrawal of medication, bed rest, a liberal fluid intake, laxatives and a light diet.

Side-effects are most likely to be due to hypercalcaemia, the first signs of which are loss of appetite, listlessness and nausea. More severe manifestations include thirst, vertigo, urgency of micturition, stupor, headache, abdominal cramps and paralysis.

Pharmaceutical precautions Store in well-closed containers protected from heat and light.

Legal category P.

Package quantities AT10 is supplied in bottles containing 15 ml with a 1 ml dropper.

Further information The hypercalcaemic action of AT10 is slower in onset and more prolonged than that of parathyroid hormone, but faster in onset and less persistent in action than calciferol. In patients who have become resistant to large doses of calciferol it may be possible to control blood calcium levels with AT10.

Product licence number 0071/5020.

BREOPRIN*

Presentation White tablets 16 mm long and 7.5 mm wide, marked  on one side and scored on the other. Each tablet contains 648 mg micro-encapsulated aspirin.

Uses Breoprin Tablets may be used where aspirin is required and therefore are recommended for the relief of pain and stiffness associated with rheumatoid and osteoarthritis, rheumatism, bursitis, sprains, strains and neuralgia.

Breoprin is also recommended for the relief of symptoms of colds and influenza and in other minor painful conditions such as headache, toothache and menorrhoea.

Usage and administration *Adults:* Breoprin Tablets should be taken at approximately eight-hourly intervals, for example at 7.00 a.m., 1.00 p.m. and 9.00 p.m. Where large doses of aspirin are usually required as in acute rheumatoid conditions, each dose should consist of 2 tablets. In other cases the dose should be 1 tablet, though patients who experience pain or stiffness in the morning on rising may increase the last dose of the day to 2 tablets. No more than 6 tablets should be taken in 24 hours.

Children: Breoprin should not be given to children below the age of 14 years.

Contra-indications, warnings, etc

Contra-indications: Breoprin should not be given to patients with active peptic ulceration because aspirin may induce (occasionally major) gastro-intestinal haemorrhage. It should also be withheld from those known to be sensitive to aspirin, including those with haemophilia and similar coagulation disorders.

Precautions: There is clinical and epidemiological evidence for the safety of aspirin in human pregnancy. However, its use should be avoided at term because aspirin may prolong labour and contribute to maternal and neonatal bleeding.

Aspirin may enhance the effects of anticoagulants and inhibit the action of uricosuric agents. Because aspirin may precipitate bronchospasm, it can induce attacks of asthma in susceptible subjects.

Overdose: Aspirin overdose may be treated by gastric lavage with 0.5% sodium bicarbonate solution. If the condition is not serious, sodium bicarbonate and fluids by mouth will speed renal excretion of salicylate. In more serious cases, an intravenous infusion of 5% dextrose should be set up, supplemented by electrolytes and alkali as indicated by blood and urine analysis. Haemolysis may be necessary. Haemorrhage may require blood transfusions. The administration of vitamin K, either orally or parenterally, will restore prothrombin time to normal.

Side-effects: The main side-effects associated with aspirin therapy are dyspepsia and other signs of gastric irritation. They are likely to occur less frequently with Breoprin than with ordinary aspirin tablets because the croscapsulation causes the major part of the aspirin to be released in the small intestine. If tinnitus occurs, the dose should be reduced.

Pharmaceutical precautions Protect from moisture in well-closed containers.

Legal category P.

Package quantities Bottles of 100 tablets.

Further information Nil.

Product licence number 0071/0091.

BRONCHILATOR*

Presentation Bronchilator is an aerosol inhalant in the form of an oral nebuliser, delivering 250 metered doses by finger depression of an actuator. Each metered dose contains 0.350 mg isotharine mesylate, and 0.070 mg Phenylephrine Hydrochloride BP.

Uses Bronchilator provides effective and relatively long-lasting relief of bronchospasm in bronchial asthma and chronic bronchitis.

Dosage and administration Bronchilator is for oral inhalation only.

Adults: The usual dose is 1 or 2 inhalations and it is not normally necessary to repeat this dose at less than half-hourly intervals. In bronchial asthma 1 or 2 inhalations more may be required, but it is important to wait one full minute after the initial 1 or 2 inhalations, to be certain that relief has not been obtained. Not more than eight treatments should be taken in 24 hours.

Bronchilator should only be administered to children under the supervision of a responsible adult and strictly as recommended by the doctor.

Contra-indications, warnings, etc Bronchilator should not be given to patients taking MAO inhibitors.

As with other sympathomimetic amines, too frequent use of Bronchilator may cause tachycardia, palpitations, nausea, headache, changes in blood pressure, etc. Patients should therefore be advised not to exceed the recommended dose. Other sympathomimetic amines should be prescribed with caution in patients using Bronchilator. Dosage should be carefully adjusted in patients with hyperthyroidism, hypertension, coronary artery disease, cardiac asthma, limited cardiac reserve and in individuals sensitive to sympathomimetic amines.

Overdose: Serious symptoms are unlikely except after massive overdose. They may be treated in the same way as those due to adrenaline overdose (i.e. injection of piperhexan or phenolamine). Slow intravenous procaine or procainamide should be used for fibrillation, and artificial respiration and oxygen for cyanosis and respiratory embarrassment.

Side-effects: When used as recommended, side-effects are rare. A small drop in pulse rate and blood pressure may follow inhalation of Bronchilator.

Pharmaceutical precautions Keep away from extreme heat.

Legal category POM.

Package quantities Complete nebuliser containing 12.5 ml of solution (equivalent to 250 doses).

Refills containing 12.5 ml.

Further information Nil.

Product licence number 0071/5024.

ERADACIN* ▼

Presentation Eradacin capsules are No. 1 opaque, red/yellow capsules filled with a white powder. Each capsule contains 150 mg acroloxacin (rosaloxacin I.N.N.)

Uses Eradacin is for the treatment of acute gonorrhoea in both male and female patients.

Dosage and administration Eradacin is for oral administration only.

Adults: Two capsules (300 mg) preferably on an empty stomach.

Children: No recommendations.

Contra-indications, warnings, etc Safe use during human pregnancy has not yet been established and Eradacin should be used only when necessitated by the anticipated bacteriological and clinical benefits.

It should be used with caution in patients with impaired renal or hepatic function.

Eradacin may cause dizziness and drowsiness. Patients should therefore be warned not to drive or operate machinery if affected. Occasionally, headaches and gastro-intestinal upsets may occur.

Eradacin has been shown to induce lesions in weight-bearing joints of young animals receiving high, single or repeated doses. The relevance of this to man is unknown but it is recommended that frequent, repeat doses should not be given to those under 18 years of age.

Overdosage: Animal toxicity studies suggest that CNS depression is a likely symptom of overdosage. If vomiting does not occur, the drug should be removed by emesis or gastric lavage, if ingestion is recent, and symptomatic treatment applied.

Pharmaceutical precautions None.

Legal category POM.

Package quantities Eradacin is supplied in packs of 20 capsules.

Further information A single dose of 300 mg Eradacin has been shown to produce a cure rate of over 90% in cases of uncomplicated gonococcal urethritis. Treatment with Eradacin may be successful in patients infected with *N. gonorrhoeae* strains resistant to penicillin and other antibiotics.

Product licence number 0071/0168.

HYPAQUE* 25% AND 45% HYPAQUE* SODIUM

Presentation Hypaque is a sterile, almost colourless aqueous solution in clear glass ampoules or infusion bottles containing either 25% w/v or 45% w/v Sodium Diatrizoate BP.

Hypaque Sodium is a white, odourless powder with a saline taste consisting of Sodium Diatrizoate BP. The anhydrous material contains 59.87% of iodine.

Uses An X-ray contrast medium suitable for intravenous and retrograde urography, angiography, venography and many other specialised procedures. It may also be used orally or rectally to examine the gastro-intestinal tract.

Dosage and administration The volume and concentration of Hypaque solution used depends on the procedure being carried out. The strengths and quantities given in the table opposite are suggested.

Examination of the gastro-intestinal tract: For adults an average dose of from 100 to 150 ml of a 25–50% solution is suggested when given by mouth or tube. From 500 ml to 1,000 ml of 20–35% solution is suggested as an enema.

For infants or children the oral or tube dose may vary from 50 ml to 120 ml of a 10–25% solution, and as an enema from 100 ml to 500 ml of a 10–15% solution may be used. The following formulae may be used to make a flavoured draught from Hypaque Sodium.

	1	2	3
Hypaque Sodium	30 g*	30 g*	30 g*
Sucrose	26.41 g	—	—
Methyl <i>p</i> -hydroxybenzoate	0.1 g	0.08 g	0.08
Propyl <i>p</i> -hydroxybenzoate	0.01 g	—	—
Butyl <i>p</i> -hydroxybenzoate	0.004 g	—	—
Sodium saccharin	0.03 g	0.3 g	0.3 g
Tween 80	0.08 g	—	0.08
Vanillin	—	0.2 g	0.2 g
Purified water q.s. ad.	75 ml	75 ml	75 ml

* Or an appropriate amount for the strength of solution required.

Contra-indications, warnings, etc Hypaque should not be used for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

It was formerly believed that the use of contrast media was contra-indicated in patients with advanced renal destruction associated with severe uraemia, and in those with severe hepatic and cardiac disorders. However, a review concludes that although there appear to be definite contra-indications, potentially hazardous situations requiring particular care are oliguric renal failure, myeloma and combined renal and hepatic failure.

Examination	Strength (%)	Amount of medium used (ml)	
		Adults	Children
Urography:			
i.v.	45	0.5–2.0/kg	as adult
infusion	25	4 ml/kg	as adult
retrograde	25–45	5–20	as adult
Cystography	10–45	500–1500	100–300
Peripheral arteriography	45	20–40	10–20
Haemorrhoidal Portal	45	30–40	15–20
Venography			
Renal cyst puncture	25–45	5–60	5–20
Orbital phlebography	45	2–4	1–2
Intraosseous venography	45	20–45	—
Cholelithochography:			
percutaneous	25–45	15	5
transhepatic			
operative	25–45	5–20	5
post-op. T tube	25–45	5–20	5
Hysterosalpingography	45	10	—
Arthrography	25–45	5–20	3–10
Sinography	45	20–40	—
Tube screening (gastric)	25	5–20	—
Gastro-intestinal (acute abdomen)	see above	see above	see above
Abdominal stab wounds	25	q.s.	q.s.
Dacryocystography	45	1–3	—
Vesiculography	45	1.5–2.0	—
		to a total of 10–12 each side	
Myelography	45	3	—
Duct mammography	25	1–2	—
Discography	45	0.5 max. 2.0	—

No attempt should be made to dehydrate the uraemic patient, nor should dehydration be carried out in a patient with myeloma. Recent evidence suggests that in the latter case it is dehydration rather than the presence of myeloma protein which has been the cause of adverse effects. Prior purgation should also be avoided. As with any other X-ray examination the hazards must be balanced against the clinical need for information.

pregnancy the examination should be delayed until 12–14 weeks after delivery whenever possible.

Should urine be tested for albumin within four to six hours after a Hypaque injection, crystals of diatrizoic acid may separate out on acidification with mineral acid, but these crystals are easily distinguished from the amorphous albumin precipitate. Hypaque does not affect acetate or heat coagulation tests.

Organic iodine contrast media are known to remain in the blood serum of patients for periods varying from two days to several years in concentrations sufficient to interfere with tests of thyroid function such as protein-bound iodine determinations. It has been reported that diatrizoic acid remains in the serum for four days. It is therefore advisable to perform such thyroid function tests before any examination involving the use of Hypaque.

Patients with a history of allergy, especially to iodine, and those with active tuberculosis require careful consideration. Because of the possibility of inducing a temporary suppression of urine, it is wise to allow an interval of at least 24 hours before repeating excretory retrograde pyelography in patients with unilateral obstruction of normal renal function.

The precise nature of the reactions which occur with contrast media are not fully understood, although some seem to be allergic, and major reactions resemble those due to histamine release. Most minor reactions such as pain, giddiness, a feeling of warmth, coughing, nausea and vomiting pass off quickly. Minor allergic disturbances such as sneezing, rhinorrhoea, lacrimation and pruritus or urticarial rashes are relatively benign and respond to antihistamine treatment. Where patients complain of headache it may possibly be due to fluid deprivation.

There is no satisfactory way of pre-testing which will allow the prediction of a severe reaction, but the following precautions may help to minimise reactions, according to some workers:

1. Obtain a history of personal or familial allergies, of previous iodine studies, and of sensitivity to iodine and other drugs.
2. Make a preliminary sensitivity test by injecting intravenously a small dose (0.5–1 ml) followed by a period of observation long enough to detect delayed reactions. (Although allergic reactions generally occur quickly, on very rare occasions they may not appear for 1 or even 15 minutes.)
3. Give preliminary antihistamine medication.
4. Have drugs on hand for emergency use.

In examination of the gastro-intestinal tract, Hypaque should be used with caution in infants and debilitated elderly patients because hypovolaemia may develop due to the osmotic activity of the contrast material in the intestines.

Pharmaceutical precautions The sterile aqueous solutions are almost colourless. Hypaque is relatively thermostable and may be autoclaved if 0.0125 w/v diatrizoic acid is added to the solution, but sterile Hypaque solutions should not be re-autoclaved because of the possibility of free amine production. Solutions should be protected from light.

Legal category Hypaque injections POM.
Hypaque Sodium Powder P.

Package quantities *Hypaque 25%*: 20 ml ampoules in boxes of 5. Infusion bottles of 250 ml or 350 ml.

Hypaque 45%: 20 ml ampoules in boxes of 5 or 20. 30 ml ampoules in boxes of 20.

Hypaque Sodium: Bottles of 500 g.

Further information Nil.

Product licence numbers

Hypaque 25% 0071/5044
Hypaque 45% 0071/5045
Hypaque Sodium 0071/5048

HYPAQUE* 65% AND 85%

Presentation Sterile, almost colourless aqueous solution in clear ampoules. Hypaque 65% contains Sodium Diatrizoate BP 25.23% w/v and meglumine diatrizoate 50.46%. (The iodine content of Hypaque 65% is equivalent to that of a 65% solution of sodium diatrizoate.)

Hypaque 85% contains Sodium Diatrizoate BP 28.33% w/v and meglumine diatrizoate 56.67% w/v.

At body temperature the solutions are clear, but at lower temperatures crystals may separate out. The solid readily dissolves when heated to 40°C or 45°C and recrystallisation does not occur for several hours.

Uses An X-ray contrast medium for angiocardiology, aortography, venography and other examinations.

Dosage and administration Hypaque is for parenteral use, oral administration for gastro-intestinal examinations and rectal administration as an enema.

The volume and concentration of Hypaque Solution used depend on the procedure being carried out.

When concentrations of Hypaque other than 85%, 65%, 45% or 25% are required, they can be obtained either by diluting a stronger medium with normal saline, or by mixing suitable amounts of two media.

The strengths and quantities given in the table on the next page are suggested.

Examination of the gastro-intestinal tract: For adults an average dose of 100–150 ml of a 25–50% solution is suggested when given by mouth or tube. From 500 ml to 1,000 ml of 20–35% solution is suggested for an enema.

For infants or children the oral or tube dose may vary from 50 ml to 120 ml of a 10–25% solution, and as an enema from 100 ml to 500 ml of a 10–15% solution may be used. The following formulae may be used to prepare a flavoured draught from Hypaque 85%:

	1	2	3
Hypaque 85%*	40 ml*	40 ml*	40 ml*
Sucrose	26.41 g	—	—
Methyl <i>p</i> -hydroxybenzoate	0.1 g	0.08 g	0.08 g
Propyl <i>p</i> -hydroxybenzoate	0.01 g	—	—
Butyl <i>p</i> -hydroxybenzoate	0.004 g	—	—
Sodium saccharin	0.03 g	0.3 g	0.3 g
Tween 80	0.08 g	—	0.08 g
Vanillin	—	0.2 g	0.2 g
Purified water q.s. ad.	75 ml	75 ml	75 ml

* Or an appropriate amount for the strength of solution required.

Contra-indications, warnings, etc Hypaque should not be used for myelography. Injection of even a small

amount into the subarachnoid space may produce convulsions and result in fatality.

It was formerly believed that the use of contrast media was contra-indicated in patients with advanced renal destruction associated with severe uraemia, and in severe hepatic and cardiac disorders. However, one review concludes that although there appear to be no definite contra-indications, potentially hazardous situations requiring particular care are oliguric renal failure, myeloma and combined renal and hepatic failure.

No attempt should be made to dehydrate the uraemic patient, nor should dehydration be carried out in a patient with myeloma. Recent evidence suggests that in the latter case, it is dehydration rather than the presence of myeloma protein which has been the cause of adverse effects. Prior purgation should also be avoided. As with any other X-ray examination the hazards must be balanced against the clinical need for information. In pregnancy the examination should be delayed until 12–16 weeks after delivery whenever possible.

Should urine be tested for albumin within four to six hours after a Hypaque injection, crystals of diatrizoic acid may separate out on acidification with mineral acid, but these crystals are easily distinguished from the amorphous albumin precipitate. Hypaque does not affect the acetic acid or heat coagulation tests.

Organic iodine contrast media are known to remain in the blood serum of patients for periods varying from two days to several years in concentrations sufficient to interfere with tests of thyroid function such as protein-bound iodine determinations. It has been reported that sodium diatrizoate remains in the serum for four days. It is therefore advisable to perform such thyroid function tests before any examination involving the use of Hypaque.

Patients with a history of allergy, especially to iodine, and those with active tuberculosis, require careful consideration. Because of the possibility of inducing a temporary suppression of urine, it is wise to allow an interval of at least 24 hours before repeating excretory or retrograde pyelography in patients with unilateral reduction of normal renal function.

Examination	Strength (%)	Amount of medium used (ml)	
		Adults	Children
Angiocardiography	65–85	40–60	20
Abdominal aortography			
'Seldinger'	65	20	10
arch	65–85	40–60	20
translumbar	65	20	10
Selective arteriography	45–65	5–30	4–10
Portal venography:			
spleno-veno-	65–85	30–40	10–15
mesenteric-	65	30–40	15–20
Peripheral venography	65	20–40	10–20
Sialography	65	1–3	1–3
Amniography	45–65	10–40	—

The precise nature of the reactions which occur with contrast media are not fully understood, although some seem to be allergic, and major reactions resemble those due to histamine release. Most minor reactions such as arm pain, giddiness, a feeling of warmth, coughing, nausea and vomiting pass off quickly. Minor allergic disturbances such as sneezing, rhinorrhoea, lacrimation and pruritus or urticarial rashes are relatively benign and

respond to antihistamine treatment. Where patients complain of headache it may possibly be due to fluid deprivation.

There is no satisfactory way of pre-testing which will allow the prediction of a severe reaction, but the following precautions may help to minimise reactions according to some workers:

1. Obtain a history of personal or familial allergies, previous iodine studies, and of sensitivity to iodine and other drugs.
2. Make a preliminary sensitivity test by injecting intravenously a small dose (0.5–1 ml) followed by a period of observation long enough to detect delayed reactions. (Although allergic reactions generally occur quickly, on very rare occasions they may not appear for 10 or even 15 minutes.)
3. Give preliminary antihistamine medication.
4. Have drugs on hand for emergency use.

In examinations of the gastro-intestinal tract, Hypaque should be used with caution in infants and debilitated elderly patients because hypovolaemia may develop due to the osmotic activity of the contrast material in the intestines.

Pharmaceutical precautions The sterile aqueous solutions are clear and almost colourless. Hypaque is relatively stable and may be autoclaved if 0.0125% w/v sodium calcium edetate is added to the solution, but solutions should not be re-autoclaved because of the possibility of free amine production. Solutions should be protected from light.

Legal category POM.

Package quantities Hypaque 65%: 20 ml ampoules in boxes of 5.

Hypaque 85%: 20 ml ampoules in boxes of 5.

Further information Nil.

Product licence numbers

Hypaque 65% 0071/5046

Hypaque 85% 0071/5047

INTEGRIN* CAPSULES

Presentation Integrin Capsules are No. 4 white opaque; hard gelatine capsules marked Integrin 10 on both cap and body and filled with a fine, off-white powder. Each capsule contains 10 mg oxypertine.

Uses Integrin Capsules are recommended for the treatment of acute and chronic anxiety states, a psychosomatic condition whether or not accompanied by depressive overlay, tension, apprehension, agitation or sleep disturbance.

Dosage and administration For oral administration only.

Adults: 10 mg three or four times daily, usually after meals. In certain cases up to 60 mg daily in divided doses may be needed.

Contra-indications, warnings, etc Because oxypertine can bring about the release of small amounts of catecholamines in experimental animals, it would be wise not to give Integrin with, or within three weeks of the use of monoamine oxidase inhibitors. Integrin may potentiate the effect of alcohol or other tranquillising agents should, therefore, be warned against excessive use of alcohol and, as with all tranquillisers, patients

ould also be warned to observe caution in car driving id similar situations. Although tests on pregnant rabbits omers' test) have revealed no teratogenic effects from yperetine the benefits of using Integrin in the first mester of pregnancy should be weighed against the ssible risks.

verdosage: Possible effects of overdosage might in- ude central and respiratory depression and hypoten- on. Gastric lavage may be indicated, otherwise treat- ent should be symptomatic and supportive.

de-effects: No serious toxic reactions have been ported with Integrin treatment. Even in high doses it as been well tolerated with only minor, often transient, de-effects appearing. As would be expected from the armacological properties of the compound, drowsi- ss may occur in some patients, and a few individuals ay complain of mild side-effects such as dry mouth and ziness.

harmaceutical precautions Protect from moisture id heat.

egal category POM.

ackage quantities Integrin 10 mg Capsules are ailable in bottles of 100.

urther information Nil.

roduct licence number 0071/5049.

ITEGRIN* TABLETS

resentation Integrin 40 mg Tablets are white, slightly eckled, flat tablets with bevelled edges, 8.7 mm in ameter, marked 'int' on one side and scored on the her. Each tablet contains 40 mg oxypertine.

ses Integrin 40 mg Tablets are recommended for the eatment of psychotics. They are particularly useful in ithdrawn schizophrenics. Integrin 40 mg Tablets may so be used in acute incidents of mental disturbances ich as acute agitation, behavioural disturbances, delir- m, and acute and subacute psychoses, including the anic phase of manic-depressive psychoses.

osage and administration For oral administration ly.

adults: The usual dose is 2-3 tablets (80-120 mg) daily idvided doses. This may be varied according to the ental state and the clinical response of the patient, but ie total daily dosage should not exceed 300 mg.

ontra-indications, warnings, etc Because oxy- rtine can bring about the release of small amounts of itecholamines in experimental animals, it would be ise not to give Integrin with or within three weeks of ie use of monoamine oxidase inhibitors. Oxypertine ay potentiate the central depressant effect of alcohol id other tranquillisers.

Although tests on pregnant rabbits (Somers' test) ave revealed no teratogenic effects from oxypertine the enefits of using Integrin in the first trimester of egnancy should be weighed against the possible risks. Patients have received up to 360 mg a day and one as received a maximum of 560 mg a day without toxic ffects.

verdosage: Possible effects of overdosage might in- ude central and respiratory depression and hypoten- on. Gastric lavage may be indicated, otherwise treat- ent should be symptomatic and supportive.

Side-effects: These are difficult to evaluate in the psychiatric patient. Adverse reactions reported have been mostly of a minor character and include extrapyr- amidal effects, sedation, dizziness and vomiting. Extra- pyramidal effects including restlessness may occur when high doses are used in the treatment of schizophrenia, but are rare at lower dose levels. Some observers have found that the incidence is less than with other commonly used psychotropic drugs. When these effects do occur they are readily controlled with appropriate therapy. Some patients complain of mild side-effects such as dry mouth and nasal congestion which are probably due to the autonomic effects of the drug.

There have been very few reports of hypotensive episodes such as occur with the phenothiazines. Mod- erately raised serum transaminase levels have been reported in some patients as well as occasional eosino- philia in high doses.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Integrin Tablets are available in bottles of 250.

Further information Nil.

Product licence number 0071/5050.

MODRENAL* ▼

Presentation Modrenal capsules are size 3, opaque, pink/black gelatin capsules, marked SRL 60, each con- taining 60 mg trilostane.

Uses Modrenal is for the control of the manifestations of adrenal cortical hyperfunction in such conditions as hypercortisolism and primary aldosteronism.

Dosage and administration Modrenal is for oral administration only.

Adults: One capsule (60 mg) four times a day for at least 3 days. Thereafter, the dose may be reduced or increased, according to the patient's clinical response and the results of appropriate biochemical tests. The normal dosage range is 120 mg to 480 mg per day in divided doses, but in a few patients the daily dose has been increased stepwise to 960 mg.

Children: There are no dosage recommendations for children.

Contra-indications, warnings, etc Modrenal is contra-indicated in pregnant patients. Steps should be taken to exclude pregnancy before starting treatment with Modrenal and non-hormonal contraceptive meas- ures should be taken during the course of treatment.

As with all drugs which are metabolised by the liver and excreted by the kidney, caution should be exercised in treating patients with renal or hepatic dysfunction.

Although Modrenal will not produce adrenal shut- down or Addisonian crisis, except in patients with a pituitary adenoma, it is advisable to monitor therapeutic response by regular assay of circulating corticosteroids and blood electrolytes until the presence of an ACTH- producing tumour has been excluded. If a patient taking Modrenal develops a severe illness or needs surgery, it may be advisable to administer corticosteroids.

Information on long-term effects is not yet available.

Drug Interaction: If Modrenal is administered concu- rently with thiazide or 'loop' type diuretics, its effect of

inhibiting aldosterone production reduces the loss of K⁺ ions in the urine usually seen with these drugs.

Overdosage: If recently ingested, the drug should be removed by emesis or gastric lavage. Subsequent treatment will depend on the effect the drug has had on blood electrolytes and circulating corticosteroids.

Side-effects: When administered as recommended above, side-effects are likely to be rare. During acute tolerance studies, side-effects were only troublesome when high initial doses (500–1,000 mg daily) were given; they included flushing, nausea, vomiting, rhinorrhoea, and palatal oedema. All were reversible on stopping treatment.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Modrenal capsules are supplied in bottles of 100.

Further information Modrenal selectively and reversibly reduces to normal limits both mineralo- and gluco-corticoids by inhibiting an enzyme system essential for their production (3 β -hydroxysteroid dehydrogenase/ Δ^5 -3-oxosteroid isomerase).

Product licence number 0071/0129.

MONODRAL*

Presentation Monodral Tablets are yellow, bi-convex tablets, 8 mm in diameter, marked 'W' on one side and scored on the other. Each tablet contains 5.0 mg penthienate methobromide.

Uses Monodral Tablets are recommended for the treatment of gastric hypermotility and hypersecretion. They may be used to relieve pain in peptic ulcer and stress dyspepsia.

Dosage and administration Monodral Tablets are for oral administration only. Dosage should be adjusted to individual needs.

Adults:

1. **Peptic ulcer:** The average dose is 1 tablet three times daily, with an additional dose at night if required. Some patients may require higher doses in the initial stages, especially when pain is severe, but a daily dose of 40 mg should be regarded as the maximum and this amount should be given for short periods only. When symptoms are controlled the dose should be reduced to the effective minimum.

2. **Stress Dyspepsia:** Small doses are often sufficient to relieve symptoms and a dosage of $\frac{1}{2}$ tablet (2.5 mg) three or four times daily is usually used.

Contra-indications, warnings, etc Monodral should not be given in the presence of glaucoma because of the possibility of a mydriatic or cycloplegic effect. Pyloric obstruction and obstruction of the neck of the urinary bladder are also contra-indications because of reduction of motility and tonus; consequently care is needed in patients with prostatic hypertrophy. Although tachycardia is rare, severe heart disease, where a possible increase in cardiac rate would be dangerous, is a further contra-indication.

Overdosage: This has not been reported with Monodral. The signs of acute toxicity would probably resemble those of atropine. Treatment should consist of gastric lavage, and physostigmine parenterally is an antidote.

Excitement may occur, but care is needed in administering sedatives because depression may occur as a late symptom of toxicity.

Side-effects: These are unusual at low doses. At high doses, atropine-like effects such as blurring of vision, difficulty of micturition and dryness of the mouth may occur.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Monodral is supplied in bottles of 100 tablets.

Further information Nil.

Product licence number 0071/5063.

MYTELASE*

Presentation Mytelase Tablets are white, bi-convex film-coated tablets, 6.4 mm in diameter, marked 'MY' and scored on one side and plain on the other side. Each tablet contains 10 mg ambenonium chloride.

Uses Mytelase Tablets are recommended for the treatment of myasthenia gravis.

Dosage and administration For oral administration only.

Adults: For the patient with moderately severe myasthenia, from 5 mg to 25 mg ($\frac{1}{2}$ –2 $\frac{1}{2}$ tablets) three or four times daily is recommended. Some patients require as little as 5 mg per dose; others require as much as 50 to 70 mg per dose.

It is recommended that treatment should start with 5 mg dose, the effect of the drug in each patient being carefully observed. The dosage may be gradually increased to determine the effective and safe dose for each patient.

In addition to the individual variation in dosage requirements, the amount of cholinergic medication necessary to control symptoms may fluctuate in each patient, depending on his activity and the current state of the disease, including spontaneous remission.

A few patients may require greater doses for adequate control of the myasthenic symptoms, but increasing the dosage above 200 mg daily requires exacting supervision by a physician well aware of the signs and treatment of overdosage with cholinergic medication.

Since the warning of overdosage is minimal and the requirements of patients vary tremendously, great care and supervision are required. That a narrow margin exists between the first appearance of side-effects and serious toxic effects must be borne in mind constantly. Caution in increasing dosage is essential.

Contra-indications, warnings, etc Atropine must not be administered routinely with Mytelase. Simultaneous administration of other antimuscarinic drugs should only take place under strict medical supervision. Use with caution in patients with asthma or with mechanical intestinal or urinary obstruction. Since warning of overdosage is minimal and the requirements of patients vary tremendously, great care and supervision are required.

Overstimulation with Mytelase has a clinical picture of increasing parasympathomimetic action which is more or less characteristic (when not masked by the use of atropine).

verdosage: Signs and symptoms of overdosage, including cholinergic crises, vary considerably. They are usually manifested by increasing gastro-intestinal stimulation with epigastric distress, abdominal cramps, arrhoea and vomiting, excessive salivation, pallor, cold sweating, urinary urgency and blurring of vision. Eventually fasciculation and paralysis of voluntary muscles including those of the tongue (thick tongue and difficulty swallowing), shoulder, neck and arms develop. Icterus, increase in blood pressure, with or without arrhythmia, and finally subjective sensations of internal trembling and often severe anxiety and panic may complete the picture. A cholinergic crisis can usually be differentiated from the weakness and paralysis of myasthenia gravis, inadequately treated with cholinergic drugs, by the fact that myasthenic weakness is not accompanied by any of the above signs and symptoms except the last two subjective ones (of anxiety and panic).

If signs of overdosage occur with Mytelase (excessive gastro-intestinal stimulation, excessive salivation, icterus and more serious fasciculations of voluntary muscles) discontinue temporarily all cholinergic medication and administer from 0.5 to 1 mg of atropine intravenously. Give other supportive treatment as indicated (artificial respiration, tracheotomy, oxygen, etc.).

pharmaceutical precautions Nil.

legal category POM.

package quantities Mytelase is available in bottles of 30 tablets.

further information Nil.

product licence number 0071/5066.

EGRAM*

presentation Negram Suspension is a deep pink, viscous suspension with a raspberry odour and taste containing 300 mg Nalidixic Acid BP per 5 ml dose.

Ne gram Tablets are beige, bi-convex tablets, 12.7 mm diameter, marked 'Negram' on one side and with a symbol on the other. Each tablet contains 500 mg of Nalidixic Acid BP.

uses Negram is recommended for the treatment of acute or chronic infections, especially those of the urinary and gastro-intestinal tracts, caused by Gram-negative pathogens sensitive to nalidixic acid.

usage and administration *Adults:* For acute infections, 1 g four times daily for at least seven days, reducing to 0.5 g four times a day for chronic infections.

Children: For those over the age of three months, the maximum recommended dose is 50 mg/kg body weight per day in divided doses.

Not recommended for those less than three months of age.

contra-indications, warnings, etc Negram is contra-indicated for patients with a history of convulsive disorders. It should be used with caution in patients with liver disease. Patients should avoid excessive exposure to sunlight. Although there is no evidence that nalidixic acid has any harmful effect during pregnancy, careful consideration should be given to its use during the first trimester. When treating women who are breast feeding, consideration should be given to the fact that traces of nalidixic acid are excreted in the milk.

When Negram is given to patients on anticoagulant therapy, it may be necessary to reduce the anticoagulant dosage. Negram may precipitate a haemolytic reaction in G-6-PD deficient individuals.

Nalidixic acid has been shown to induce lesions in weight-bearing joints of young animals. The relevance of this to man is unknown. The possible risk of late degenerative joint changes in young patients receiving nalidixic acid preparations should therefore be considered. If symptoms of arthralgia occur, treatment with nalidixic acid should be stopped.

Although care should be exercised in treating patients with renal failure, the full dosage of Negram may be administered in patients with creatinine clearance of more than 20 ml/min and half the normal dosage in patients with creatinine clearance less than this. Nalidixic acid in therapeutic doses can interfere with the estimation of urinary 17-ketosteroids and may cause high results in the assay of urinary vanilmandelic acid (Pisano method).

Active proliferation of the organisms is a necessary condition for the antibacterial action of nalidixic acid: the action of Negram may therefore be inhibited by the presence of other antibacterial substances.

When testing for glycosuria in patients receiving Negram, glucose-specific methods based on glucose oxidase should be used because copper reduction methods may give false-positive results.

Overdosage: In adults, symptoms of overdosage have been noted following single doses of 20 and 25 g. These have included toxic psychosis, convulsions and metabolic acidosis.

In an emergency, it is suggested that the stomach should be emptied, and symptomatic treatment applied as necessary, a particular watch being kept for central or respiratory depression.

Side-effects: Gastro-intestinal effects, skin reactions or subjective visual disturbances may occur but are readily reversible on reduction or discontinuation of therapy. There are isolated reports of convulsive episodes usually associated with overdosage or certain predisposing factors, and of raised intracranial pressure in infants. These are reversible when the drug is discontinued.

Pharmaceutical precautions Where doses of less than 5 ml are ordered, Negram Suspension may be diluted with Syrup BP so that the standard 5 ml spoonful can be given. Such dilutions will remain stable for two to three weeks.

Legal category POM.

Package quantities *Negram Suspension:* Bottles of 150 ml or 500 ml.

Negram Tablets: Boxes of 56 tablets (7 strips of 8 tablets) and (for hospitals only) bottles of 500 tablets.

Further information Nil.

Product licence numbers

Negram Suspension 0071/5067

Negram Tablets 0071/5068.

STROMBA*

Presentation 1. Stromba Tablets are flat, white tablets 9.5 mm in diameter, marked Stromba on one side and scored in quarters on the other side. Each tablet contains 5 mg stanozolol.

2. Stromba Injection consists of clear glass ampoules,

2 ml capacity, each containing stanozolol 50 mg in 1 ml aqueous suspension.

Uses Stromba Tablets may be used in the management of post-menopausal and senile osteoporosis and in patients suffering from anorexia, asthenia or chronic debilitating diseases where dietary measures alone have proved unsuccessful.

Stromba has been shown to significantly increase plasminogen activator activity measured by euglobulin clot lysis time and plasma plasminogen as well as significantly reducing plasma fibrogen and α_2 macroglobulin, a plasmin inhibitor.

Stromba Tablets may, therefore, be used for the control of the vascular symptoms of cutaneous vasculitis, Raynaud's syndrome in patients with scleroderma, and in the vasculitis of Behçet's disease; for the prevention of recurrent venous thrombosis as occurs with antithrombin III deficiency and the treatment of the complications of deep vein thrombosis as in venous lipodermatosclerosis.

Stromba Injection may be used to treat severe conditions where an anabolic effect is required to correct a negative nitrogen balance, as, for example, in major trauma, severe burns or emaciating diseases. It may also be of value in the management of anaemias (including those associated with neoplastic disease) and in the management of terminal cancer patients.

Dosage and administration

1. *Stromba Tablets: Adults:* One 5 mg tablet daily. For vascular complications, up to 10 mg daily is recommended.

Children: Under 6 years – $\frac{1}{2}$ tablet daily.

6–10 years – $\frac{1}{2}$ –1 tablet daily.

It is suggested that the tablets should be administered to children in short courses of six to eight weeks. More than one course may be given with an interval of one month between courses.

2. *Stromba Injection: Adults:* 50 mg (1 ml) administered by deep intramuscular injection once every 2–3 weeks.

Contra-indications, warnings, etc Stromba should not be used in cases of cancer of the prostate because the condition is androgen-dependent. Because of possible virilising effects on a female foetus, Stromba should not be administered to pregnant women.

Stromba should be used with caution in the presence of impaired renal or cardiac function as it may encourage sodium and water retention.

Care should be taken in administering Stromba in patients with liver dysfunction. Such patients should be monitored by means of routine liver function tests and treatment discontinued if signs of deterioration are observed.

Tumours of the liver have been reported occasionally in patients subjected to prolonged treatment with androgenic-anabolic steroids, especially patients with Fanconi's syndrome and aplastic anaemia. These tumours, however, are not typical of primary hepatocellular carcinoma and, in some cases, discontinuation of steroids has resulted in tumour regression without other therapy. The possibility that these compounds may induce or enhance the development of such hepatic tumours cannot at present be excluded and this should be considered when the use of this product is proposed for long-term treatment, particularly in young people who are not suffering from life-threatening disorders. The use of stanozolol may result in an alteration in the ratio of

high and low density lipoproteins. The significance of this is not understood.

Anabolic steroids may increase sensitivity to anticoagulants; therefore, the dose of the latter may have to be decreased in order to maintain the prothrombin time at the desired therapeutic level.

Prolonged use in children may lead to premature closure of the epiphyses.

Overdosage: There are no reports of chronic or acute overdosage with Stromba. By analogy with other substances of this type, one would expect chronic overdosage to be associated with the signs and symptoms caused by excessive circulating androgens. It is unlikely that any immediate serious reactions would be seen in a single excessive dose (in animals acute toxicity cannot be measured). In such an event, however, the patient should be kept under observation in case of delayed reactions.

Side-effects: Because of the structural relationship to the male hormones, some androgenic side-effects are to be expected, but, because the ratio of anabolic to androgenic properties is high, these effects will be minimal at the recommended dosage. The androgenic effects so far reported have been mild and are usually only seen in young people. Other effects, not related to androgenicity, such as headache, euphoria, depression and cramp have also occurred occasionally. There have been occasional reports of cholestatic jaundice.

Pharmaceutical precautions Each ampoule should be thoroughly shaken before use. Protect from light.

Legal category POM.

Package quantities 1. *Stromba Tablets:* Bottles of 50 or 200 tablets.

2. *Stromba Injection:* Plastic boxes each containing 1 ampoules.

Further information Nil.

Product licence numbers

Stromba Tablets 0071/5092

Stromba Injection 0071/0031

TELEPAQUE*

Presentation Telepaque Tablets are off-white to buff bi-convex tablets, 10.3 mm in diameter and plain on both sides. Each tablet contains 500 mg lipoic acid BP.

Uses Telepaque Tablets are recommended for oral cholecystography and cholangiography.

Dosage and administration Telepaque Tablets are usually given 10–14 hours before cholecystography.

Adults:

1. The usual dose is 6 Telepaque Tablets swallowed whole with at least one full glass of water. Eight tablets may be given to very obese patients. For repeat examinations on the same day as the original procedure an additional 6 tablets may be administered. However if the repeat examination is to be performed with double dose of Telepaque a period of five to seven days should be allowed between the two examinations. No more than 12 tablets should be taken during a 24-hour period.

2. In order to obtain better visualisation of the extrahepatic ducts, 9–12 tablets may be given in 2 doses. Three to six tablets are given four hours after a fatty meal.

n the day preceding the examination, and then a full dose of 6 tablets after a fat-free meal in the evening.

Another technique is to administer a double dose (12 tablets) of Telepaque after a 12-hour fast, followed by ml Camphorated Opium Tincture BP to close the sphincter of Oddi. Films may be taken 5–14 hours later, and any sphincter pain caused by the tincture may be eased with an anticholinergic. As noted above, 12 tablets is the maximum dose which should be administered in 4 hours.

3. Certain biliary calculi only become radiographically opaque after prolonged exposure to the contrast medium. Such prolonged exposure to Telepaque can be obtained by the following regimen. Patients are instructed to take two Telepaque Tablets after each of the three main meals, daily for four days. During this time the meals should be relatively fat-free. The X-ray examination is made on the morning of the fifth day, the patient fasting.

Contra-indications, warnings, etc Telepaque is contra-indicated in patients with advanced hepatorenal disease or severe impairment of renal function. It should not be given to patients with gastro-intestinal disorders which interfere with absorption and result in inadequate isualisation. Telepaque may also be contra-indicated in patients who are sensitive to iodine compounds. Caution is also necessary in patients suffering from cholangitis or marked hyperthyroidism.

In patients with severe advanced liver disease, renal function should be assessed before cholecystography, and renal output and hepatic function should be observed for a few days after the procedure. Observation of renal function after multiple doses of the contrast medium has also been recommended. Iopanoic acid has a uricosuric effect approximately equivalent to that of probenecid. Although this action cannot be definitely linked with nephrotoxicity, it has been strongly recommended that adequate hydration should be encouraged as a possible means of decreasing the risk of renal complications.

Patients with pre-existing renal disease should not receive double doses of cholecystographic media. It is possible that renal irritation in susceptible individuals could result in reflex vascular spasm with partial or complete renal shutdown. It is therefore suggested that kidney function in patients with renal disease should be assessed before administration of cholecystographic media, and for several days afterwards.

Fatal coronary occlusion in four patients with arteriosclerotic heart disease who had taken a cholecystographic agent has been reported and premedication with tropine is a reasonable prophylactic measure against vagal stimulation if cholecystography is necessary in patients with recent symptoms of coronary artery disease. However, the connection between these fatalities and the administration of the contrast media (iopanoic acid in two cases and iodoaliphonic acid in the other two) may have been wholly fortuitous. It has also been suggested that the administration of large doses of other aromatic iodine compounds like urographic and angiographic agents with or shortly following cholecystographic agents may increase the likelihood of toxic reactions.

The most frequently reported adverse reactions have been mild and transient nausea, vomiting, diarrhoea and cramps. A stinging sensation during urination occurs occasionally and has been attributed to urethral irritation. It does not indicate any renal or upper urinary tract trouble. Skin reactions such as urticaria, pruritus and flushing rarely occur.

Thrombocytopenia after two 3 g doses has been reported in a patient with a history of conjunctival haemorrhages. Acute renal failure with complete recovery has been reported in four patients, three of whom were given doses of Telepaque which were higher than those recommended.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Cartons of 36 tablets packed in aluminium foil strips of 6.

Further information Nil.

Product licence number 0071/5095.

TRANCOPRIN®

Presentation White, flat-bevelled edge tablets 11 mm in diameter, marked with a 'T' on one face and scored on the other. Each tablet contains Aspirin BP 300 mg and chlormezanone 100 mg.

Uses For the treatment of painful conditions where the combination of an analgesic and a mild tranquilliser/muscle relaxant would be of value. Such conditions include musculoskeletal disorders associated with muscle spasm, headache and painful menstrual disorders.

Dosage and administration Trancoprin tablets are for oral administration only. The usual adult dose is 1 or 2 tablets three times a day. Not more than 8 tablets should be taken daily. There are no specific recommendations for children.

Contra-indications, warnings, etc Trancoprin tablets should not be given to patients with a known hypersensitivity to chlormezanone or aspirin (including those with haemophilia and similar coagulation disorders) nor to those who are also taking monoamine oxidase inhibitors. They should not be taken by patients with a history of peptic ulcer because aspirin may induce (occasionally major) intestinal haemorrhage. Chlormezanone in high doses may modify the patient's reactions (performance of skilled tasks, alertness, etc.) to a varying extent, depending upon individual susceptibility. Therefore, patients should be advised not to drive or operate machinery during treatment if affected. If Trancoprin is administered with CNS depressants, it is possible that their sedative effect may be intensified. As with other drugs acting on the central nervous system, patients should avoid alcohol while receiving Trancoprin since the response cannot be predicted.

There is clinical and epidemiological evidence of the safety of aspirin (but not of chlormezanone) in human pregnancy. Because aspirin may prolong labour and contribute to maternal and neonatal bleeding, the use of Trancoprin is best avoided at term. Aspirin may enhance the effect of anticoagulants and inhibit the action of uricosuric agents: because it may precipitate bronchospasm, it may induce attacks of asthma in susceptible subjects.

Overdosage should be treated by gastric lavage (if the product has been recently ingested) together with the usual measures taken for salicylate toxicity. There are likely to be additional symptoms due to the excessive amount of chlormezanone absorbed, such as somnolence, depression and prostration. There may also be muscular incoordination, blurred vision, weakness and

memory disturbances. In severe cases, hypotension, respiratory depression and loss of consciousness may occur. Symptomatic treatment is suggested for chlormezanone overdosage.

Side-effects: Adverse effects have been infrequent with Trancoprin. As would be expected with chlormezanone, a compound having mild tranquillising properties, drowsiness and dizziness have been the commonest.

There have also been occasional reports of constipation, flushing, dry mouth, nausea, weakness and rash. Very rarely reversible cholestatic jaundice has been reported in patients who have taken chlormezanone.

The dependence potential of chlormezanone is not known.

Pharmaceutical precautions Trancoprin tablets should be kept in well-closed containers protected from moisture.

Legal category POM.

Package quantities Amber glass bottles, each containing 100 tablets.

Further information Nil.

Product licence number 0071/0093.

VERIPAQUE*

Presentation Veripaque Powder is a fine, white powder containing 50 mg oxyphenisatin in 3 g.

Uses Veripaque is recommended: a) for adding to barium enemas in radiological examination of the large intestine; b) as a cleansing enema to remove colonic gas and faeces before plain abdominal radiography, intravenous pyelography, cholecystography, proctosigmoidoscopy, etc; c) for pre-operative cleansing of the large intestine.

Dosage and administration Veripaque Powder is used for the preparation of enemas for rectal administration.

Adults: Veripaque enemas should be administered slowly

over a period of five to eight minutes with the fluid level 18–24 inches above the hips.

As a cleansing enema prior to diagnostic or surgical procedures, 3 g of Veripaque Powder is dissolved in litres of water.

When used as an adjuvant to a barium enema, 3 Veripaque Powder is mixed thoroughly with 2 litres of barium enema suspension.

Contra-indications, warnings, etc Care is needed in patients with an irritable colon or inflammatory diseases of the large intestine; in such cases Veripaque should be used in smaller than usual doses. As with other enemas Veripaque is not recommended in cases of appendicitis, gross bleeding from the bowel, intestinal obstruction, severe spasm or severe diarrhoea, or where there is danger of intestinal perforation. Reduced dosage is recommended for elderly or debilitated patients. Although when used in small and infrequent doses as in preparations for radiography it may well be harmless, regular, prolonged use should be discouraged because of the possibility of liver toxicity. Minor side-effects such as cramps, diarrhoea, nausea and vomiting, sweating or tachycardia may occur infrequently and can usually be obviated by decreasing the dosage. The cramps, which occur in about 8% of cases, usually produce only mild discomfort and do not interfere with completion of the procedure.

As with tannic acid, more serious side-effects such as syncope may occur occasionally; they are usually caused by administration of too large a dose.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Boxes of 6 vials each containing 3 g Veripaque Powder.

Further information Nil.

Product licence number 0071/5099.

* Trade Mark



CETOXYL* 2.5

Presentation Acetoxyl 2.5 contains 2.5% benzoyl peroxide in an aqueous acetone gel base. The gel is visible and non-greasy when applied to the skin.

Uses Acetoxyl 2.5 is indicated as an aid in the treatment of acne vulgaris.

The gel base allows the active substance, benzoyl peroxide, to penetrate into the acne follicle, where it exerts an antibacterial effect against *Propionobacterium* *acnes*.

Dosage and administration The gel should be carefully applied to the affected areas once daily. Washing with soap and water prior to application greatly enhances the efficacy of the preparation.

The response to benzoyl peroxide can vary from patient to patient and in some cases the higher strength, cetoxyl 5, may be required.

Contra-indications, warnings, etc Patients with a known sensitivity to benzoyl peroxide should not use this product.

Take care to keep the product away from the mouth, the eyes and other mucous membranes to avoid irritation. The product should only be applied to other sensitive areas, such as the skin of the neck, with caution.

For external use only.

In normal use a mild burning sensation will probably be felt on first application and a moderate reddening and peeling of the skin will occur within a few days. During the first few weeks of treatment a sudden increase in peeling will occur in most patients. This is not harmful and will subside in a day or two if the treatment is temporarily discontinued.

If discomfort such as burning, redness or excess peeling occurs, discontinue treatment temporarily or consult a doctor.

Keep out of reach of children.

The product may bleach coloured fabrics.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities Acetoxyl 2.5 is available in tubes containing 40 g.

Further information Nil.

Product licence number 0174/0041.

CETOXYL* 5

Presentation Acetoxyl 5 contains 5% benzoyl peroxide in an aqueous acetone gel base. The gel is invisible and non-greasy when applied to the skin.

Uses Acetoxyl 5 is indicated as an aid in the treatment of acne vulgaris.

The gel base allows the active substance, benzoyl

peroxide, to penetrate into the acne follicle, where it exerts an antibacterial effect against *Propionobacterium* *acnes*.

Dosage and administration The gel should be carefully applied to the affected areas once daily. Washing with soap and water prior to application greatly enhances the efficacy of the preparation.

The response to benzoyl peroxide can vary from patient to patient. Should any undue reaction occur, it may be necessary to use the lower strength, Acetoxyl 2.5.

Contra-indications, warnings, etc Patients with a known sensitivity to benzoyl peroxide should not use this product.

Take care to keep the product away from the mouth, the eyes and other mucous membranes to avoid irritation. The product should only be applied to other sensitive areas, such as the skin of the neck, with caution.

For external use only.

In normal use a mild burning sensation will probably be felt on first application and a moderate reddening and peeling of the skin will occur within a few days. During the first few weeks of treatment a sudden increase in peeling will occur in most patients. This is not harmful and will subside in a day or two if the treatment is temporarily discontinued.

If discomfort such as burning, redness or excess peeling occurs, discontinue treatment temporarily or consult a doctor.

Keep out of reach of children.

The product may bleach coloured fabrics.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities Acetoxyl 5 is available in tubes containing 40 g.

Further information Nil.

Product licence number 0174/0039.

BENOXYL* 5

Presentation Benoxyl 5 is available as a white lotion or cream containing benzoyl peroxide 5%. It is non-greasy, odourless and non-staining – completely invisible on the skin.

Uses Benoxyl 5 is indicated in the treatment of acne vulgaris. The active ingredient, benzoyl peroxide, is an antibacterial and mild keratolytic agent.

Benoxyl may be applied in conjunction with other topical preparations such as salicylic acid and antibacterials.

Dosage and administration Benoxyl 5 lotion or cream should be applied to the affected areas once daily.

Washing with soap and water prior to application greatly enhances the efficacy of the preparation.

Should discomfort such as burning, redness or excessive peeling occur at any point, treatment should be discontinued and resumed when discomfort subsides.

As the skin becomes tolerant to Benoxyl 5, peeling will diminish. When this occurs Benoxyl 10 should be used.

Contra-indications, warnings, etc Allergic sensitivity to Benoxyl is rare.

A mild burning sensation may be noticed on first application and moderate erythema and desquamation appear within a few days. Indiscriminate application may produce a marked erythema. Such conditions will subside if treatment is discontinued for a few days. Benoxyl may bleach clothing, bed linen and, very rarely, eyebrows and hair.

Pharmaceutical precautions Benoxyl lotions and creams should be stored in a cool, dark place.

Legal category P.

Package quantities *Cream:* 40 g. *Lotion:* 30 ml.

Further information Nil.

Product licence numbers

Lotion 0174/5003

Cream 0174/5007

BENOXYL* 5 WITH SULPHUR

Presentation Benoxyl 5 with Sulphur is available as an off-white lotion or cream. It contains benzoyl peroxide 5% and sulphur 2%. It is non-greasy, odourless and non-staining – completely invisible on the skin.

Uses Benoxyl 5 with Sulphur is indicated in the treatment of acne vulgaris. The active ingredient, benzoyl peroxide, is an antibacterial and mild keratolytic agent. In Benoxyl 5 with Sulphur the activity of the benzoyl peroxide is enhanced by the addition of sulphur.

While the traditional remedies, sulphur and resorcinol, cause marked epidermal reactions, the combination of benzoyl peroxide and sulphur acts predominantly at a deeper level, closer to the site of acne pathology. Benoxyl may be applied in conjunction with other topical preparations such as salicylic acid and antibacterials.

Dosage and administration Benoxyl 5 with Sulphur lotion or cream should be applied to the affected areas once daily. Washing with soap and water prior to application greatly enhances the efficacy of the preparation.

In cases of severe or resistant acne, Benoxyl 10 with Sulphur may eventually be required.

Contra-indications, warnings, etc Allergic sensitivity to Benoxyl is rare.

A mild burning sensation may be noticed on first application and moderate erythema and desquamation appear within a few days. Indiscriminate application may produce a marked erythema. Such conditions will subside if treatment is discontinued for a few days. Benoxyl may bleach clothing, bed linen and, very rarely, eyebrows and hair.

Pharmaceutical precautions Benoxyl lotions and creams should be stored in a cool, dark place.

Legal category P.

Package quantities *Cream:* 40 g. *Lotion:* 30 ml.

Further information Nil.

Product licence numbers

Lotion 0174/5004

Cream 0174/5008

BENOXYL* 10

Presentation Benoxyl 10 is available as a white lotion containing benzoyl peroxide 10%. It is non-greasy, odourless and non-staining – completely invisible on the skin.

Uses Benoxyl 10 is indicated in the treatment of acne vulgaris. The active ingredient, benzoyl peroxide, is an antibacterial and mild keratolytic agent.

Benoxyl 10 may be applied in conjunction with other topical preparations such as salicylic acid and antibacterials.

Dosage and administration Benoxyl 10 lotion should be applied to the affected areas once daily. Washing with soap and water prior to application greatly enhances the efficacy of the preparation.

Should discomfort such as burning, redness or excessive peeling occur at any point, treatment should be discontinued and resumed when discomfort subsides. Alternatively Benoxyl 5 (5% benzoyl peroxide) may be used.

Contra-indications, warnings, etc Allergic sensitivity to Benoxyl is rare.

A mild burning sensation may be noticed on first application and moderate erythema and desquamation appear within a few days. Indiscriminate application may produce a marked erythema. Such conditions will subside if treatment is discontinued for a few days. Benoxyl may bleach clothing, bed linen and, very rarely, eyebrows and hair.

Pharmaceutical precautions Benoxyl lotion should be stored in a cool, dark place.

Legal category P.

Package quantities Lotion: 30 ml.

Further information Nil.

Product licence number Lotion 0174/0034.

BENOXYL* 10 WITH SULPHUR

Presentation Benoxyl 10 with Sulphur is available as an off-white lotion or cream. It contains benzoyl peroxide 10% and sulphur 5%. It is non-greasy, odourless and non-staining – completely invisible on the skin.

Uses Benoxyl 10 with Sulphur is indicated in the treatment of acne vulgaris. The active ingredient, benzoyl peroxide, is an antibacterial and mild keratolytic agent. In Benoxyl 10 with Sulphur the activity of the benzoyl peroxide is enhanced by the addition of sulphur.

While the traditional remedies, sulphur and resorcinol caused marked epidermal reactions, the combination of benzoyl peroxide and sulphur acts predominantly at a deeper level, closer to the site of acne pathology. Benoxyl may be applied in conjunction with other topical preparations such as salicylic acid and antibacterials.

usage and administration Treatment should normally start with Benoxyl 5 (5% benzoyl peroxide). As the skin becomes tolerant to Benoxyl 5, peeling will diminish. When this occurs, Benoxyl 5 with Sulphur (5% benzoyl peroxide with 2% sulphur) should be used.

Benoxyl 10 with Sulphur lotion or cream should be applied to the affected areas once daily. Washing with soap and water prior to application greatly enhances the efficacy of the preparation.

contra-indications, warnings, etc Allergic sensitivity to Benoxyl is rare.

A mild burning sensation may be noticed on first application and moderate erythema and desquamation appear within a few days. Indiscriminate application may produce a marked erythema. Such conditions will subside if treatment is discontinued for a few days. Benoxyl may bleach clothing, bed linen and, very rarely, eyebrows and hair.

pharmaceutical precautions Benoxyl lotions and creams should be stored in a cool, dark place.

legal category P.

package quantities *Cream*: 40 g. *Lotion*: 30 ml.

further information Nil.

product licence numbers

Lotion 0174/5005

Cream 0174/5009

BRASIVOL

Presentation Benoxyl 20 Lotion contains benzoyl peroxide 20% in a stabilised lotion base.

Uses Benoxyl 20 Lotion is indicated in the management of Cutaneous Ulcers.

Dosage and administration Apply a protective ointment to the skin area bordering the ulcer. Cut a thick dressing such as an abdominal pad, or cotton wool between gauze layers to fit the size and shape of the ulcer exactly. Moisten the dressing with normal saline or water. Saturate the dressing with Benoxyl 20 and apply to the ulcer with sterile forceps, and apply over this a piece of thin plastic film to extend just beyond the ulcer margin.

Change the dressing every eight hours for large ulcers and every 12 hours for small ulcers. To hold the dressing in place cover it with a large pad, such as an amputation pad, and tape this firmly in place with hypoallergenic tape. For ulcers with cavities, saturate surgical ribbon gauze with Benoxyl 20 Lotion and pack into the cavities with sterile forceps, so that the Benoxyl 20 comes into contact with every area of the ulcer cavity, and then proceed as above. Renew packing at each dressing. In lesions of the legs a supporting bandage may be advantageous.

Contra-indications, warnings, etc Keep away from the mouth, eyes and other mucous membranes to avoid irritation. Avoid normal skin. Irritant dermatitis has been reported in 2.5% to 3% of cases, if undue skin irritation develops, the use of the product should be discontinued. The product may bleach coloured fabrics. For external use only.

pharmaceutical precautions Store in a cool place.

legal category POM.

Package quantities Benoxyl 20 Lotion is supplied in bottles containing 100 ml.

Further information For excess granulation growth use a dilute Silver Nitrate preparation to reduce it to just below epidermal level. Analgesics may be needed for the first few days of treatment.

Product licence number 0174/0036.

BRÄSIVOL

Presentation Bräsivol is an abrasive cleansing paste in three grades, each containing graded particles of fused synthetic aluminium oxide in a non-irritant soap-detergent base.

Bräsivol No. 1 Fine is an off-white paste containing 38.09% aluminium oxide.

Bräsivol No. 2 Medium is a light-blue paste containing 52.2% aluminium oxide.

Bräsivol No. 3 Coarse is a light-green paste containing 65.2% aluminium oxide.

Uses Bräsivol is indicated in the treatment of acne vulgaris. Bräsivol effectively cleanses and removes debris from blocked pores and removes excess sebum from the skin, thus maintaining patency of the pore duct openings.

Dosage and administration The patient should commence treatment with Bräsivol No. 1 Fine. The abrasive cleansing paste should be applied by the patient to the wetted skin and rubbed gently but firmly over the affected area with a circular motion for about 30 seconds, then rinsed off thoroughly with water. This routine may be repeated one to three times daily, replacing ordinary soap and water.

In more severe conditions, after the use of Bräsivol No. 1 Fine for several weeks, the skin may require the slightly more abrasive action of Bräsivol No. 2 Medium and subsequently the longer-term maintenance may require the use of Bräsivol No. 3 Coarse.

Contra-indications, warnings, etc Bräsivol is contra-indicated in the presence of superficial venules and telangiectasia (actinic sequelae).

Care should be taken to avoid using Bräsivol close to the eyes or mouth and male patients using an electric razor should shave before applying Bräsivol.

A degree of dryness and redness will be seen during the first few days of treatment. Over-enthusiastic use, however, can cause irritation and, if this occurs, treatment should be interrupted for a day or two and then resumed.

Pharmaceutical precautions Protect from heat.

Legal category GSL.

Package quantities

Bräsivol No. 1 Fine. 70 g.

Bräsivol No. 2 Medium. 85 g.

Bräsivol No. 3 Coarse. 100 g.

Further information Bräsivol satisfies the patient's need to take an active part in the treatment of his condition but reduces to a minimum the desire for self-manipulation in the form of squeezing and picking of lesions.

Product licence numbers

Bräsivol No. 1 Fine 0174/5000

Bräsivol No. 2 Medium 0174/5001

Bräsivol No. 3 Coarse 0174/5002

DRICLOR*

Presentation Driclor is a clear colourless alcoholic solution containing 20% w/w aluminium chloride hexahydrate.

Uses Driclor is indicated for the treatment of hyperhidrosis of the axillae, the hands and the feet.

Dosage and administration Last thing at night carefully dry the affected areas and apply the product. Wash off in the morning. Do not re-apply the product during the day.

Initially the product may be applied each night until sweating stops during the day. The frequency of application may then be reduced to twice a week. Subsequently if sweating is still absent the frequency of application may be reduced to once a week or in some cases less frequently.

Contra-indications, warnings, etc Ensure that the affected areas to be treated are perfectly dry.

Do not apply the product to broken or irritated areas of skin.

Do not bathe immediately before application of the product. Allow at least one hour following bathing.

Do not shave armpits for 24 hours before or after use of the product.

Avoid direct contact with clothing and polished metal surfaces.

The product is inflammable.

For external use only.

Keep out of the reach of children.

Keep away from the eyes.

The reduction in sweating which the product causes may produce some temporary irritation or redness. If this becomes excessive stop the treatment temporarily and if necessary consult a doctor.

Pharmaceutical precautions The cap of Driclor should always be replaced tightly after use.

Driclor should be stored in an upright position.

Store in a cool place.

Legal category POM.

Package quantities 60ml in roll-on applicator plastic bottle.

Further information Driclor may cause irritation which is troublesome but not severe enough to warrant discontinuing its use. In these circumstances the irritation may be alleviated by the use of a weak hydrocortisone cream.

Product licence number 0174/0044.

DUOFILM*

Presentation Duofilm is an almost colourless, clear, mobile liquid supplied in an amber screw-capped bottle, internally fitted with a brush applicator.

Duofilm is a collodion based product containing:

Salicylic Acid BP 16.70% w/w

Lactic Acid BP 16.70% w/w

Uses Duofilm is for topical application only and is indicated in the treatment of plantar and mosaic warts.

Dosage and administration The patient should be instructed as follows:

1. Soak warts in hot water for five minutes.

2. Rub surface of warts carefully with pumice stone or manicure emery board.

3. Apply Duofilm taking care to avoid normal skin.

4. Allow to dry thoroughly and cover with plaster wart is large or on the foot.

5. Continue treatment until the wart is completely cleared and ridge lines of the skin have been restored.

Contra-indications, warnings, etc Duofilm is product formulated for the controlled corrosion of keratin. Care must be taken to apply the product to the wart only. Avoid applying to normal skin.

Duofilm should not be used on the face or anogenital regions.

Keep away from naked flame.

Pharmaceutical precautions Highly inflammable. Store in a cool place. Keep out of the reach of children.

Legal category P.

Package quantities Duofilm is available in an amber screw-capped applicator bottle containing 15 ml.

Further information Duofilm is prescribable on FP10.

Product licence number 0174/0025.

LACTICARE*

Presentation Lacticare contains Lactic Acid 5% and Sodium Pyrrolidone Carboxylate 2.5% in an oil-in-water viscous lotion base.

Uses Lacticare is indicated for the symptomatic relief of hyperkeratotic and other chronic dry skin condition and for dry skin conditions caused by low humidity or the use of detergents.

Dosage and administration Use as required on affected areas or as directed by a doctor. Shake well before use.

Contra-indications, warnings, etc Occasionally a transient mild stinging sensation may occur. Should prolonged irritation develop when used on abraded or inflamed skin, discontinue use.

Keep away from the eyes and mucous membranes. Should contact with the eyes occur, remove with water.

Keep out of the reach of children.

For external use only.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Bottles containing 150 ml.

Further information Nil.

Product licence number 0174/0038

OILATUM* CREAM

Presentation Oilatum Cream is a white, stable, oil-in-water cream containing Arachis Oil BP 21%. Impermeability is provided by the incorporation of 1% polyvinyl pyrrolidone (PVPK 30) in the oil phase.

Mineral oil and lanolin derivatives are avoided.

Uses Oilatum Cream is indicated in cases of dry sensitive skin, lanolin sensitivity, alkali intolerance, ichthyosis and similar conditions.

The use of Oilatum Cream in such conditions reduces:

moisture loss from the stratum corneum and thus restores flexibility.

The use of an inert plastic in the oil phase ensures a continuous residual film which tends to be more occlusive and longer-lasting than ordinary vegetable oils.

Dosage and administration Oilatum Cream, which may be used as often as required, is applied to the affected area and rubbed well in. It is especially effective immediately after washing, when the normal acid condition of the skin may be disturbed and when the sebaceous content of the stratum corneum may be depleted.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Protect from heat.

Legal category P.

Package quantities Oilatum Cream is available in tubes containing 40 g.

Further information The rapid symptomatic relief obtainable with Oilatum Cream is achieved by the use of an oil-in-water cream which provides a higher moisture content than is possible with water-in-oil preparations. After the evaporation and absorption of the water phase, the residual oil droplets coalesce to form an occlusive film.

Oilatum Cream is prescribable on FP10.

Product licence number 0174/5014.

OILATUM* EMOLLIENT

Presentation Oilatum Emollient is a semi-dispersing emulsion additive producing an emulsion of dispersed oil in bath water and a homogenised film on the surface. Oilatum Emollient, which is a colourless liquid, contains the following active ingredients:

Octylated wool alcohols	5.0%
liquid paraffin	63.7%

Uses Oilatum Emollient is indicated in the treatment of contact dermatitis, atopic dermatitis, senile pruritus, ichthyosis and related dry skin conditions. Oilatum emollient replaces oil and water and hydrates the keratin. Oilatum Emollient is particularly suitable for infant bathing. The preparation also overcomes the problem of cleansing the skin in conditions where the use of soaps, soap substitutes and colloid or oat-meal baths proves irritating.

Dosage and administration Oilatum Emollient should always be used with water, either added to the bath or applied to wet skin.

1. **Bath:** Add 1–3 capsul to an 8 inch bath of water. Soak for 10–20 minutes.

2. **For infant bathing:** Add ½–2 capsul to a wash-basin of water. Apply gently over entire body with sponge and bat dry.

3. **Direct to skin:** Wet the skin of the affected area and rub in a small quantity of Oilatum Emollient. Rinse and bat dry.

Where conditions permit, and particularly in cases of extensive areas of dry skin, Oilatum Emollient should be used as a bath oil, ensuring complete coverage by immersion. In addition to the therapeutic benefits, this method of use provides a means of sedating tense patients, particularly relevant in cases of acute pruritic

dermatoses where relaxation of tension appears to relieve symptoms.

Contra-indications, warnings, etc The patient should be advised to use care to avoid slipping in the bath.

Pharmaceutical precautions Protect from heat.

Legal category P.

Package quantities Oilatum Emollient is available in bottles containing 150 ml and 350 ml. A dispensing pack containing 1 litre is also available.

Further information Oilatum Emollient is prescribable on FP10.

Product licence number 0174/5010.

PANOXYL* 5 ACNE GEL PANOXYL* 10 ACNE GEL

Presentation Panoxyl 5 contains 5% benzoyl peroxide in a white gel base formulated with colloidal magnesium aluminium silicate, hydroxypropylmethyl-cellulose ethyl alcohol, polyoxyethylene lauryl ether, citric acid and purified water.

Panoxyl 10 contains 10% benzoyl peroxide in a gel base formulated as mentioned above for Panoxyl 5.

Uses Panoxyl 5 and 10 are each indicated for use as an aid in the treatment of acne. Benzoyl peroxide provides a drying and desquamative action, enhanced by the gel base, which is also invisible on the skin.

Dosage and administration Treatment should normally commence with Panoxyl 5. Apply the gel to the affected areas once daily. Washing with soap and water prior to application greatly enhances the efficacy of the preparation. The reaction of the skin to benzoyl peroxide differs in individual patients, and for this reason the higher percentage of benzoyl peroxide in Panoxyl 10 may be required in order to provide a satisfactory drying and desquamative action.

Contra-indications, warnings, etc Panoxyl 5 and 10 should not be prescribed for patients with a known sensitivity to benzoyl peroxide. Application to sensitive areas such as the neck should be made with caution; to avoid irritation there should be no contact with eyes, mouth and other mucous membranes.

In normal use, a mild burning sensation will probably be felt on first application and a moderate reddening and peeling of the skin will occur within a few days. During the first few weeks of treatment a sudden increase in peeling will occur in most patients; this is not harmful and will subside within a day or two if treatment is temporarily discontinued.

Panoxyl 5 and Panoxyl 10 may bleach dyed fabrics and thus care should be taken with clothing and bed linen if coloured.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities Panoxyl 5 and Panoxyl 10 are supplied in tubes each containing 40 g.

Further information Nil.

Product licence numbers

Panoxyl 5 0174/0019

Panoxyl 10 0174/0020

POLYTAR* EMOLLIENT

Presentation Polytar Emollient is a black liquid concentrated tar bath additive containing a unique combination of tars. The ingredients are as follows:

Tar BP	7.5%
Cade Oil BPC	7.5%
Coal Tar Solution	2.5%
Arachis oil extract of crude coal tar	7.5%
Liquid Paraffin BP	35%

Polytar Emollient makes available more active tar per ml than other bath additives containing only extracts in solution.

Uses Polytar Emollient is indicated in the treatment of psoriasis, eczema, atopic and pruritic dermatoses. The use of Polytar Emollient may be combined with ultraviolet radiation and other adjunctive therapy.

Polytar Emollient is also of value in removing loose psoriatic scales and paste following dithranol treatment.

Dosage and administration Two to four capful of Polytar Emollient should be added to an 8 inch bath and the patient instructed to bathe for 20 minutes.

Clinical studies have revealed that this is the optimum period for maximum absorption; after this time the rate of absorption decreases rapidly.

Contra-indications, warnings, etc Patients should be instructed to guard against slipping when entering or leaving the bath.

If irritation occurs and persists, discontinue use.

Pharmaceutical precautions Protect from heat.

Legal category GSL.

Package quantities Polytar Emollient is available in bottles of 250 ml. A dispensing pack containing 1 litre is also available.

Further information Studies have confirmed that Polytar Emollient ranks highly in terms of patient acceptability.

Unlike liquor picis carbonis, Polytar Emollient will not stain the bath, hair or skin. Furthermore, Polytar Emollient contains a bath oil to eliminate any drying of the skin.

Polytar Emollient is prescribable on FP10 for the treatment of psoriasis, eczema, atopic and pruritic dermatoses.

Product licence number 0174/5011.

POLYTAR* LIQUID

Presentation Polytar Liquid is a light-brown liquid concentrated, antiseptic, tar-medicated scalp cleanser adjusted to pH 5.5, containing the following active ingredients:

Tar BP	0.3%
Cade Oil BPC	0.3%
Coal Tar Solution	0.1%
Arachis oil extract of crude coal tar	0.3%
Oleyl alcohol	1.00%

Uses Polytar Liquid is indicated in the treatment of scalp disorders such as psoriasis, dandruff, seborrhoea, eczema and pruritus. Polytar Liquid is also of value in the removal of pastes and pomades used in the treatment of psoriasis.

Dosage and administration The hair should be wetted and sufficient Polytar Liquid applied to produce

an abundant lather. The scalp and adjacent areas should be vigorously massaged with the fingertips. The hair should then be thoroughly rinsed and the procedure repeated.

Polytar Liquid should be used once or twice weekly

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Protect from heat.

Legal category GSL.

Package quantities Polytar Liquid is available in bottles of 65 ml, 150 ml and 350 ml. A dispensing pack containing 1 litre is also available.

Further information Polytar Liquid is prescribable on FP10 for psoriasis, eczema and seborrhoea of the scalp and dandruff.

Product licence number 0174/5016.

POLYTAR PLUS*

Presentation Polytar Plus is a concentrated antiseptic tar-medicated scalp cleanser containing the following active ingredients:

Tar BP	0.3%
Cade Oil BPC	0.3%
Coal Tar Solution	0.1%
Arachis Oil extract of crude coal tar	0.3%
Oleyl alcohol	1.0%
Hydrolysed Animal Protein	3.0%

Uses Polytar Plus is indicated in the treatment of scalp disorders such as dandruff, psoriasis, seborrhoea, eczema and pruritus. Polytar Plus is also of value in the removal of pastes and pomades used in the treatment of psoriasis.

Dosage and administration The hair should be wetted and sufficient Polytar Plus applied to produce an abundant lather. The scalp and adjacent areas should be vigorously massaged with the fingertips. The hair should then be thoroughly rinsed and the procedure repeated.

Polytar Plus should be used once or twice weekly.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Store in a cool place.

Legal category P.

Package quantities Polytar Plus is available in bottles of 150 ml and 350 ml.

Further information Nil.

Product licence number 0174/0037.

SPECTRABAN* 4

Presentation Spectraban 4 contains isoamyl-p-N, N dimethylaminobenzoate 2.5% in ethyl alcohol. The lotion which is non-greasy and invisible on the skin, is blue in colour.

Uses Spectraban 4 is a protective sunscreen lotion indicated in patients at risk from exposure to ultraviolet light within the wavelength range 290–320 nanometres. It is this narrow waveband of ultraviolet light which is responsible for burning and tanning of the skin in summer. Use of the product should allow 4 times normal exposure to sunlight before burning.

Spectraban 4 is indicated in sun-sensitive conditions such as polymorphic light eruptions and solar urticaria.

id any condition made worse by UVB light such as pus erythematosus.

usage and administration Apply evenly and liberally to areas to be exposed or protected only by light clothing. Allow 45 minutes before swimming or sweating reducing exercise. A single application may give day long protection but the product should be re-applied during prolonged sunning, after excessive sweating and swimming or as directed by a doctor.

contra-indications, warnings, etc Sunscreen preparations occasionally produce a sensitivity reaction. Although such occurrences are rare with Spectraban 4, treatment should be discontinued if a skin rash or irritation develops. For external use only. Avoid contact with the eyes. Avoid flame. May stain clothing. Keep out of the reach of children.

pharmaceutical precautions Keep in a cool dark place.

legal category P.

package quantities Spectraban 4 is available in bottles containing 150 ml.

further information Spectraban 4 is prescribable on FP10 for patients who require protection from ultraviolet radiation in photodermatoses. Severe photosensitivity, which may occur in patients with porphyria is usually the result of long wavelength ultraviolet radiation or visible light. The protective qualities of Spectraban 4 are within the erythral range, 290–320 nanometres.

product licence number 0174/5013.

SPECTRABAN* 15

Presentation Spectraban 15 contains isoamyl-p-N, l-dimethylaminobenzoate 2.5% and para-aminobenzoic acid 5% in ethyl alcohol. The lotion, which is non-greasy and invisible on the skin, is pink in colour.

Uses Spectraban 15 is a protective sunscreen lotion indicated in patients at risk from exposure to ultraviolet light within the wavelength range 290–320 nanometres. It is this narrow waveband of ultraviolet light which is responsible for burning and tanning of the skin in man. Use of the product should allow 15 times normal exposure to sunlight before burning.

Spectraban 15 is indicated in sun-sensitive conditions such as polymorphic light eruptions and solar urticaria and any condition made worse by UVB light such as pus erythematosus.

Dosage and administration Apply evenly and liberally to areas to be exposed or protected only by light clothing. Allow 45 minutes before swimming or sweating reducing exercise. A single application may give day long protection but the product should be re-applied during prolonged sunning, after excessive sweating and swimming or as directed by a doctor.

Contra-indications, warnings, etc Sunscreen preparations occasionally produce a sensitivity reaction. Although such occurrences are rare with Spectraban 15, treatment should be discontinued if a skin rash or irritation develops. For external use only. Avoid contact with the eyes. Avoid flame. Keep out of the reach of children. May stain clothing.

Pharmaceutical precautions Keep in a cool dark place.

Legal category P.

Package quantities Spectraban 15 is available in bottles containing 150 ml.

Further information Spectraban 15 is prescribable on FP10 for patients who require protection from ultraviolet radiation in photodermatoses. Severe photosensitivity, such as may occur in patients with porphyria is usually the result of long wavelength ultraviolet radiation or visible light. The protective qualities of Spectraban 15 are within the erythral range, 290–320 nanometres.

Product licence number 0174/0035.

STIE-LASAN* OINTMENT

Presentation Dithranol BP 0.4% in a pomade base containing cetyl alcohol, mineral oil, white soft paraffin and sodium lauryl sulphate with 0.4% w/w salicylic acid.

Uses As an aid in the treatment of psoriasis, Dithranol has been shown to inhibit enzyme metabolism and reduce the mitotic turnover which is accelerated in the psoriatic epidermis. Stie-Lasan Ointment has demonstrated a high degree of efficacy for scale removal and plaque resolution in resistant psoriasis.

Dosage and administration *When used on the skin:* At bedtime, apply Stie-Lasan Ointment to plaque sites, being careful to avoid surrounding normal areas. A protective film of soft white paraffin applied to areas surrounding the plaques may be helpful. In the morning, remove any remaining Stie-Lasan Ointment with warm oil, followed by a tar bath.

When used on the scalp: Before applying Stie-Lasan Ointment, a thin protective film of soft white paraffin should be applied to the ears and scalp margin to minimise any irritation in these areas. Stie-Lasan Ointment, which should be applied at bedtime, should be massaged generously into the affected areas of the scalp, using a pair of plastic gloves to avoid staining the hands. The Ointment may easily be removed each morning with a shampoo. Soap alone is not sufficient. When scales are gone, plaques flattened and no palpable differences exist between the site of the lesions and normal surrounding skin, treatment may be reduced to a maintenance level.

Contra-indications, warnings, etc Dithranol is a powerful irritant and Stie-Lasan Ointment must not be used on or near the eyes or in areas where inflammation is present. Do not use in acute eruptions, only on quiescent or chronic patches.

If any reaction indicating sensitivity is observed, discontinue use. If excessive erythema is observed on adjacent normal skin, reduce the frequency of application.

Wash hands thoroughly after use.

For external use only.

Stie-Lasan Ointment will stain fabrics and temporarily stain hair and surrounding skin areas.

Pharmaceutical precautions Store in a cool dark place. The use of diluents is not recommended.

Legal category P.

Package quantities 110 g.

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STIEFEL LABORATORIES (UK) LIMITED

Further information Nil.

Product licence number 0174/0018.

ZEASORB* POWDER

Presentation ZeaSORB is an off-white, highly absorbent, soft, antiseptic dusting powder containing the following:

Finely pulverised maize core	45%
Chloroxylanol BPC	0.5%
Aluminium dihydroxyallantoinate	0.2%

Uses Intertrigo, hyperhidrosis, bromidrosis, prevention of tinea pedis and any other condition in which the absorption of fluid from the surface of the skin is desirable.

Dosage and administration The affected areas should be dried as thoroughly as possible before applying ZeaSORB Powder. The powder should be smoothed over the surface of the skin, between joints and in folds.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Store in a cool dry place.

Legal category P.

Package quantities ZeaSORB Powder is available in sifter-top plastic containers of 30 g.

Further information ZeaSORB Powder absorbs more than twice as much moisture as any of the leading 1 dusting powders with which it has been compared.

Furthermore, many dusting powders cake after the absorption of moisture, forming small irritating masses. This has been overcome with ZeaSORB, which remains soft upon saturation.

Product licence number 0174/5015.

**Trade Mark*

Stuart Pharmaceuticals Limited
Carr House, Carrs Road
Cheadle
Cheshire SK8 2EG



ANTASIL* LIQUID AND TABLETS

Presentation Antasil is presented as a white liquid and as white tablets, marked Stuart.

Each 5 ml of liquid contains Dried Aluminium Hydroxide Gel USP 400 mg, Magnesium Hydroxide USP 100 mg and Activated Polydimethylsiloxane 150 mg.

Each tablet contains Dried Aluminium Hydroxide Gel JSP 400 mg, Magnesium Hydroxide USP 400 mg and Activated Polydimethylsiloxane 250 mg.

Uses As an antacid/defatulant for symptomatic treatment of peptic ulcer, dyspepsia of functional or organic origin, heartburn in hiatus hernia or pregnancy, flatulence and abdominal distension, gastritis, oesophagitis and other conditions where hyperacidity or flatulence may be present.

Dosage and administration Antasil liquid – 5–30 ml is required, preferably between meals and at bedtime. Antasil tablets – one or two to be sucked or chewed as required, preferably between meals and at bedtime.

Contra-indications, warnings, etc

Contra-indications: There is no known contra-indication.

Precautions: Care should be taken in patients suffering from hypophosphataemia. It is probably wise to avoid any drug, including antacids, during the first trimester of pregnancy unless there are compelling reasons for their use.

Aluminium hydroxide may form a complex with tetracyclines and reduce absorption when given concomitantly.

Although the antacids in Antasil are balanced to minimise bowel reaction, mild diarrhoea may be experienced at high doses.

Pharmaceutical precautions *Storage conditions:* Antasil liquid and tablets should not be stored at extremes of temperature.

Legal category P.

Package quantities Antasil liquid is supplied in bottles containing 300 ml and the tablets in cartons of 60 (6 strips of 10 tablets).

Further information The antacids in Antasil are balanced to minimise bowel reaction. Activated Polydimethylsiloxane assists in breaking down bubble-trapped gas, allowing the antacids to disperse quickly reducing hyperacidity and protecting the gastric mucosa from the inflammatory effect of high acid levels.

Product licence numbers

Tablets 0029/0118
Liquid 0029/0119

DISADINE* DP (DRY POWDER SPRAY)

Presentation Disadine DP is presented in an aerosol can which dispenses a brown powder. It is a dry powder spray containing 0.5% Povidone Iodine USP in BP propellants.

Uses Disadine DP is a wide-spectrum antiseptic for topical use. It presents all the bactericidal, fungicidal and virucidal properties of iodine with little if any risk of the skin sensitisation associated with elemental iodine. Disadine DP is indicated for topical application in the treatment and prevention of infection in wounds, including burns, varicose ulcers and bed sores.

Dosage and administration The aerosol can of Disadine DP must be shaken before use. The area requiring treatment is sprayed from a distance of 6–10 inches (15–25 cm) until a light dusting of powder is deposited. When dry this forms a protective antiseptic layer over the area which has been sprayed.

Contra-indications, warnings, etc Care must be taken when Disadine DP is used on known iodine-sensitive subjects, although these do not normally react to povidone iodine.

Disadine DP must not be used on patients with non-toxic nodular colloid goitre.

In very rare cases Disadine DP may produce skin reactions with iodine-sensitive subjects. These reactions subside on cessation of treatment.

Avoid getting the powder into the eyes or nose.

In cases of overdosage, treatment must be symptomatic.

Povidone iodine can be absorbed systemically during the topical treatment of burns, the degree of absorption being proportional to the depth and extent of the burn. Prolonged treatment with povidone iodine of patients with severe and extensive burns may cause metabolic acidosis, hypernatraemia, and renal impairment. In patients at risk Disadine DP should be used with caution. Excessively high serum levels may be reduced by haemodialysis. Absorption of povidone iodine may interfere with thyroid function tests by causing an increase in protein bound iodine levels.

Pharmaceutical precautions The aerosol can of Disadine DP must be stored away from direct heat and must not be autoclaved. The product should be used directly from the aerosol container. The container must not be punctured or destroyed by burning, even when empty.

Legal category GSL.

Package quantities Disadine DP is supplied in a 150 g aerosol can.

Further information Nil.

Product licence number 0029/5903.

DISPRAY* ANTIBIOTIC POWDER SPRAY

Presentation Dispray Antibiotic Powder Spray is presented in an aerosol can which dispenses a white or faintly yellow sterile powder. Approximately 1.2 g of powder is contained in each can. Dispray Antibiotic Powder Spray contains a sterile antibiotic powder with the following composition:

Neomycin Sulphate PhEur	650,000 units
Bacitracin Zinc BP	10,000 units
Polymyxin B Sulphate PhEur	165,000 units

in BP propellants.

Uses Dispray Antibiotic Spray is a wide-spectrum antibiotic spray. It is intended for topical application to wounds, cuts, lacerations and burns, and is particularly suitable for use in destroying pathogens which may contaminate tissues during surgical procedures.

Dosage and administration Spray the area to be treated with a light dusting of powder from a distance of 25 cm (10 inches).

Adults: The maximum recommended application is one can per day for seven days. The dose of neomycin should not exceed 1 g daily for seven days (or its equivalent when smaller daily doses are administered).

Children: Particular care must be exercised when using this product for any indication in children. The maximum dose should be reduced in proportion to body weight as an absorbed dose of neomycin exceeding 15 mg/kg body weight/day* may be associated with ototoxic effects. Greater caution should be exercised when treating infants.

* Note: A 10 second burst from a Dispray container delivered 68 mg (range 55–81 mg) of the antibiotic powder mixture over a 5" diameter area (approximately 129 cm²). Spraying should, therefore, not exceed 2 seconds/kg body weight/day.

Contra-indications, warnings, etc Contra-indicated in patients with hypersensitivity to neomycin, bacitracin or polymyxin.

Ototoxicity (including irreversible hearing loss) and nephrotoxicity, which may also result in ototoxicity, have been reported in association with inappropriate dosing with neomycin and also with polymyxin B. Nephrotoxicity has also been reported with inappropriate dosing with bacitracin. Significant absorption of the three antibiotics may occur from broken or inflamed skin. The spray should not be used on large denuded areas, including those due to burns, sunburn, chronic ulcers and chronic inflammatory dermatoses. Special care should be exercised in the treatment of patients with established hearing loss.

Dispray Antibiotic is not indicated for the treatment of pruritus and minor skin disorders.

Concurrent administration with other preparations containing aminoglycoside antibiotics is not recommended.

The inappropriate use of topical antibiotics has been associated with the emergence of resistant strains of bacteria.

In patients with renal impairment the dose should be reduced accordingly.

Neomycin may rarely cause neuromuscular blockade and because it potentiates skeletal muscle-relaxant drugs, it may cause respiratory depression and arrest. The use of this product in the immediate pre- and post-operative period is not, therefore, advisable.

All the antibiotics used in Dispray Antibiotic are known to cause delayed hypersensitivity reactions when used topically.

Because insufficient evidence is available on the use of the product in pregnant or lactating mothers special precautions should be exercised in its use in these situations.

Avoid inhaling the spray.

In the case of overdosage the treatment should be symptomatic.

Pharmaceutical precautions Dispray aerosols must be protected from heat and direct sunlight and must not be autoclaved. The container must not be punctured or destroyed by burning, even when empty. The product should be used directly from the aerosol container.

Legal category POM.

Package quantities Dispray Antibiotic Spray is presented as an aerosol spray which has a net weight of 110 g (79 ml).

Further information Nil.

Product licence number 0029/5905.

DISPRAY* 1 QUICK PREP

Presentation Dispray 1 Quick Prep is supplied in a printed tin-plate aerosol can which dispenses a colourless liquid containing Chlorhexidine Gluconate Solution BP 2.5% (chlorhexidine gluconate 0.5% w/v) in 70% total alcohols as industrial methylated spirit with BP propellant.

Uses Dispray 1 is a powerful disinfectant used for rapid disinfection of the skin before operations, subcutaneous or intramuscular injections or before venepuncture.

Dosage and administration Dispray 1 Quick Prep is sprayed on to the surface to be disinfected from a distance of 4–8 inches (10–20 cm).

It is suitable for both adults and children.

Contra-indications, warnings, etc Dispray 1 Quick Prep is flammable and must not be used near fires or flames. It must only be applied externally and must be kept away from the eyes and aural canals.

Only very occasional cases of skin sensitivity to chlorhexidine gluconate have been reported. As the product is supplied as an aerosol spray, it is unlikely that the liquid will be ingested. Any product which enters the eyes, ears or mouth must be washed out immediately with water.

Pharmaceutical precautions Dispray 1 Quick Prep spray should be protected from heat, including exposure to bright sunlight and radiators. The aerosol must not be punctured or destroyed by burning even when empty.

The product should be used directly from its container. Hypochlorite bleaches may cause the development of brown stains in fabrics which have previously been in contact with chlorhexidine preparations. Oxidising bleaches such as sodium perborate should be used.

Legal category GSL.

Package quantities Dispray 1 Quick Prep is supplied as an aerosol can containing 400 ml.

Further information Nil.

Product licence number 0029/5900.

METOSYN* FAPG CREAM AND OINTMENT

Presentation Metosyn consists of the corticosteroid fluciclonide presented as FAPG Cream and as Ointment.

Metosyn FAPG Cream, fluciclonide 0.05% w/w is dissolved completely in propylene glycol with fattycohols added to produce a white, homogeneous, semisolid preparation. Metosyn Ointment contains fluciclonide 0.05% w/w completely dissolved in a petroleum base.

Uses Metosyn contains an effective topical corticosteroid, and is suitable for treating a wide variety of local inflammatory, pruritic and allergic disorders of the skin. It is indicated for topical application in the following conditions.

Eczema and dermatitis: Atopic eczema, seborrhoeic dermatitis, discoid eczema, pompholyx, contact dermatitis, neurodermatitis, intertrigo.

Non-specific ano-genital pruritus: prurigo. Psoriasis, lichen planus. Discoid lupus erythematosus.

Metosyn FAPG Cream may be used for wet or dry lesions. Metosyn Ointment, with its emollient effects, is particularly suitable for dry scaly lesions.

Dosage and administration A small quantity of Metosyn FAPG Cream or Metosyn Ointment should be applied three to four times daily to the affected area and massaged well in.

Once improvement is apparent, usage may be reduced to twice or even once daily. These instructions apply to both adults and children.

It is recommended that Metosyn is used undiluted (see Pharmaceutical precautions).

Contra-indications, warnings, etc

Contra-indications: Metosyn is contra-indicated in rosacea, acne and peri-oral dermatitis, all of which can be treated with oral tetracyclines and hydrocortisone if a topical steroid is required. As with all topical steroids, Metosyn is contra-indicated in tuberculous, syphilitic, fungal and viral infections of the skin.

Precautions: Where there is bacterial infection associated with an inflammatory skin condition, Metosyn should only be administered if adequate antibacterial cover is also given. Topical administration of corticosteroids to pregnant animals has been shown to cause abnormalities of foetal development. Although the relevance of this finding to human application has not been established, when topical steroid treatment is considered necessary during pregnancy, both the amount applied and the length of treatment should be minimised. Long-term continuous topical steroid therapy should be avoided since adrenal suppression can occur, particularly when infants are being treated.

Side-effects: As with all topical steroids, striae may occur after extensive use of Metosyn. Occasionally a stinging or mild itching sensation may be noticed on application of FAPG Cream.

Overdose: A 25 g tube of Metosyn FAPG Cream or Ointment contains 12.5 mg of fluciclonide. Toxic effects are not likely to occur following accidental oral ingestion. Similarly, the components of the vehicles, singly or collectively, have not been shown to produce toxic effects in these quantities.

Pharmaceutical precautions Metosyn should be stored in the original tube and protected from heat. It is recommended that the product be used undiluted. However, if dilution of Metosyn Ointment is required,

white soft paraffin should be used and special FAPG diluent should be used to dilute FAPG Cream.

Legal category POM.

Package quantities Tubes of 25 g and 100 g FAPG Cream.

Tubes of 25 g and 100 g Ointment.

Further information Metosyn FAPG Cream and Metosyn Ointment do not contain lanolin or parabens.

Product licence numbers

Metosyn FAPG Cream 0029/5071

Metosyn Ointment 0029/0133

SORBICHEW*

Presentation Sorbichew tablets contain isosorbide dinitrate.

The Chewable tablets are round, green, scored tablets embossed Stuart, each containing 5 mg isosorbide dinitrate.

Uses *Angina Pectoris:* Sorbichew tablets are to prevent or abort the acute attack.

Dosage and administration Sorbichew tablets are scored for easier dose adjustment.

Treatment of the acute attack: Either one or two Sorbichew tablets should be chewed until dissolved completely and swallowed.

Prevention of an expected attack: Immediately prior to the stressful event either one or two Sorbichew tablets should be chewed until dissolved completely and swallowed.

Contra-indications, warnings, etc

Contra-indications: A known sensitivity to the drug.

Warnings: The following adverse effects may be seen with isosorbide dinitrate.

1. Cutaneous vasodilation, headache, dizziness and weakness may occur. If headache is a problem, a temporary lowering of the dose, and the use of analgesics, may be necessary. In the majority of patients, headache diminishes or disappears after 1-3 weeks and optimum dosage may be achieved.

2. Postural hypotension.

3. The drug can act as a physiological antagonist to noradrenaline, acetylcholine, histamine and other agents.

4. Dry rash and/or exfoliative dermatitis may occasionally occur.

Overdose: Overdose should be treated symptomatically. The main symptom is likely to be hypotension and this may be treated by elevation of the legs to promote venous return.

Pharmaceutical precautions *Storage:* Although Sorbichew tablets are very stable and no special storage precautions are required, it is advised that in accordance with good pharmaceutical practice the tablets should be stored protected from heat and moisture.

Legal category P.

Package quantities Sorbichew: 5 mg chewable tablets are supplied in aluminium tubes of 100 and 500.

Further information Unlike glyceryl trinitrate, Sorbichew tablets are very stable and therefore loss of potency when carried by the patient does not normally occur.

Sorbichew has an approximate onset of action of two minutes and duration of action up to two hours.

Product licence number

Sorbichew 5 mg 0029/0109

SORBID* S.A.

Presentation Sorbid S.A. tablets contain isosorbide dinitrate.

Sorbid S.A. tablets are yellow, round, flat, bevel-edged tablets, embossed 'Stuart' on one side and '880' on the reverse side. Each tablet contains 40 mg of isosorbide dinitrate; 10 mg for immediate release and 30 mg in a sustained action formulation.

Uses *Angina Prophylaxis:* The tablets are swallowed for protection against angina pectoris.

Dosage and administration *Angina Prophylaxis:* 1–2 Sorbid S.A. tablets should be swallowed twice daily.

Contra-indications, warnings, etc *Contra-indications:* A known sensitivity to the drug.

Warnings: The following adverse effects may be seen with isosorbide dinitrate.

1. Cutaneous vasodilation, headache, dizziness and weakness may occur. If headache is a problem, a temporary lowering of the Sorbid S.A. dose, and the use of analgesics, may be necessary. In the majority of patients, headache diminishes or disappears after 1–3 weeks and optimum dosage of Sorbid S.A. may be achieved.

2. Postural hypotension.

3. The drug can act as a physiological antagonist to noradrenaline, acetylcholine, histamine and other agents.

4. Dry rash and/or exfoliative dermatitis may occasionally occur.

Overdosage: Overdose should be treated symptomatically. The main symptom is likely to be hypotension and this may be treated by elevation of the legs to promote venous return.

Pharmaceutical precautions *Storage:* Although Sorbid S.A. tablets are very stable and no special storage precautions are required, it is advised that in accordance with good pharmaceutical practice the tablets should be stored protected from heat and moisture.

Legal category P.

Package quantities Sorbid S.A. 40 mg tablets are supplied in aluminium tubes of 60.

Further information Unlike glyceryl trinitrate, Sorbid S.A. tablets are very stable and therefore loss of potency when carried by the patient does not normally occur.

The duration of action of the Sorbid S.A. tablet is estimated to be up to 12 hours.

Product licence number

Sorbid S.A. tablets 40 mg 0029/0149

SORBITRATE*

Presentation Sorbitrate tablets contain isosorbide dinitrate. Sorbitrate tablets are available containing 10 mg and 20 mg isosorbide dinitrate. The 10 mg tablets are oval, yellow, scored tablets embossed Stuart. The 20 mg tablets are oval, blue, scored tablets embossed Stuart.

Uses *Angina Prophylaxis:* The tablets are taken orally for protection against angina pectoris.

Congestive Cardiac Failure: The tablets are taken as adjunctive therapy in the management of severe acute or chronic congestive cardiac failure.

Dosage and administration The tablets are scored for easier dose adjustment.

Angina Prophylaxis: 1–4 Sorbitrate 10 mg tablets or $\frac{1}{2}$ –Sorbitrate 20 mg tablets should be taken three or four times a day. The individual dose required for adequate cover should be determined.

Congestive Cardiac Failure: In severe congestive cardiac failure Sorbitrate tablets may be taken in doses of 10–40 mg three or four times daily depending on patient requirements. In this situation optimal individual dose is best determined by continuous haemodynamic monitoring. The use of Sorbitrate in severe congestive cardiac failure should be considered adjunctive therapy to more conventional treatment (e.g. digitalis, diuretics, etc.).

Contra-indications, warnings, etc

Contra-indications: A known sensitivity to the drug.

Warnings: The following adverse effects may be seen with isosorbide dinitrate.

1. Cutaneous vasodilation, headache, dizziness and weakness may occur. If headache is a problem, a temporary lowering of the Sorbitrate dose, and the use of analgesics, may be necessary. In the majority of patients, headache diminishes or disappears after 1–3 weeks and optimum dosage of Sorbitrate may be achieved.

2. Postural hypotension.

3. The drug can act as a physiological antagonist to noradrenaline, acetylcholine, histamine and other agents.

4. Dry rash and/or exfoliative dermatitis may occasionally occur.

Overdosage: Overdose should be treated symptomatically. The main symptom is likely to be hypotension and this may be treated by elevation of the patient's legs to promote venous return.

Pharmaceutical precautions *Storage:* Although Sorbitrate tablets are very stable and no special storage precautions are required, it is advised that in accordance with good pharmaceutical practice the tablets should be stored protected from heat and moisture.

Legal category P.

Package quantities Sorbitrate tablets: 20 mg tablets are supplied in aluminium tubes of 100.

10 mg tablets are supplied in aluminium tubes of 100 and 500.

Further information Unlike glyceryl trinitrate, Sorbitrate tablets are very stable and therefore loss of potency when carried by the patient does not normally occur. The duration of action of the tablets is estimated to be four to six hours.

Product licence numbers

Sorbitrate Tablets 20 mg 0029/0145

Sorbitrate Tablets 10 mg 0029/0111

STUART SILICONE PROTECTIVE

Presentation Stuart Silicone Protective presents Dimethyl Silicone Fluid BPC in a convenient aerosol form. It is presented in a printed tin-plate aerosol can which dispenses the product as a colourless liquid spray.

Uses Stuart Silicone Protective is a water repellent and brilliant preparation which provides surface protection of the skin against bed sores without the need to rub areas at risk in sensitive patients.

Dosage and administration The area to be protected could be cleaned and dried before spraying with Stuart Silicone Protective. Stuart Silicone Protective is applied by spraying for a few seconds from a distance of 4–8 cm (10–20 cm).

Contra-indications, warnings, etc Stuart Silicone Protective is for external use only and should not be used on broken, acutely inflamed or weeping skin, and must be kept away from the eyes and ears. Cases of infection should be treated symptomatically.

Pharmaceutical precautions Stuart Silicone Protective aerosols must be stored away from heat and must not be autoclaved. They must not be punctured or destroyed by burning, even when empty. Stuart Silicone Protective must be used directly from the aerosol.

Legal category GSL.

Package quantities Stuart Silicone Protective is supplied in aerosol cans of 200 g.

Further information Nil.

Product licence number 0029/5902.

STUART TINCT. BENZ. CO. SPRAY

Presentation Stuart Tinct. Benz. Co. Spray presents Compound Benzoin Tincture BPC in a convenient aerosol form. It is presented in a printed tin-plate aerosol can which dispenses the product as a tacky, dark brown resin with the distinct odour of gum benzoin. It contains 5% Compound Benzoin Tincture BPC.

Uses Stuart Tinct. Benz. Co. Spray has the local antiseptic, astringent and protective properties of Tinct. Benz. Co. It is used to reduce the sensitivity of skin to adhesive plaster, and to prevent skin irritation.

Dosage and administration Stuart Tinct. Benz. Co. Spray is applied by holding the aerosol can about 4–8 cm (10–20 cm) away from the area to be treated and spraying thinly.

Contra-indications, warnings, etc Although it has mild antiseptic properties, Stuart Tinct. Benz. Co. Spray must not be used on infected areas. It must not be used near the eyes or on broken skin.

Rare cases of contact dermatitis have been reported after topical use of Compound Benzoin Tincture BPC.

Cases of ingestion should be treated symptomatically.

Pharmaceutical precautions Stuart Tinct. Benz. Co. Aerosols must be stored away from heat and must not be autoclaved. The product should be used directly from the aerosol container. Containers must not be punctured or destroyed by burning even when empty.

Legal category GSL.

Package quantities Stuart Tinct. Benz. Co. Spray is presented as an aerosol spray the contents of which weigh 150 g.

Further information Nil.

Product licence number 0029/5904.

TENORETIC*

Presentation White film-coated tablets, imprinted with the lettering 'Tenoretic' and bisected on the reverse side. Each tablet contains 100 mg atenolol and 25 mg chlorthalidone.

Uses In mild and moderate hypertension.

Mode of action: Tenoretic combines the antihypertensive effects of the cardioselective beta-blocker atenolol and the diuretic chlorthalidone.

Dosage and administration One tablet daily.

Adults: Most patients with hypertension will give a satisfactory response to a single tablet daily of Tenoretic. There is little or no further fall in blood pressure with increased dosage, and where necessary another antihypertensive drug, such as a vasodilator, can be added. Patients can be transferred directly to Tenoretic from other antihypertensive treatments, with the exception of clonidine (see precautions below).

Children: There is no paediatric experience with Tenoretic; therefore this preparation is not recommended for children.

Contra-indications, warnings, etc

Contra-indications: Tenoretic should not be given to patients with second or third degree heart block. Beta-blockers should not be given with verapamil and neither drug should be administered within several days of discontinuing the other.

Precautions *Cardiac:* Untreated cardiac failure. Tenoretic should not be used in patients with untreated cardiac failure, but may be introduced when the failure has been controlled.

Pulse rate: One of the pharmacological actions of Tenoretic is to reduce the heart rate. In the rare instances that symptoms may be attributable to the slow heart rate, the dose may be reduced.

Sudden withdrawal in ischaemic heart disease: As with other beta-blockers, treatment in patients with ischaemic heart disease should not be discontinued abruptly.

Obstructive airways disease: Tenoretic contains the cardioselective beta-blocker atenolol and may therefore be used in patients with obstructive airways disease. However, an increase in airways resistance may be provoked in asthmatic patients. In contrast to preparations containing non-selective beta-blockers, this bronchospasm may usually be reversed by commonly used dosage of bronchodilator preparations such as salbutamol or isoprenaline.

Metabolic effects: The metabolic effects of chlorthalidone are dose-related and, at the low dose contained in the Tenoretic tablet, are unlikely to be troublesome.

Potassium Status: Tenoretic is associated with only minor changes in potassium status. Total body potassium is unaltered on chronic therapy, and changes in serum potassium are minor and probably clinically unimportant. Thus, in cases of uncomplicated hypertension, concurrent potassium supplements should be unnecessary. However, care should be taken with patients who are receiving digitalis preparations for cardiac failure, taking abnormal (low in potassium) diets, or suffering from gastro-intestinal complaints.

Serum Uric Acid: Tenoretic is generally associated with only a minor increase in serum uric acid. In cases of prolonged elevation the concurrent use of a uricosuric agent will reverse the hyperuricaemia.

Diabetes: Tenoretic contains chlorthalidone, which may decrease glucose tolerance. During prolonged therapy regular tests for glycosuria should be carried out.

Renal failure: In patients with severe renal impairment, a reduction in the daily dose or in frequency of administration may be necessary.

Anaesthesia: As with all beta-receptor blocking drugs it may be decided to withdraw Tenoretic before surgery. In this case 48 hours should be allowed to elapse between the last dose and anaesthesia. If treatment is continued care should be taken when using anaesthetic agents such as ether, cyclopropane and trichloroethylene. Vagal dominance, if it occurs, may be corrected with atropine (1–2 mg i.v.).

Concurrent clonidine therapy: If atenolol and clonidine are given concurrently, the clonidine should not be discontinued until several days after the withdrawal of the beta-blocker (see also manufacturer's prescribing information on clonidine).

Pregnancy: Like other drugs Tenoretic should not be given in pregnancy unless its use is essential.

Side-effects: Tenoretic is well tolerated. Side-effects associated with it are infrequent and generally mild. Cold extremities and transient muscle fatigue may occur, but the sleep disturbances which are associated with some other beta-blocking preparations are rare. There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuance of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-blocker should be gradual. Nausea and dizziness have been reported occasionally with chlorthalidone, and idiosyncratic drug reactions such as thrombocytopenia and leucopenia have occurred rarely.

Overdosage: From first principles, excessive bradycardia may be countered by atropine, 1–2 mg intravenously, and, if necessary, this may be followed by a beta-stimulant, such as isoprenaline 25 micrograms initially, or orciprenaline 0.5 mg given as a slow intravenous injection. Care must be taken to ensure that the blood pressure does not fall too low if the dose of the beta-receptor agonist has to be increased. Excessive diuresis may be countered by maintaining normal fluid and electrolyte balance.

Pharmaceutical precautions Protect from heat, light and moisture.

Legal category POM.

Package quantities Calendar packs of 28 or 10 × 28 tablets.

Further information When the combined anti-hypertensive effect of a beta-blocker and a diuretic is required, Tenoretic is a simple, convenient and acceptable therapy which may be expected to improve patient compliance. The effect of Tenoretic following a single oral dose is sustained for at least twenty-four hours.

Product licence number 0029/0139

TENORET* 50 ▼

Presentation White film-coated tablets, imprinted with the lettering Tenoret 50 on one face. Each tablet

contains 50 mg atenolol and 12.5 mg chlorthalidone. The tablets are presented in calendar packs.

Uses Hypertension: Particularly suited to the older patient. The combination of low effective doses of beta-blocking drug and diuretic may be suited to older patients where full doses of both may be considered inappropriate.

Mode of Action: Tenoret 50 combines the antihypertensive effects of the cardioselective beta-blocker atenolol (Tenormin*) and the diuretic chlorthalidone.

Dosage and administration One tablet daily.

Adults: Older patients with hypertension who do not respond to low dose therapy with a single agent should have a satisfactory response to a single tablet daily of Tenoret 50. Where hypertensive control is not achieved addition of a small dose of a third agent, e.g. a vasodilator may be appropriate.

Contra-indications, warnings, etc Contra-indications: Tenoret 50 should not be given to patients with second- or third-degree heart block. Beta-blockers should not be given with verapamil and neither drug should be administered within several days of discontinuing the other.

Precautions Cardiac: Untreated cardiac failure. Tenoret 50 should not be used in patients with untreated cardiac failure, but may be introduced when the failure has been controlled.

Pulse rate: One of the pharmacological actions of Tenoret 50 is to reduce heart rate. In the rare instances that symptoms may be attributable to the slow heart rate the dose may be reduced.

Sudden withdrawal in ischaemic heart disease: As with other beta-blockers, treatment in patients with ischaemic heart disease should not be discontinued abruptly.

Obstructive airways disease: Tenoret 50 contains the cardioselective beta-blocker atenolol and may therefore be used with caution in patients with obstructive airways disease. However, an increase in airways resistance may be provoked in asthmatic patients. In contrast to preparations containing non-selective beta-blockers, this bronchospasm may usually be reversed by a commonly used dosage of bronchodilator preparations such as salbutamol or isoprenaline.

Metabolic effects: The metabolic effects of chlorthalidone are dose-related and, at the low dose contained in the Tenoret 50 tablet, are most unlikely to be troublesome.

Potassium status: Experience even with a full dose of this beta-blocker and diuretic combination in Tenoretic has been associated with only minor changes in potassium status. Total body potassium is unaltered on chronic therapy, and changes in serum potassium are minor and probably clinically unimportant. Thus, in cases of uncomplicated hypertension, concurrent potassium supplements should be unnecessary. However, in the older patient who may be receiving digitalis preparations for cardiac failure, taking an abnormal (low in potassium) diet or suffering from gastrointestinal complaints, occasional measurement of potassium levels is appropriate.

Serum uric acid: Experience, again with Tenoretic, has generally been associated with only a minor increase in serum uric acid. In cases of prolonged elevation the concurrent use of a uricosuric agent will reverse the hyperuricaemia.

Diabetes: Tenoret 50 contains chlorthalidone which may

decrease glucose tolerance. During prolonged therapy regular tests for glycosuria should be carried out.

Renal impairment: In patients with severe renal impairment a reduction in the frequency of administration may be necessary.

anaesthesia: As with all beta-receptor blocking drugs it may be decided to withdraw Tenoret 50 before surgery. In this case 48 hours should be allowed to elapse between the last dose and anaesthesia. If treatment is continued care should be taken when using anaesthetic agents such as ether, cyclopropane and trichloroethylene. Vagal dominance, if it occurs, may be corrected with atropine (1–2 mg i.v.).

Concurrent clonidine therapy: If atenolol and clonidine are given concurrently, the clonidine should not be discontinued until several days after the withdrawal of the beta-blocker (see also manufacturers prescribing information on clonidine).

Fertility: Like other drugs, Tenoret 50 should not be given in pregnancy unless its use is essential.

Side effects: Cold extremities and transient muscle fatigue may occur, but the sleep disturbances which are associated with some other beta-blocking preparations are rare. There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuance of the drug should be considered if any such reaction is not otherwise explicable. Nausea and dizziness have been reported occasionally with chlorthalidone, and idiosyncratic drug reactions such as thrombocytopenia and leucopenia have occurred rarely.

Overdosage: From first principles, excessive bradycardia may be countered by atropine, 1–2 mg intravenously, and, if necessary, this may be followed by a beta-stimulant, such as isoprenaline 25 micrograms initially, or orciprenaline 0.5 mg, given as a slow intravenous injection. Care must be taken to ensure that the blood pressure does not fall too low if the dose of the beta-receptor agonist has to be increased. Excessive diuresis may be countered by maintaining normal fluid and electrolyte balance.

Pharmaceutical precautions Protect from heat, light and moisture.

Legal category POM.

Package quantities Calendar packs, each containing 28 tablets.

Further information When the combined anti-hypertensive effect of a beta-blocker and a diuretic is required, Tenoret 50 one tablet daily is a simple, convenient and acceptable therapy which may be expected to improve patient compliance.

Product licence number 0029/0156

TENORMIN* TABLETS

Presentation Tenormin tablets containing atenolol 100 mg are round, bi-convex, orange and film coated. They are imprinted on one face with the name Tenormin and are bisected on the reverse face.

Uses Management of hypertension, angina pectoris and dysrhythmias.

Mode of action: Tenormin (atenolol) is a beta-adrenoceptor blocking drug which is cardioselective (i.e. acts preferentially on beta-adrenergic receptors in the heart). It is without intrinsic sympathomimetic and membrane stabilising activities. It is probably the action of Tenormin in reducing cardiac rate and contractility which makes it effective in eliminating or reducing the symptoms of patients with angina. As with other beta-adrenoceptor blocking drugs its mode of action in the treatment of hypertension is unclear. It is effective as a beta adrenoceptor blocking drug on the heart for at least 24 hours following a single oral dose. Human studies indicate that it crosses the blood brain barrier only to a negligible extent.

Dosage and administration Adults:

Hypertension: One tablet daily. Most patients respond to 100 mg daily given as a single dose. The effect will be fully established after one to two weeks. A further reduction in blood pressure may be achieved by combining Tenormin with other antihypertensive agents. For example, co-administration of Tenormin with a diuretic, as in Tenoretic, provides a highly effective and convenient antihypertensive therapy.

Patients can be transferred to Tenormin from other antihypertensive treatments with the exception of clonidine (see precautions below).

Angina: Most patients with angina pectoris will respond to 100 mg daily given as a single or divided dose. It is unlikely that additional benefit will be gained by increasing the dose.

Dysrhythmias: Having controlled the dysrhythmias with intravenous Tenormin (see entry for Tenormin Injection) a suitable oral maintenance dosage is 50–100 mg daily.

Children: There is no paediatric experience with Tenormin and for this reason it is not recommended for children.

Contra-indications, warnings, etc

Contra-indications: Tenormin is contra-indicated in patients with second-degree or third-degree heart block. Beta-blockers should not be given with verapamil and neither drug should be administered within several days of discontinuing the other.

Precautions: Tenormin must not be used in patients with untreated cardiac failure, but may be introduced with care when the failure has been brought under control. Where congestive cardiac failure appears during treatment with Tenormin, the drug may be temporarily withdrawn until the failure has been controlled.

One of the pharmacological actions of Tenormin is to reduce heart rate. In the rare instances that symptoms may be attributable to the slow heart rate, the dose may be reduced.

Tenormin acts preferentially on cardiac beta-receptors. It can be used in patients with chronic obstructive airways disease. However, an increase in airways resistance may be provoked in asthmatic patients. In contrast to non-selective beta-blockers this bronchospasm may usually be reversed by commonly used dosage of broncho-dilator preparations such as salbutamol or isoprenaline.

In patients suffering from ischaemic heart disease, as with other beta-blocking agents, treatment should not be discontinued abruptly.

If Tenormin and clonidine are given concurrently the clonidine should not be discontinued until several days

after the withdrawal of the beta-blocker (see also prescribing information on clonidine).

Anaesthesia: As with all beta receptor blocking drugs it may be decided to withdraw Tenormin before surgery. In this case 48 hours should be allowed to elapse between the last dose and anaesthesia. If treatment is continued care should be taken when using anaesthetic agents such as ether, cyclopropane and trichloroethylene. Vagal dominance, if it occurs, may be corrected with atropine (1–2 mg i.v.).

Renal failure: Since Tenormin is excreted via the kidneys dosage should be adjusted in cases of severe impairment of renal function. No significant accumulation of Tenormin occurs at a GFR greater than 35 ml/min/1.73 m² (normal range is 100–150 ml/min/1.73 m²). For patients with a creatinine clearance of 15–35 ml/min/1.73 m² (equivalent to serum creatinine of 300–600 mcmol/litre) the dose should be 50 mg daily or 100 mg on alternate days. For patients with a creatinine clearance of < 15 ml/min/1.73 m² (equivalent to serum creatinine of 600 mcmol/litre) the dose should be 50 mg on alternate days or 100 mg every fourth day.

Patients on haemodialysis should be given 50 mg after each dialysis; this should be done under hospital supervision as marked falls in blood pressure can occur.

Pregnancy: Like all other drugs, Tenormin should not be given in pregnancy unless its use is essential. There is no evidence of teratogenicity in animal studies.

Side-effects: In clinical studies the side-effects reported are usually attributable to its pharmacological actions and include coldness of the extremities, muscular fatigue and, in isolated cases, bradycardia. Sleep disturbances of the type noted with other beta-blockers have rarely been reported. There have been reports of skin rashes and/or dry eyes associated with the use of beta adrenergic blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuance of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta-blocker should be gradual.

Overdosage: From first principles, excessive bradycardia may be countered by atropine, 1–2 mg intravenously, and, if necessary, this may be followed by a beta stimulant, such as isoprenaline 25 micrograms initially or orciprenaline 0.5 mg given as a slow intravenous injection. Care must be taken to ensure that the blood pressure does not fall too low if the dose of the beta-receptor agonist has to be increased.

Pharmaceutical precautions Tenormin tablets should be protected from heat, light and moisture.

Legal category POM.

Package quantities 100 mg tablets in calendar packs of 28 or 10 × 28.

Further information Tenormin facilitates compliance with antihypertensive therapy by its acceptability to patients and simplicity of dosing. The narrow dose range and early patient response ensure that the effect of the drug in individual patients is quickly demonstrated. Tenormin is fully compatible with diuretics and other hypotensive agents. Since it acts preferentially on beta receptors in the heart, Tenormin may, with care, be used successfully in the treatment of patients with respiratory disease who cannot tolerate non-selective beta-blockers.

Product licence number 0029/0122.

TENORMIN* INJECTION ▼

Presentation Tenormin Injection containing 5 mg atenolol in 10 ml isotonic, citrate buffered aqueous solution.

Uses Management of dysrhythmias.

Mode of action: Tenormin (atenolol) is a beta-adrenoceptor blocking drug which is cardioselective (i.e. act preferentially on beta-adrenergic receptors in the heart). It is without intrinsic sympathomimetic and membranestabilising activities. Human studies indicate that it crosses the blood-brain barrier only to a negligible extent.

Dosage and administration *Adults: Dysrhythmias* A suitable initial dose of Tenormin is 2.5 mg (5 ml injected intravenously over a 2.5 minute period (i.e. 1 mg/minute). This may be repeated at 5 minute interval until a response is observed up to a maximum dosage of 10 mg. If Tenormin is given by infusion, 0.15 mg/kg body weight may be administered over a 20 minute period. If required, the injection or infusion may be repeated every 12 hours. Having controlled the dysrhythmias with intravenous Tenormin a suitable oral maintenance dosage is 50–100 mg daily (see entry for Tenormin Tablets).

Children: There is no paediatric experience with Tenormin and for this reason it is not recommended for children.

Contra-indications, warnings, etc Tenormin is contra-indicated in patients with second-degree or third-degree heart block. Beta-blockers should not be given with verapamil and neither drug should be administered within several days of discontinuing the other.

Precautions: Tenormin must not be used in patients with untreated cardiac failure, but may be introduced with care when the failure has been brought under control. Where congestive cardiac failure appears during treatment with Tenormin, the drug may be temporarily withdrawn until the failure has been controlled.

One of the pharmacological actions of Tenormin is to reduce heart rate. In the rare instances that symptoms may be attributable to the slow heart rate, the dose may be reduced.

Tenormin acts preferentially on cardiac beta-receptors. It can be used in patients with chronic obstructive airways disease. However, an increase in airways resistance may be provoked in asthmatic patients. In contrast to non-selective beta-blockers this bronchospasm may usually be reversed by commonly used dosage of bronchodilator preparations such as salbutamol or isoprenaline.

In patients suffering from ischaemic heart disease, as with other beta-blocking agents, treatment should not be discontinued abruptly. If Tenormin and clonidine are given concurrently the clonidine should not be discontinued until several days after the withdrawal of the beta-blocker (see also 'Prescribing Information' on clonidine).

Anaesthesia: As with all beta-receptor blocking drugs it may be decided to withdraw Tenormin before surgery. In this case 48 hours should be allowed to elapse between the last dose and anaesthesia. If treatment is continued care should be taken when using anaesthetic agents such as ether, cyclopropane and trichloroethylene. Vagal dominance, if it occurs, may be corrected with atropine (1–2 mg i.v.).

Renal failure: Since Tenormin is excreted via the kidneys dosage should be adjusted in cases of severe impairment

renal function. No significant accumulation of Tenormin occurs at a GFR greater than 35 ml/min/1.73 m² (normal range is 100–150 ml/min/1.73 m²). For patients with a creatinine clearance of 15–35 ml/min/1.73 m² (equivalent to serum creatinine of 300–600 µmol/litre) the oral dose should be 50 mg daily or 100 mg on alternate days. For patients with a creatinine clearance < 15 ml/min/1.73 m² (equivalent to serum creatinine > 600 µmol/litre) the oral dose should be 50 mg on alternate days or 100 mg every fourth day.

Patients on haemodialysis should be given 50 mg orally after each dialysis; this should be done under hospital supervision as marked falls in blood pressure can occur.

regnancy: Like all other drugs, Tenormin should not be given in pregnancy unless its use is essential. There is no evidence of teratogenicity in animal studies.

side effects: In clinical studies, the side effects reported are usually attributable to its pharmacological actions and include coldness of the extremities, muscular fatigue and, in isolated cases, bradycardia. Sleep disturbances of the type noted with other beta-blockers have rarely been reported.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuance of the drug should be considered any such reaction is not otherwise explicable. Cessation of therapy with a beta-blocker should be gradual.

overdose: From first principles, excessive bradycardia may be countered by atropine, 1–2 mg intravenously, and, if necessary, this may be followed by a beta stimulant, such as isoprenaline 25 micrograms initially, or orciprenaline 0.5 mg given as a slow intravenous injection. Care must be taken to ensure that the blood pressure does not fall too low if the dose of the beta-receptor agonist has to be increased.

pharmaceutical precautions Tenormin Injection should be protected from light.

note: Dilutions of Tenormin Injection in Dextrose Injection BP, Sodium Chloride Injection BP or Sodium Chloride and Dextrose Injection BP may be used.

legal category POM.

package quantities Injection: 10 ml ampoules in boxes of 10.

further information Since it acts preferentially on beta-receptors in the heart, Tenormin may, with care, be used successfully in the treatment of patients with respiratory disease who cannot tolerate non-selective beta-blockers.

product licence number 0029/0087

TENORMIN[®] LS

presentation Tenormin LS tablets, containing atenolol 50 mg are round, bi-convex, white and film coated. They are imprinted on one face with the name Tenormin 50.

uses Management of hypertension, angina pectoris and dysrhythmias in patients with impaired renal function.

mode of action: Tenormin LS (atenolol) is a beta-adrenoceptor blocking drug which is cardioselective (i.e.

acts preferentially on beta adrenergic receptors in the heart). It is without intrinsic sympathomimetic and membrane stabilising activities. It is probably the action of Tenormin LS in reducing cardiac rate and contractility which makes it effective in eliminating or reducing the symptoms of patients with angina. As with other beta-adrenoceptor blocking drugs, its mode of action in the treatment of hypertension is unclear. It is effective as a beta-adrenoceptor blocking drug on the heart for at least 24 hours following a single oral dose. Human studies indicate that it crosses the blood brain barrier only to a negligible extent.

Dosage and administration *Adults:* In patients having normal renal function the doses of Tenormin recommended are:

<i>Hypertension:</i>	100 mg once daily
<i>Angina Pectoris:</i>	100 mg daily in single or divided doses
<i>Dysrhythmias:</i>	50–100 mg daily

Patients with impaired renal function, as defined below will respond to 50 mg of atenolol taken daily or on alternate days.

<i>Glomerular Filtration Rate (ml/min/1.73 m²)</i>	<i>Atenolol Dose (mg)</i>
35 or more	100 daily
15–35	50 daily
less than 15	50 on alternate days

Patients on haemodialysis should be given 50 mg after each dialysis; this should be done under hospital supervision as marked falls in blood pressure can occur.

The effect of Tenormin LS therapy will be fully established after one–two weeks.

Unlike many other beta-adrenoceptor blocking drugs, atenolol is metabolised to only a slight extent (10%). There is no first pass effect due to extensive hepatic metabolism, and no accumulation of metabolites of unknown pharmacological activity. It is, therefore, possible to adjust the dosage in patients with renal disease in proportion to the degree of renal impairment, without the need to determine optimum dose by titration for each patient.

Patients can be directly transferred to Tenormin LS from other antihypertensive treatments with the exception of clonidine (see precautions below).

Children: There is no paediatric experience with Tenormin LS, and for this reason it is not recommended for children.

Contra-indications, warnings, etc

Contra-indications: Tenormin LS is contra-indicated in patients with second-degree or third-degree heart block. Beta blockers should not be given with verapamil, and neither drug should be administered within several days of discontinuing the other.

Precautions: Tenormin LS must not be used in patients with untreated cardiac failure, but may be introduced with care when the failure has been brought under control. Where congestive cardiac failure appears during treatment with Tenormin LS the drug may be temporarily withdrawn until the failure has been controlled.

One of the pharmacological actions of atenolol is to reduce heart rate. In the rare instances that symptoms may be attributable to the bradycardia, the dose may be reduced by giving a tablet of Tenormin LS on alternate days.

Tenormin LS acts preferentially on cardiac beta receptors. It can be used in patients with chronic obstructive airways disease. However, an increase in airways resistance may be provoked in asthmatic patients. In contrast to non-selective beta blockers, this bronchospasm may usually be reversed by commonly used doses of broncho-dilator preparations such as salbutamol or isoprenaline.

In patients suffering from ischaemic heart disease, as with other beta blocking agents, treatment should not be discontinued abruptly.

If Tenormin LS and clonidine are given concurrently, the clonidine should not be discontinued until several days after the withdrawal of the beta blocker (see also prescribing information on clonidine).

Anaesthesia: As with all beta receptor blocking drugs, it may be decided to withdraw Tenormin LS before surgery. In this case, 48 hours should be allowed to elapse between the last dose and anaesthesia. If treatment is continued, care should be taken when using anaesthetic agents such as ether, cyclopropane, and trichloroethylene. Vagal dominance, if it occurs, may be corrected with atropine (1–2 mg i.v.).

Pregnancy: Like all other drugs, Tenormin LS should not be given in pregnancy unless its use is essential. There is no evidence of teratogenicity in animal studies.

Side-effects: In clinical studies, the side effects reported are usually attributable to its pharmacological actions and include coldness of the extremities, muscular fatigue, and in isolated cases bradycardia. Sleep disturbances of the type noted with other beta blockers have rarely been reported.

There have been reports of skin rashes and/or dry eyes associated with the use of beta adrenergic blocking drugs. The reported incidence is small and in most cases

the symptoms have cleared when treatment was withdrawn. Discontinuance of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy with a beta blocker should be gradual.

Overdosage: From first principles, excessive bradycardia may be countered by atropine, 1–2 mg, intravenous and if necessary this may be followed by a beta stimulant such as isoprenaline 25 micrograms initially, or orciprenaline 0.5 mg given as a slow intravenous injection. Care must be taken to ensure that the blood pressure does not fall too low if the dose of the beta receptor agonist has to be increased.

Pharmaceutical precautions Tenormin LS tablets should be protected from heat, light, and moisture.

Legal category POM.

Package quantities 50 mg tablets in tubes of 100.

Further information Tenormin LS facilitates compliance with anti-hypertensive therapy by its acceptability to patients and simplicity of dosing. The narrow dose range and early patient response ensure that the effect of the drug in individual patients is quickly demonstrated. Tenormin LS is fully compatible with diuretics and other hypotensive agents. Since it acts preferentially on beta receptors in the heart, Tenormin LS may, with care, be used successfully in the treatment of patients with respiratory disease who cannot tolerate non-selective beta blockers.

Product licence number 0029/0086.

**Trade Mark*

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51 Ives Road
Maidenhead
Berkshire SL6 1RD



ANAPOLON* 5

Presentation Each Anapolon Tablet contains oxymetholone 5 mg. The white tablets are marked ANAPOLON on one face and SYNTEX on the other.

Uses Anapolon Tablets are recommended for conditions in which a potent tissue-building or protein-sparing action is desired, such as convalescence after severely debilitating diseases, surgical cases, osteoporosis, pituitary dwarfism, following corticosteroid therapy and after burns.

Dosage and administration Hormone therapy is adjunctive to and not a replacement for conventional therapy. Duration of therapy will depend on the response to the condition and the appearance of adverse reactions. Therapy should be intermittent. Adequate amounts of calories and protein must be given if a beneficial effect is to be obtained.

Adults: The recommended dosage is 1 to 2 tablets per day (5–10 mg) for four to six weeks, with breaks of 10–15 days between each course.

Children: In children up to 12 years of age, adequate response has been observed on doses of $\frac{1}{2}$ to 1 tablet per day (2.5–5 mg). Four to six weeks of therapy should be followed by one month without therapy. X-rays should often be taken to determine the amount of bone maturation. As skeletal stimulation may continue for six months after therapy has been stopped, the drug should be discontinued well before bone maturation reaches the norm for the chronological age.

Contra-indications, warnings, etc

Contra-indications: Carcinoma of the prostate or breast in male patients; pregnancy (primarily because of masculinisation of the foetus); infancy; nephrosis or the ephrotic phase of nephritis; hepatic dysfunction; hypersensitivity to oxymetholone.

Warnings and precautions: Oxymetholone should not be used to promote weight gain in adults or children who are healthy. Oxymetholone should not be used to enhance athletic ability.

Tumours of the liver have been reported occasionally in patients subjected to prolonged treatment with anabolic steroids. The possibility that these compounds may induce or enhance the development of hepatic tumours cannot at present be excluded and this should be considered when the use of the product is proposed, especially in young people who are not suffering from life-threatening disorders.

Caution is required when administering anabolic steroids to patients with cardiac, renal or hepatic disease or with benign prostatic hypertrophy. Oedema may occur occasionally.

Anabolic steroids may increase sensitivity to anticoagulants. Dosage of the anticoagulant may have to be decreased to maintain the prothrombin time at the desired therapeutic level.

Anabolic steroids have been shown to alter glucose

tolerance tests. Diabetics should be followed carefully and the dosage of insulin or oral hypoglycaemic agents adjusted accordingly.

Disturbance of liver function tests, elevation of serum bilirubin and jaundice may occur. Liver function should be checked at regular intervals in patients receiving Anapolon Tablets. The following adverse reactions may occur:

1. *In males:* Pre-pubertal phallic enlargement and increased frequency of erections; post-pubertal inhibition of testicular function and oligospermia and gynaecomastia.
2. *In females:* Hirsutism, male-pattern baldness, deepening of the voice and clitoral enlargement (these changes are usually irreversible even after prompt discontinuation of therapy); menstrual irregularities.
3. *In both sexes:* Increased or decreased libido; acne (especially in females and pre-pubertal males); premature closure of the epiphyses in children.

Pharmaceutical precautions Anapolon Tablets should be kept under normal storage conditions.

Legal category POM.

Package quantities Anapolon Tablets are available in canisters of 100 tablets.

Further information A higher-strength presentation, Anapolon 50 Tablets, is specifically indicated in aplastic and refractory hypoplastic anaemias. Full prescribing information should be consulted for that presentation if it is to be used.

Product licence number 0286/5008.

ANAPOLON* 50

Presentation Each Anapolon 50 Tablet contains oxymetholone 50 mg. The white tablets are scored and stamped with the number '50' on one side and SYNTEX on the other.

Uses Anapolon 50 is recommended for the treatment of aplastic and refractory anaemias (including acquired, idiopathic and congenital aplasias). Anapolon 50 is also recommended as adjunctive therapy in patients with malignant diseases where treatment with cytotoxic agents or radiotherapy is likely to cause bone-marrow depression.

The exact mode of action of oxymetholone is as yet uncertain. It is thought, however, that oxymetholone stimulates the production of erythropoietin, which in turn acts on the primitive stem cells increasing the rate of differentiation into red cell precursors. It has also been demonstrated that oxymetholone increases the mitotic rate of the stem cells, stimulating the extension of healthy tissue into hypoplastic areas of the bone marrow. Oxymetholone has a beneficial effect on haemoglobin

synthesis as shown by an increased plasma iron clearance.

Dosage and administration The recommended dosage when treating aplasias is from 2 mg to 5 mg per kg body weight daily for adults, and from 2 mg to 4 mg per kg body weight daily for children in divided doses. The selected dose will depend on the severity of the condition.

1. Initial therapy should be continued for a period of six months or until a response is seen (whichever is the shorter time). Therapy must be maintained for at least three months before a response can be expected.

2. From the time of response the same dose should be continued for a further three months.

3. At this time the dose should be halved and, if the remission is maintained, continued for three months.

4. During the next three months gradual withdrawal should be attempted.

5. Should a relapse occur at any time whilst the dose is being reduced the initial dosage regime should be re-instituted. When administering oxymetholone as an adjunctive to cytotoxic therapy and radiotherapy the recommended dosage is up to 150 mg per day.

Contra-indications, warnings, etc

Contra-indications: Carcinoma of the prostate or breast in male patients; pregnancy (primarily because of masculinisation of the foetus); infancy; nephrosis or the nephrotic phase of nephritis; hepatic dysfunction; hypersensitivity to oxymetholone.

Precautions and warnings: Tumours of the liver have been reported occasionally in patients subjected to prolonged treatment with androgenic-anabolic steroids. The possibility that these compounds may induce or enhance the development of hepatic tumours cannot at present be excluded and this should be considered when the use of this product is proposed, especially in young people who are not suffering from life-threatening disorders.

Care should be exercised in incipient cardiac failure and the elderly male in whom benign enlargement of the prostate is evident. When anticoagulant therapy is used concomitantly, dosage of the anticoagulant may have to be decreased in order to maintain the prothrombin time at the desired therapeutic level. This is because Anapolon, like other anabolic steroids, may enhance blood fibrinolytic activity.

Oxymetholone exhibits only slight androgenic activity in low doses, but in the high dosage levels employed in the treatment of aplastic anaemias, it may lead to virilisation in women and pre-pubertal children. Disturbance of liver function tests, elevation of serum bilirubin and jaundice may occur, together with other signs of liver disturbance. Should this happen, the dosage should be halved. If liver function tests do not improve within one week then oxymetholone therapy should be withdrawn. Peliosis hepatis and hepatocellular carcinoma have occasionally been observed in patients with congenital and acquired aplastic anaemia treated with oxymetholone and other oral androgens for prolonged periods. In some cases withdrawal of the drug has been associated with regressions of the hepatic lesions.

With prolonged high dosage any sodium retention that may occur is usually responsive to diuretic therapy.

Leukaemia has been observed in patients with aplastic anaemia treated with oxymetholone. The role, if any, of oxymetholone is unclear since malignant transformation has been seen in blood dyscrasias and leukaemia has

been reported in patients with aplastic anaemia who have not been treated with oxymetholone.

The following adverse reactions may occur:

1. *In males:* Pre-pubertal phallic enlargement or erections; post-pubertal inhibition of testicular function an oligospermia and gynaecomastia.

2. *In females:* Hirsutism, male-pattern baldness, deepening of the voice and clitoral enlargement (these changes are usually irreversible even after prompt discontinuation of therapy); menstrual irregularities.

3. *In both sexes:* Increased or decreased libido; acne (especially in females and pre-pubertal males); premature closure of the epiphyses in children.

Pharmaceutical precautions Anapolon 50 should be kept under normal storage conditions.

Legal category POM.

Package quantities Anapolon 50 is available in canisters of 100 tablets.

Further information A lower-strength preparation (Anapolon 5 Tablets, oxymetholone 5 mg), is specifically indicated for conditions where tissue-building or protein sparing action is desired. Full prescribing information should be consulted for that presentation if it is to be used.

Product licence number 0286/5009.

BREVINOR®

Presentation A 21-tablet calendar pack: each white tablet contains norethisterone 0.5 mg (500 mcg) and ethinyloestradiol 35 mcg. The tablets are marked B on one side.

Uses Brevinor is indicated for oral contraception, with the benefit of a low intake of oestrogen.

The mode of action of Brevinor is similar to that of other progestogen/oestrogen oral contraceptives; its activity is exerted through a combined effect on one or more of the following: hypothalamus, anterior pituitary ovary, endometrium and cervical mucus.

Dosage and administration The dosage of Brevinor for the initial cycle of therapy is 1 tablet taken daily from the 5th to the 25th day of the menstrual cycle, counting the first day of menstrual flow as 'Day 1'. For the subsequent cycles, no tablets are taken for seven days; then a new course is started of 1 tablet daily for 21 days. This sequence of 21 days on treatment, seven days off treatment is repeated for as long as contraception is required.

To provide added protection during the first cycle only the patient should be instructed to use an additional method of contraception for the first 14 days.

Tablet omissions: Tablets must be taken daily in order to maintain adequate hormone levels. If a tablet is missed it should be taken as soon as possible, within 24 hours of the correct time even if this means that 2 tablets are taken together. If 2 tablets are missed, a tablet should be taken as soon as possible so medication is re-established. An additional method of contraception should be used for the remainder of that tablet cycle. If more than 2 tablets have been missed, oral contraceptive therapy should be discontinued immediately and a method of non-hormonal contraception should be used until menstruation has appeared or pregnancy has been excluded.

Switching from another oral contraceptive: Brevinor could be started seven days after completing the last course of the other product. An additional mechanical or chemical contraceptive should be used for the first 14 days of tablet-taking.

Use after childbirth, miscarriage or abortion: After childbirth, oral contraception is usually started when spontaneous menstruation has resumed. Another method of contraception should be used in the meantime, unless the first course of tablets is started within seven days of delivery. After a miscarriage or abortion, oral contraception can normally be started on the fifth day.

Contra-indications, warnings, etc

Contra-indications: As with all combined progestogen/oestrogen oral contraceptives, the following conditions should be regarded as contra-indications:

-) Thrombophlebitis, thromboembolic disorders, cerebral apoplexy, or a history of these conditions.
-) Acute or severe chronic liver disease, Dubin-Johnson or Rotor syndrome, history during pregnancy of idiopathic jaundice or severe pruritus.
-) Known or suspected carcinoma of the breast.
-) Known or suspected oestrogen-dependent neoplasia.
-) Undiagnosed abnormal vaginal bleeding.
-) Pregnancy.

Side-effects and precautions: As with all oral contraceptives, there may be slight nausea at first, weight gain or breast discomfort, which soon disappear.

Spotting or bleeding may occur during the first few cycles. Usually menstrual bleeding becomes light and occasionally there may be no bleeding during the tablet-free days.

Hypertension, which is usually reversible on discontinuing treatment, has occurred in a small percentage of women taking oral contraceptives. Oestrogen-progestogen preparations should be used with caution in patients with a history of hepatic dysfunction or hypertension.

A statistical association between the use of oral contraceptives and the occurrence of thrombosis, embolism or haemorrhage has been reported. Patients on such treatments should be kept under regular surveillance, in view of the possibility of development of such conditions as thromboembolism.

Risk of coronary artery disease in women taking oral contraceptives is increased by the presence of other predisposing factors such as cigarette smoking, hypercholesterolaemia, obesity, diabetes, history of pre-lamptic toxemia and increasing age. After the age of forty-five years, the patient and physician should carefully re-assess the risk/benefit ratio of using combined oral contraceptives as opposed to alternative methods of contraception.

Benign and malignant liver tumours have been associated with oral contraceptive use. The relationship between occurrence of liver tumours and use of female sex hormones is not known at present. These tumours are very rare but they may rupture causing intra-abdominal bleeding. If the patient presents with a mass tenderness in the right upper quadrant or an acute abdomen, the possible presence of a tumour should be considered.

The use of this product in patients suffering from epilepsy, migraine, asthma or cardiac dysfunction may result in exacerbation of these disorders, because of fluid retention.

A decreased glucose tolerance may occur in diabetic patients on this treatment, and their control must be carefully supervised.

An increased risk of congenital anomalies, including heart defects and limb defects, has been reported following the use of sex hormones, including oral contraceptives, in pregnancy. If the patient does not adhere to the prescribed schedule, the possibility of pregnancy should be considered at the time of the first missed period and further use of oral contraceptives should be withheld until pregnancy has been ruled out. It is recommended that for any patient who has missed two consecutive periods, pregnancy should be ruled out before continuing the contraceptive regimen. If pregnancy is confirmed the patient should be apprised of the potential risks to the foetus and the advisability of continuing the pregnancy should be discussed in the light of these risks. It is advisable to discontinue Brevinor three months before a planned pregnancy.

Gastro-intestinal upsets may interfere with the absorption of the tablets. Some drugs may modify the metabolism of Brevinor reducing its effectiveness; these include certain sedatives, antibiotics, anti-epileptic and anti-arthritis drugs. During the time such agents are used concurrently, it is advisable that mechanical contraceptives also be used.

Women taking oral contraceptives require careful observation if they have or have had any of the following conditions: breast nodules; fibrocystic disease of the breast or an abnormal mammogram; a history of severe depressive states; varicose veins; sickle-cell anaemia; diabetes; hypertension; high blood cholesterol levels; epilepsy; asthma; otosclerosis; multiple sclerosis; porphyria; tetany; disturbed liver functions; gallstones; cardiovascular disease; kidney disease; chloasma; herpes of pregnancy. The worsening or first appearance of any of these conditions may indicate that the oral contraceptive should be stopped. Contact lenses may become uncomfortable.

Brevinor should be discontinued at least six weeks before elective operations and during immobilisation.

Women with a history of oligomenorrhoea or secondary amenorrhoea or young women without regular cycles may have a tendency to remain anovulatory or to become amenorrhoeic after discontinuation of oral contraceptives. Women with these pre-existing problems should be advised of this possibility and encouraged to use other contraceptive methods.

The risk of arterial thrombosis associated with combined oral contraceptives increases with age, and this risk is aggravated by cigarette smoking. The use of combined oral contraceptives by women in the older age group, especially those who are cigarette smokers, should therefore be discouraged and alternative methods advised.

Treatment of overdose: Overdosage may be manifested by nausea, vomiting, breast enlargement and vaginal bleeding. There is no specific antidote and treatment should be symptomatic. Gastric lavage may be employed if the overdose is large and the patient is seen sufficiently early (within four hours).

Pharmaceutical precautions Brevinor should be kept under normal storage conditions.

Legal category POM.

Package quantities Brevinor is available in calendar packs of 3 x 21 tablets.

Further information Nil.

Product licence number 0286/0054.

EMKO* CONTRACEPTIVE FOAM

Presentation A pressurised metal canister which delivers into the applicator provided a foam containing nonoxynol-9 8% w/v and benzethonium chloride 0.2% w/v.

Uses Spermicidal contraceptive agent. As with other spermicidal preparations, an additional method of contraception, for example, diaphragm, cap or intra-uterine device, must be used with Emko Foam.

When pregnancy is medically contra-indicated, the choice of contraceptive should be made in consultation with a doctor.

Dosage and administration The contents of the applicator to be introduced into the vagina not more than one hour before intercourse. Emko Foam must be used each time physical contact is repeated.

If a diaphragm or cap is used, Emko Foam may be used as a lubricant, spread around the rim.

Contra-indications, warnings, etc There are no known contra-indications to the use of Emko Contraceptive Foam.

On rare occasions irritation of the vagina or penis may occur; if it does, use of Emko should be discontinued and medical advice should be sought.

Douching is unnecessary; following sexual intercourse, an interval of at least six hours must elapse before douching for cleansing purposes.

Pharmaceutical precautions Store in a cool place.

Legal category GSL.

Package quantities Emko Contraceptive Foam Kit containing 40 g aerosol container and an applicator.

40 g refill aerosol pack.

90 g refill aerosol pack.

Further information In one study (1), Emko Contraceptive Foam was used by 2,932 women for 28,322 cycles; a pregnancy-rate of 3.98 pregnancies per 100 woman-years was reported. Another study (2), in 130 women who used Emko Contraceptive Foam for 2,737 women-months, showed a pregnancy-rate of 1.75 pregnancies per 100 woman-years. Both study reports emphasised the need for giving adequate, careful instructions to the patients.

References:

1. *Contraception* 1971; **3**: 37-43.
2. *Pacific Medicine and Surgery* 1965; **73**: 353-5.

Product licence number 0286/0051.

MASTERIL*

Presentation Each Masteril ampoule contains drostanolone propionate 100 mg in 1 ml of clear oily solution.

Uses Masteril is indicated for the amelioration of disseminated mammary carcinoma, used either alone or in conjunction with other medication or surgery. Masteril is thought to work by blocking the uptake of oestrogen by oestrogen-dependent carcinoma cells.

Dosage and administration The recommended dose is 300 mg (3 ampoules) weekly given by intramuscular injection. Therapy should be continued until such time as the patient ceases to derive benefit from Masteril.

Contra-indications, warnings, etc There are no known contra-indications to the recommended use of Masteril.

Virilisation may be encountered during prolonged therapy. Other side-effects are very unlikely.

Pharmaceutical precautions Masteril should not be stored in direct sunlight.

Legal category POM.

Package quantities Masteril is available in ampoules of 1 ml (100 mg) packed in boxes of 10.

Further information Nil.

Product licence number 0286/5010.

NAPROSYN* TABLETS

NAPROSYN* 500 TABLETS

NAPROSYN* SUPPOSITORIES

NAPROSYN* SUSPENSION

Presentation Naprosyn (naproxen) is d-2-(6'-methoxy-2-naphthyl) propionic acid, a non-steroidal anti-inflammatory agent, developed by Syntex Research. It is presented as a yellow half-scored tablet containing 250 mg of naproxen, inscribed NAPROSYN on one side and SYNTEX on the other, an oblong, scored yellow tablet containing 500 mg of naproxen inscribed NAPROSYN 500 on one side, a flavoured yellow suspension containing 25 mg/ml naproxen and as suppositories each containing 500 mg naproxen.

Uses Naprosyn is indicated for the treatment of rheumatoid arthritis, osteoarthritis (degenerative arthritis), ankylosing spondylitis, juvenile rheumatoid arthritis, acute gout, and acute musculoskeletal disorders (such as sprains and strains, direct trauma, lumbosacral pain, cervical spondylitis, tenosynovitis and fibrositis).

Naprosyn has been shown to have striking anti-inflammatory analgesic and antipyretic properties when tested in classical animal test systems. It exhibits its anti-inflammatory effect even in adrenalectomised animals, indicating that its action is not mediated through the pituitary-adrenal axis. It inhibits prostaglandin synthetase, as do other non-steroidal anti-inflammatory agents. As with other agents, however, the exact mechanism of its anti-inflammatory action is not known.

Dosage and administration For rheumatoid arthritis, osteoarthritis and ankylosing spondylitis, the usual dose is 500 mg to 1 g per day taken in two doses at 12-hour intervals.

Where 1 g per day is needed, the suggested regime is one Naprosyn 500 tablet twice daily.

In the following cases a loading dose of 750 mg or 1 g per day for the acute phase is recommended:

- (a) In patients reporting severe night-time pain and/or morning stiffness.
- (b) In patients being switched to Naprosyn from a high dose of another anti-rheumatic compound.
- (c) In osteoarthritis where pain is the predominant symptom.

For the patient who requires 750 mg per day and whose night-time pain and/or morning stiffness are most

troublesome, 500 mg should be taken before retiring and 100 mg upon awakening. For the patient whose day-time pain and reduced mobility are most troublesome, 100 mg should be taken upon awakening and 250 mg on retiring.

For the treatment of juvenile rheumatoid arthritis in children over five years of age, the usual dosage is 1 mg/kg/day taken in two doses at 12-hour intervals. In acute gout, the recommended dosage is 750 mg at ce, then 250 mg every eight hours until the attack has ssed.

For the treatment of acute musculoskeletal disorders, e recommended dose is 250 mg twice or thrice daily; ost patients will require only seven days' treatment but me patients may require up to 14 days' treatment.

Naprosyn Suppositories are recommended for patients whom rectal administration may be preferable. One ppository is to be inserted at night.

contra-indications, warnings, etc

contra-indications: Active peptic ulceration.

pecial precautions and warnings: Naprosyn has been und to be well tolerated by patients exhibiting /pepsia with other similar agents. None the less isodes of gastro-intestinal bleeding have been erted in patients with Naprosyn therapy. Naprosyn ould be given under close supervision to patients with history of gastro-intestinal disease.

Due to the high plasma protein binding of Naprosyn, tients simultaneously receiving hydantoins, anti-co- ulants or a highly protein-bound sulphonamide should :bserved for signs of overdosage of these drugs. :obenecid given concurrently increases Naprosyn asma levels and extends its half-life considerably.

Occasional skin rashes and angio-oedema have been ported. Patients who have exhibited aspirin hypersen- itivity in the past (usually as the angio-oedema/asthma ndrome) may exhibit the same phenomenon on aprosyn. Bronchospasm may be precipitated in patients ffering from, or with a previous history of, bronchial thma or allergic disease. The following additional currences have been reported with Naprosyn: nausea, mting, abdominal discomfort, epigastric distress, adache, inability to concentrate, insomnia, tinnitus id vertigo. Thrombocytopenia, granulocytopenia, jaun- ce, aplastic anaemia, haemolytic anaemia, peptic ceration and nephropathy may occur rarely.

Sporadic abnormalities in laboratory tests (e.g. liver nction tests) have occurred in patients on Naprosyn erapy, but no definite trend was seen in any test dicating toxicity.

Naprosyn decreases platelet aggregation and prolongs eeding time. This effect should be kept in mind when eeding times are determined.

It is suggested that Naprosyn therapy be temporarily scontinued 48 hours before adrenal function tests are rformed because Naprosyn may artifactually interfere ith some tests for 17-ketogenic steroids. Similarly, aprosyn may interfere with some assays of urinary 5-/droxyindoleacetic acid.

Mild peripheral oedema has been observed in a few stients receiving Naprosyn. Although sodium retention as not been reported in metabolic studies, it is possible at patients with questionable or compromised cardiac nction may be at a greater risk when taking Naprosyn. aprosyn should be used only with caution in patients ith renal dysfunction, particularly if long-term usage is nder consideration.

Teratology studies in rats and rabbits, at dose levels equivalent on a human multiple basis to those which have produced foetal abnormality with certain other non-steroidal anti-inflammatory agents, e.g. aspirin, have not produced evidence of foetal damage with Naprosyn. As with other drugs of this type Naprosyn produces delay in parturition in animals. The relevance of this finding to human patients is unknown. However, good medical practice indicates minimal drug usage in pregnancy, and use of this class of therapeutic agents requires cautious balancing of possible benefits against potential risks to the mother and foetus.

The use of Naprosyn should be avoided in patients who are breast-feeding.

Overdosage: Significant overdosage of the drug may be characterised by drowsiness, heartburn, indigestion, nausea or vomiting. No evidence of toxicity or late sequelae have been reported 5–15 months after ingestion, for three to seven days, of doses of up to 3 g/day. One patient ingested a single dose of 25 g of naproxen and experienced mild nausea and indigestion. It is not known what dose of the drug would be life-threatening. Should a patient ingest a large amount of naproxen accidentally or purposefully, the stomach may be emptied and usual supportive measures employed. Animal studies indicate that the prompt administration of activated charcoal in adequate amounts would tend to reduce markedly the absorption of the drug.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities Naprosyn Tablets are supplied in canisters of 60 and 250 tablets. Naprosyn 500 Tablets are supplied in canisters of 100 tablets. Naprosyn Suspension is supplied in 500 ml bottles. Naprosyn Suppositories are supplied in boxes containing 10 suppositories.

Further information In addition to the excellent therapeutic efficacy demonstrated by Naprosyn in comparative clinical trials, good tolerance has been demonstrated, even in patients exhibiting multiple intolerance to other commonly used non-steroidal anti-inflammatory agents.

Product licence numbers

Naprosyn Tablets	0286/0031
Naprosyn 500 Tablets	0286/0061
Naprosyn Suspension	0286/0047
Naprosyn Suppositories	0286/0053

NORIDAY*

Presentation Each pack contains 28 yellow tablets, each containing norethisterone 0.35 mg. Each tablet is stamped NORIDAY on one side and SYNTEX on the other.

Uses Noriday is a progestogen-only oral contraceptive. It is particularly useful for women for whom oestrogens may not be appropriate. Although the mode of action of NORIDAY tablets has not yet been fully defined it is thought that alterations occur in the cervical mucus which inhibit the penetration of sperm, there is substantial inhibition of ovulation, and changes occur in the endometrium which inhibit implantation of the fertilised egg.

Dosage and administration The first Noriday tablet is taken on the FIRST DAY of menstrual bleeding. Thereafter, 1 tablet is taken continuously at the same time every day even during menstrual bleeding.

When starting oral contraception with Noriday tablets, additional precautions must be used for the first 14 days of tablet-taking. Suitable methods are sheaths, caps plus spermicides, and intrauterine devices. The rhythm, temperature and cervical-mucus methods cannot be used.

Tablet omissions: Tablets must be taken daily in order to maintain adequate hormone levels. If a tablet is missed, it should be taken as soon as possible, with the next tablet being taken at the usual time so that two tablets are taken on that date. An additional method of contraception should be used for the next 14 days. If two or more tablets are missed, NORIDAY should be discontinued immediately and a method of non-hormonal contraception should be used until menses has appeared or pregnancy has been excluded.

Contra-indications, warnings, etc

Contra-indications: A history during pregnancy of idiopathic jaundice or severe pruritus; Dubin-Johnson or Rotor syndrome; acute or severe chronic liver diseases; undiagnosed irregular vaginal bleeding; a history of thromboembolic disorders; pregnancy. Special caution should be observed in the presence of pre-existing breast or genital-tract cancer.

Warnings, side-effects: Hypertension, which is usually reversible on discontinuing treatment, has occurred in a small percentage of women taking oral contraceptives. NORIDAY should be used with caution in patients with a history of hepatic dysfunction or hypertension.

A statistical association between the use of oral contraceptives and the occurrence of thrombosis, embolism or haemorrhage has been reported. Patients on such treatments should be kept under regular surveillance, in view of the possibility of development of such conditions as thromboembolism. Risk of coronary artery disease in women taking oral contraceptives is increased by the presence of other predisposing factors such as cigarette smoking, hypercholesterolaemia, obesity, diabetes, history of pre-eclamptic toxemia and increasing age. After the age of thirty-five years, the patient and physician should carefully re-assess the risk/benefit ratio of using oral contraceptives as opposed to alternative methods of contraception.

It is advisable to discontinue Noriday at least six weeks before elective operations and during immobilisation.

Benign and malignant liver tumours have been associated with oral contraceptive use. The relationship between occurrence of liver tumours and use of female sex hormones is not known at present. These tumours may rupture causing intra-abdominal bleeding. If the patient presents with a mass or tenderness in the right upper quadrant or an acute abdomen, the possible presence of a tumour should be considered.

An increased risk of congenital anomalies, including heart defects and limb defects, has been reported following the use of sex hormones, including oral contraceptives, in pregnancy. If the patient does not adhere to the prescribed schedule, the possibility of pregnancy should be considered at the time of the first missed period and further use of oral contraceptives should be withheld until pregnancy has been ruled out. It is recommended that for any patient who has missed two consecutive periods, pregnancy should be ruled out before continuing the contraceptive regimen. If preg-

nancy is confirmed the patient should be apprised of the potential risks to the foetus and the advisability of continuing the pregnancy should be discussed in the light of these risks. It is advisable to discontinue the use of oral contraceptives three months before a planned pregnancy.

Progestogen-only oral contraceptives such as Norida may offer less protection against ectopic pregnancy than against intra-uterine pregnancy.

The incidence of side-effects in clinical trials was lower than that experienced with oestrogen-containing oral contraceptives. Side-effects which did occur included some cycle irregularity during the first few months of therapy, spotting or breakthrough bleeding, amenorrhoea, and occasionally, breast discomfort.

Circumstances requiring additional contraceptive precautions other than the temperature, rhythm and cervical-mucus methods:

1. When changing to Noriday tablets from other hormonal contraceptives, additional contraceptive measures should be employed until 14 consecutive tablets have been taken regularly.

2. Vomiting or diarrhoea may reduce the effectiveness of the tablets by preventing them from being fully absorbed. In the case of repeated vomiting or continued diarrhoea, additional contraceptive measures should be employed for 14 days after the symptoms have subsided.

3. Interaction with other drugs. Some drugs accelerate the metabolism of oral contraceptives taken concurrently. Drugs suspected of having the capacity to reduce the efficacy of oral contraceptives include certain sedatives, antibiotics, anti-epileptic and anti-arthritis drugs.

It is therefore advisable to use non-hormonal methods of contraception during treatment with such drugs.

Menstrual pattern: A usual feature of all progestogen-only oral contraceptives is that they produce an initial irregularity of the bleeding pattern, but such irregularity tends to decrease with time. The patient should be informed before starting Noriday tablets that her menstrual pattern is likely to alter.

Irregular bleeding is, from a medical point of view, no reason for discontinuation of therapy, as long as organic causes and pregnancy can be ruled out. The patient should be instructed that if two or more consecutive periods are missed, she should consult her physician in order to rule out pregnancy.

Use after delivery or abortion: Although after delivery or abortion it is customary to start oral contraception at the end of the first biphasic menstrual cycle, Noriday tablet may be started as early as the seventh day post-partum. Additional contraceptive measures should be employed for the first 14 days of tablet-taking.

Use during breast-feeding: There is no evidence that Noriday tablets diminish the yield of breast milk. Small amounts of steroid materials appear in the milk; their effect on the breast-fed child has not been determined.

Reasons for stopping oral contraception immediately First signs of thrombophlebitis or thromboembolism, jaundice or pregnancy.

Overdosage: Overdosage may be manifested by nausea, vomiting, breast enlargement and vaginal bleeding. There is no specific antidote and treatment should be symptomatic. Gastric lavage may be employed if the overdosage is large and the patient is seen sufficiently early (within four hours).

Pharmaceutical precautions Noriday tablets should be kept under normal storage conditions.

Pharmaceutical category POM.

Pack quantities Noriday tablets are available in blister packs of 3 x 28 tablets.

Further information Nil.

Product licence number 0286/0024.

DRIMIN[®]

Presentation A 21-tablet calendar pack; each yellow tablet contains norethisterone 1.0 mg and ethinyloestradiol 35 mcg.

Uses Norimin is indicated for oral contraception, with the benefit of a low intake of oestrogen. The mode of action of Norimin is similar to that of other progestogen/oestrogen oral contraceptives; its activity is exerted through a combined effect on one or more of the following: hypothalamus, anterior pituitary, ovary, endometrium and cervical mucus.

Dosage and administration The dosage of Norimin for the initial cycle of therapy is 1 tablet taken daily from the 5th to the 25th day of the menstrual cycle, counting the first day of menstrual flow as 'Day 1'. For subsequent cycles, no tablets are taken for seven days, then a new course is started of 1 tablet daily for 21 days. This sequence of 21 days on treatment, seven days off treatment is repeated for as long as contraception is required.

To provide added protection during the first cycle only, the patient should be instructed to use an additional method of contraception for the first 14 days.

Tablet omissions: Tablets must be taken daily in order to maintain adequate hormone levels. If a tablet is missed, it should be taken as soon as possible within 24 hours of the correct time even if this means that 2 tablets are taken together. If 2 tablets are missed, a tablet should be taken as soon as possible so medication is re-established. An additional method of contraception should be used for the remainder of that tablet cycle. If more than 2 tablets have been missed, oral contraceptive therapy should be discontinued immediately and a method of non-hormonal contraception should be used until menstruation has appeared or pregnancy has been excluded.

Changing from another oral contraceptive: Norimin could be started seven days after completing the last course of the other product. An additional mechanical or chemical contraceptive should be used for the first 14 days of tablet-taking.

Use after childbirth, miscarriage or abortion: After childbirth, oral contraception is usually started when spontaneous menstruation has resumed. Another method of contraception should be used in the meantime, unless the first course of tablets is started within seven days of delivery. After a miscarriage or abortion, oral contraception can normally be started on the fifth day.

Contra-indications, warnings, etc

Contra-indications: As with all combined progestogen/oestrogen oral contraceptives, the following conditions should be regarded as contra-indications:

- (i) Thrombophlebitis, thromboembolic disorders, cerebral apoplexy, or a history of these conditions.

- (b) Acute or severe chronic liver disease, Dubin-Johnson or Rotor syndrome, history during pregnancy of idiopathic jaundice or severe pruritus.
- (c) Known or suspected carcinoma of the breast.
- (d) Known or suspected oestrogen-dependent neoplasia.
- (e) Undiagnosed abnormal vaginal bleeding.
- (f) Pregnancy.

Side-effects and precautions: As with all oral contraceptives, there may be slight nausea at first, weight gain or breast discomfort, which soon disappear.

Spotting or bleeding may occur during the first few cycles. Usually menstrual bleeding becomes light and occasionally there may be no bleeding during the tablet-free days.

Hypertension, which is usually reversible on discontinuing treatment, has occurred in a small percentage of women taking oral contraceptives. Progestogen/oestrogen preparations should be used with caution in patients with a history of hepatic dysfunction or hypertension.

A statistical association between the use of oral contraceptives and the occurrence of thrombosis, embolism or haemorrhage has been reported. Patients on such treatments should be kept under regular surveillance in view of the possibility of development of such conditions as thromboembolism.

Risk of coronary artery disease in women taking oral contraceptives is increased by the presence of other predisposing factors such as cigarette smoking, hypercholesterolaemia, obesity, diabetes, history of pre-eclamptic toxemia and increasing age. After the age of thirty-five years, the patient and physician should carefully re-assess the risk/benefit ratio of using combined oral contraceptives as opposed to alternative methods of contraception.

Benign and malignant liver tumours have been associated with oral contraceptive use. The relationship between occurrence of liver tumours and use of female sex hormones is not known at present. These tumours are very rare but they may rupture causing intra-abdominal bleeding. If the patient presents with a mass or tenderness in the right upper quadrant or an acute abdomen, the possible presence of a tumour should be considered.

The use of this product in patients suffering from epilepsy, migraine, asthma or cardiac dysfunction may result in exacerbation of these disorders, because of fluid retention.

A decreased glucose tolerance may occur in diabetic patients on this treatment, and their control must be carefully supervised.

An increased risk of congenital anomalies, including heart defects and limb defects, has been reported following the use of sex hormones, including oral contraceptives, in pregnancy. If the patient does not adhere to the prescribed schedule, the possibility of pregnancy should be considered at the time of the first missed period and further use of oral contraceptives should be withheld until pregnancy has been ruled out. It is recommended that for any patient who has missed two consecutive periods, pregnancy should be ruled out before continuing the contraceptive regimen. If pregnancy is confirmed the patient should be apprised of the potential risks to the foetus and the advisability of continuing the pregnancy should be discussed in the light of these risks. It is advisable to discontinue Norimin three months before a planned pregnancy.

Gastro-intestinal upsets may interfere with the absorption of the tablets. Some drugs may modify the metabolism of Norimin reducing its effectiveness; these include certain sedatives, antibiotics, anti-epileptic and anti-arthritis drugs. During the time such agents are used concurrently, it is advisable that mechanical contraceptives also be used.

Women taking oral contraceptives require careful observation if they have or have had any of the following conditions: breast nodules; fibrocystic disease of the breast or an abnormal mammogram; a history of severe depressive states; varicose veins; sickle-cell anaemia; diabetes; hypertension; high blood cholesterol levels; epilepsy; asthma; otosclerosis; multiple sclerosis; porphyria; tetany; disturbed liver functions; gallstones; cardiovascular disease; kidney disease; chloasma; herpes of pregnancy. The worsening or first appearance of any of these conditions may indicate that the oral contraceptive should be stopped. Contact lenses may become uncomfortable.

Norimin should be discontinued at least six weeks before elective operations and during immobilisation.

Women with a history of oligomenorrhoea or secondary amenorrhoea or young women without regular cycles may have a tendency to remain anovulatory or to become amenorrhoeic after discontinuation of oral contraceptives. Women with these pre-existing problems should be advised of this possibility and encouraged to use other contraceptive methods.

The risk of arterial thrombosis associated with combined oral contraceptives increases with age, and this risk is aggravated by cigarette smoking. The use of combined oral contraceptives by women in the older age group, especially those who are cigarette smokers, should therefore be discouraged and alternative methods advised.

Treatment of overdosage: Overdosage may be manifested by nausea, vomiting, breast enlargement and vaginal bleeding. There is no specific antidote and treatment should be symptomatic. Gastric lavage may be employed if the overdose is large and the patient is seen sufficiently early (within four hours).

Pharmaceutical precautions Norimin should be kept under normal storage conditions.

Legal category POM.

Package quantities Norimin is available in calendar packs of 3 × 21 tablets.

Further information Nil.

Product licence number 0286/0059.

NORINYL* - 1

NORINYL* - 1/28

Presentation Norinyl-1 consists of 21 white tablets, stamped NORINYL on one side and SYNTEX on the other. Each tablet contains norethisterone 1 mg and mestranol 0.05 mg. Norinyl-1/28 has, in addition to 21 white tablets, seven orange tablets containing lactose, stamped SYNTEX on one side.

Uses Norinyl-1 and Norinyl-1/28 are oral contraceptives. They are also useful in the treatment of certain menstrual disorders, e.g. heavy, irregular or painful periods. Activity is exerted through a combined effect on one or more of the following: hypothalamus, anterior pituitary, ovary, endometrium and cervical mucus.

Dosage and administration *Norinyl-1:* the very first tablet is taken by mouth on the *fifth* day of a menstrual period. One tablet is then taken at the same time of day every day, until all 21 tablets are used. The next pack started after *seven tablet-free* days: this sequence repeated for as long as contraception is required.

Norinyl-1/28: The very first tablet is taken on the *first* day of a menstrual period. Tablets should be taken at the same time of day, every day, until all 28 are used. The next pack is started on the *following* day. The first tablet of every course should be chosen from the red section in accordance with the instructions on the pack. Strict care should be exercised to ensure that the tablets are taken in their proper sequence.

The patient should be advised that, during the first 14 days of starting Norinyl-1 (and Norinyl-1/28), an additional mechanical or chemical method of contraception should be used.

Tablet omissions: Tablets must be taken daily in order to maintain adequate hormone levels. If a tablet is missed it should be taken as soon as possible within 24 hours of the correct time even if this means that 2 tablets are taken together. If 2 tablets are missed, a tablet should be taken as soon as possible so medication is re-established. An additional method of contraception should be used for the remainder of that tablet cycle. If more than 2 tablets have been missed, oral contraceptive therapy should be discontinued immediately and a method of non-hormonal contraception should be used until menses has appeared or pregnancy has been excluded.

Changing from another oral contraceptive: Norinyl should be started seven days after completing the last course of the other product. An additional mechanical or chemical contraceptive should be used for the first 7 days of tablet-taking.

Use after childbirth, miscarriage or abortion: After childbirth, oral contraception is usually started when spontaneous menstruation has resumed. Another method of contraception should be used in the meantime unless the first course of tablets is started within seven days of delivery. After a miscarriage or abortion, oral contraception can normally be started on the fifth day.

Contra-indications, warnings, etc

Contra-indications: As with all combined progestogen/oestrogen oral contraceptives, the following conditions should be regarded as contra-indications:

- Thrombophlebitis, thromboembolic disorders, cerebral apoplexy, or a history of these conditions.
- Acute or severe chronic liver disease, Dubin-Johnson or Rotor syndrome, history during pregnancy of idiopathic jaundice or severe pruritus.
- Known or suspected carcinoma of the breast.
- Known or suspected oestrogen-dependent neoplasia.
- Undiagnosed abnormal vaginal bleeding.
- Pregnancy.

Side-effects and precautions: As with all oral contraceptives, there may be slight nausea at first, weight gain, breast discomfort, which soon disappear.

Spotting or bleeding may occur during the first few cycles. Usually menstrual bleeding becomes light or occasionally there may be no bleeding during the tablet-free days.

Hypertension, which is usually reversible on discontinuing treatment, has occurred in a small percentage

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Gastro-intestinal upsets may interfere with the absorption of the tablets. Some drugs may modify the metabolism of Norinyl reducing its effectiveness; these include certain sedatives, antibiotics, anti-epileptic and anti-arrhythmic drugs. During the time such agents are used concurrently, it is advisable that mechanical contraceptives also be used.

Women taking oral contraceptives require careful observation if they have or have had any of the following conditions: breast nodules; fibrocystic disease of the breast or an abnormal mammogram; a history of severe depressive states; varicose veins; sickle-cell anaemia; diabetes; hypertension; high blood cholesterol levels; epilepsy; asthma; otosclerosis; multiple sclerosis; porphyria; tetany; disturbed liver functions; gallstones; cardiovascular disease; chloasma; herpes of pregnancy; or worsening or first appearance of any of these conditions may indicate that the oral contraceptive

should be stopped. Contact lenses may become uncomfortable.

Norinyl should be discontinued at least 6 weeks before elective operations and during immobilisation.

Women with a history of oligomenorrhoea or secondary amenorrhoea or young women without regular cycles may have a tendency to remain anovulatory or to become amenorrhoeic after discontinuation of oral contraceptives. Women with these pre-existing problems should be advised of this possibility and encouraged to use other contraceptive methods.

The risk of arterial thrombosis associated with combined oral contraceptives increases with age, and this risk is aggravated by cigarette smoking. The use of combined oral contraceptives by women in the older age group, especially those who are cigarette smokers, should therefore be discouraged and alternative methods advised.

Treatment of overdose: Overdosage may be manifested by nausea, vomiting, breast enlargement and vaginal bleeding. There is no specific antidote and treatment should be symptomatic. Gastric lavage may be employed if the overdose is large and the patient is seen sufficiently early (within four hours).

Pharmaceutical precautions Norinyl-1 and Norinyl-1/28 should be kept under normal storage conditions.

Legal category POM.

Package quantities Norinyl-1 is available in packs of 3 x 21 tablets.

Norinyl-1/28 is available in 'push-packs' of 28 tablets (seven placebos).

Further information Nil.

Product licence number 0286/5000.

STAYCEPT* PESSARIES

Presentation Smooth, torpedo-shaped, solid white pessaries containing nonoxynol-9 6% w/w.

Uses Spermicidal contraceptive agent. As with other spermicidal preparations, additional methods of contraception, for example, diaphragm, cap or intra-uterine device, must be used with Staycept pessaries.

When pregnancy is medically contra-indicated, the choice of contraceptive should be made in consultation with a doctor.

Dosage and administration One to be inserted into the vagina before intercourse. When used with a diaphragm or cap, one pessary should be placed inside the diaphragm or cap before it is put into position; a second pessary is then inserted into the vagina as far as possible.

Contra-indications, warnings, etc There are no known contra-indications to the use of Staycept Pessaries.

Pharmaceutical precautions Store in a cool place.

Legal category GSL.

Package quantities Pack of 10 pessaries.

Further information Nil.

Product licence number 0286/5012.

STAYCEPT* JELLY

Presentation A smooth, clear jelly containing octoxynol 1% w/w.

Uses Spermicidal contraceptive agent. As with other spermicidal preparations, additional methods of contraception, for example, diaphragm, cap or intra-uterine device, must be used with Staycept Jelly.

When pregnancy is medically contra-indicated, the choice of contraceptive should be made in consultation with a doctor.

Dosage and administration

- Used with diaphragm. Two 1-inch strips of jelly to be applied to either side of diaphragm and spread in a thin layer over cap and rim.
- Used with intra-uterine device. Two to three inches applied into the vagina, from an applicator.

Contra-indications, warnings, etc There are no known contra-indications to the use of Staycept Jelly.

Pharmaceutical precautions Store in a cool place.

Legal category GSL.

Package quantities 80 g tube.

Further information Staycept Jelly can be used as a lubricant by women who experience difficulty with intercourse because of a dry vagina.

Product licence number 0286/5011.

SYNFLEX*

Presentation Opaque, orange, size 1, hard gelatin capsules marked SYNTEX, each containing naproxen sodium 275 mg (equivalent to naproxen 250 mg).

Uses Synflex is indicated for the treatment of: acute musculo-skeletal disorders (such as sprains and strains, direct trauma, lumbo-sacral pain, cervical spondylitis, fibrositis, bursitis and tendinitis); chronic pain in conditions such as musculo-skeletal disorders and peripheral vascular disease; dysmenorrhoea; uterine pain following IUCD insertion; pain following orthopaedic surgery; postoperative pain; post-partum pain.

Synflex has been shown to have potent analgesic, antipyretic and anti-inflammatory properties when tested in classical animal test systems. It inhibits prostaglandin synthetase, as do other non-steroidal anti-inflammatory agents. As with other agents, however, the exact mechanism of its anti-inflammatory action is not known.

Dosage and administration 1 capsule contains 275 mg of naproxen sodium.

Adults: For bursitis, tendinitis and musculo-skeletal disorders the recommended dosage is 550 mg at once, then 275 mg three or four times daily; most patients will require only seven days' treatment but some patients may require up to fourteen days' treatment.

For dysmenorrhoea and chronic pain the recommended dosage is 550 mg initially followed by 275 mg three or four times daily as needed.

For postoperative and orthopaedic pain the recommended regime is 550 mg initially, followed by 275 mg three to five times daily as needed, with a maximum daily dose after the first day of 1,375 mg (5 capsules).

For post-partum pain a single dose of 550 mg is recommended.

Children: As safety and efficacy studies are not complete, Synflex is not recommended for use in child under 16 years of age.

Contra-indications, warnings, etc

Contra-indication: Active peptic ulceration.

Special precautions: Synflex has been found to be tolerated by patients exhibiting dyspepsia with other similar agents. Nonetheless episodes of gastro-intestinal bleeding have been reported in patients with Synflex therapy. Synflex should be given under close supervision to patients with a history of gastro-intestinal disease.

Due to the high plasma protein binding of Synflex patients simultaneously receiving hydantoins, anti-coagulants, or a highly protein-bound sulphonamide should be observed for signs of overdosage of these drugs. Probenecid given concurrently increases Synflex plasma levels and extends its half-life considerably.

Occasional skin rashes and angio-oedema have been reported. Patients who have exhibited aspirin hypersensitivity in the past (usually as the angio-oedema/asthma syndrome) may exhibit the same phenomenon with Synflex. Bronchospasm may be precipitated in susceptible patients and in patients suffering from, or with a history of, bronchial asthma or allergic disease. The following additional occurrences have been reported with Synflex: nausea, vomiting, abdominal discomfort, epigastric distress, headache, inability to concentrate, insomnia, tinnitus and vertigo. Thrombocytopenia, granulocytopenia, jaundice, aplastic anaemia, haemolytic anaemia, peptic ulceration and nephropathy may occur rarely. Sporadic abnormalities in laboratory tests (e.g. liver function tests) have occurred in patients on Synflex therapy, but no definite trend was seen in any test indicating toxicity.

Synflex decreases platelet aggregation and prolongs bleeding time. This effect should be kept in mind when bleeding times are determined.

It is suggested that Synflex therapy be temporarily discontinued 48 hours before adrenal function tests are performed, because Synflex may artifactually interfere with some tests for 17-ketogenic steroids. Similarly, Synflex may interfere with some assays of urinary hydroxyindoleacetic acid.

Mild peripheral oedema has been observed in some patients receiving Synflex. Although sodium retention has not been reported in metabolic studies, it is possible that patients with questionable or compromised cardiac function may be at a greater risk when taking Synflex. Synflex should be used only with caution in patients with renal dysfunction, particularly if long-term usage is under consideration.

Teratology studies in rats and rabbits, at dose levels equivalent on a human multiple basis to those which have produced foetal abnormality with certain other non-steroidal anti-inflammatory agents, e.g. aspirin, have not produced evidence of foetal damage with Synflex. As with other drugs of this type Synflex delays parturition in animals. The relevance of this finding to human patients is unknown. However, good medical practice indicates minimal drug usage in pregnancy, and use of this class of therapeutic agent requires cautious balancing of possible benefit against potential risk to mother and foetus.

The use of Synflex should be avoided in patients who are breast-feeding.

Overdosage: Significant overdosage of the drug may be characterised by drowsiness, heartburn, indigestion.

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Synflex Capsules
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of an immediate effect should be explained to the patient
in order to ensure cooperation and continuation of
treatment with the regular dosage schedule.

There is no evidence that exceeding the maximum
recommended dosage is more effective; higher dosage
should therefore be avoided.

For full information on using the device, see patient
instruction insert.

Contra-indications, warnings, etc

Contra-indications:

1. Untreated fungal, bacterial or viral nasal infections.
2. Hypersensitivity to the formulation.

Warnings, precautions, side-effects: Glucocorticoids
may mask some signs of infection and new infections
may appear during their use.

Syntaris Nasal Spray is not recommended in the first
three months of pregnancy. If used in the second or third
trimester, the expected benefits should be weighed
against the potential hazards to the foetus.

Care must be taken when transferring patients from
systemic steroid therapy to Syntaris Nasal Spray if there
is reason to suspect that their adrenal function is
impaired.

Although adrenal suppression or atrophy of the nasal
mucosa have not been observed in clinical trials, the
potential for these effects should be considered with
prolonged excessive usage.

Adverse reactions noted in clinical trials with Syntaris
Nasal Spray have been consistent with what one would
expect when applying topical medication to an already
inflamed membrane. The most frequently observed side-
effect was a mild transient nasal burning and stinging
which was occasionally severe enough to warrant
discontinuation of treatment. Other side-effects noted,
in order of decreasing prevalence were: nasal irritation,
epistaxis, runny and stuffy nose, sore throat, hoarseness
and throat irritation. If severe these may require discon-
tinuation of therapy.

Treatment of overdosage: Administration of large
amounts of flunisolide over a short period may produce
suppression of hypothalamic-pituitary-adrenal function.
In such event, Syntaris Nasal Spray should be reduced
immediately to the recommended dosage.

Pharmaceutical precautions Do not refrigerate.

Legal category POM.

Package quantities Each pack of Syntaris contains
one 24 ml bottle and the metered pump/nozzle device.

Further information Nil.

Product licence number 0286/0057.

SYNTEX MENOPHASE*

Presentation Syntex Menophase consists of 28
tablets in a bubble pack. This is a sequential oestrogen-
progestogen product comprising six different formula-
tions arranged so that 1 tablet is taken daily starting with
5 pink, and continuing with 8 orange, 2 yellow, 3 green,
6 blue and 4 lavender tablets.

Composition: Syntex Menophase comprises six
formulations:

	(mg)	(mcg)	Tablets
1. Mestranol	0.0125	(12.5)	5 pink
2. Mestranol	0.025	(25.0)	8 orange
3. Mestranol	0.050	(50.0)	2 yellow
4. Norethisterone	1.00		
Mestranol	0.025	(25.0)	3 green
5. Norethisterone	1.50		
Mestranol	0.030	(30.0)	6 blue
6. Norethisterone	0.75		
Mestranol	0.020	(20.0)	4 lavender

Uses Syntex Menophase is designed for the treatment of hot flushes and sweats and the amelioration of symptoms associated with the climacteric. Problems which can be associated with failure of endogenous oestrogen production and which have improved in clinical studies include: hot flushes and sweats, depression, lack of concentration, emotional lability, nervousness, lethargy, insomnia, loss of libido, senile vaginitis, pruritus, dry skin, arthritis and neuralgia due to senile osteoporosis.

Dosage and administration The patient is advised to take her first tablet on a Sunday and thereafter to take one tablet at the same time each day in sequential order round the pack. She starts a new pack the day after she has taken her last lavender tablet from the previous pack.

Though menopausal symptoms are likely to improve during the first month of treatment, it will be necessary to maintain therapy for 6–12 months. If symptoms recur after discontinuation, further courses can be prescribed.

Contra-indications, warnings, etc

Contra-indications: As with other oestrogen/progestogen containing compounds, previous thromboembolism, active liver disease, pregnancy and undiagnosed irregular vaginal bleeding should be regarded as contra-indications. Caution should be observed in the presence of pre-existing breast or genital-tract cancer.

Precautions:

1. Syntex Menophase is not an oral contraceptive.
2. Syntex Menophase provides sequential graded doses of hormones; the post-menopausal patient with an intact uterus may therefore experience a small, regular monthly bleed. If forewarned of this possibility, it usually causes no distress.

3. Because Syntex Menophase has not been designed as a contraceptive agent, in the event of a tablet omission the patient should discard the tablets missed and take only that tablet appropriate to the day of the week.

4. Hypertension, which is usually reversible on discontinuing treatment, has occurred in a small percentage of women receiving oestrogen/progestogen medication. A statistical association between the use of certain oestrogen/progestogen-containing preparations and a risk of thromboembolism has been reported, although no cause and effect relationship has been proved. Foetal abnormalities have been reported to occur in the offspring of women who have taken progestogens and/or oestrogens during pregnancy. Pregnancy should be ruled out before initiating or continuing the regimen.

Side-effects: The incidence of side-effects is extremely low. Occasionally breast tenderness and nausea may occur in the first month or two, but usually improve during treatment.

Overdosage: May be manifested by: nausea, vomiting, breast enlargement and vaginal bleeding. There is no

specific antidote and treatment should be symptomatic. Gastric lavage may be employed if the overdose is large and the patient is seen sufficiently early (within 6 hours).

Pharmaceutical precautions Syntex Menophase should be stored in a cool place.

Legal category POM.

Package quantities Push-through bubble-pack containing 28 tablets.

Further information Nil.

Product licence number 0286/0027.

TOPILAR* TOPILAR* OINTMENT

Presentation Topilar and Topilar Ointment contain flucilorolone acetonide, which is a topical anti-inflammatory corticosteroid.

Topilar contains flucilorolone acetonide 0.025% w/w completely dissolved in the specially formulated FAF cream base (a combination of fatty alcohols and propylene glycol). The FAPG cream base is a white, non-aqueous hydrophilic, semi-solid vehicle with slight pearly sheen.

Topilar Ointment contains flucilorolone acetonide 0.025% w/w dissolved in an emollient ointment base.

Uses Topilar and Topilar Ointment are indicated for the treatment of steroid-responsive skin conditions such as psoriasis and dermatitis (eczema), e.g. contact, atopic and seborrhoeic dermatitis.

Topilar has the advantage in that it may be used for dermatoses where, because of the character and site of the lesion and the possible use of polythene occlusion supervening infection is a potential hazard. If *fracture* infection supervenes, appropriate anti-infective therapy should be instituted.

Dosage and administration In adults and children a thin smear is applied to the affected areas twice daily. This regimen should be followed until the acute phase has passed. Treatment should be continued for at least one week thereafter with one application daily. The course is completed by a further short period, e.g. two weeks, during which one application is made on alternate days.

Polythene occlusion may be required for difficult cases.

Contra-indications, warnings, etc Topilar and Topilar Ointment are contra-indicated in viral, tuberculous and frank bacterial infections of the skin. In such cases appropriate anti-infective therapy should be instituted according to the doctor's normal practice.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively, i.e. in large amounts or for prolonged periods, in the first trimester of pregnancy.

In infants, the long-term administration of large quantities of topical steroids should be avoided; adrenal suppression may occur even without occlusion. Adrenal suppression occasionally occurs in the long-term treatment of adults, especially if occlusion is used although the effect on the adrenal gland is general

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extreme, or there is delay in removing the drug from the
stomach, administration of a para-symphathomimetic
drug should be considered.

Side-effects: In clinical trials, comparing Urispas with
other antispasmodic agents, the incidence of side-effects
was low. Those adverse reactions that have been
recorded include headache, nausea, fatigue, diarrhoea,
blurred vision and dry mouth.

Pharmaceutical precautions No special precautions
are required.

Legal category POM.

Package quantities Containers of 100.

Further information Nil.

Product licence number 0286/5005.

UTOVLAN*

Presentation Each Utovlan Tablet contains norethis-
terone 5 mg. The white tablets are uncoated, circular
bevel-edged and with a break-line.

Uses At low dosage Utovlan is indicated for dysfunc-
tional uterine bleeding, endometriosis, polymenorrhoea,
menorrhagia, metropathia haemorrhagica, postpone-
ment of menstruation, and premenstrual syndrome. At
high dosage Utovlan is recommended for disseminated
carcinoma of the breast.

Dosage and administration Low dosage

*Dysfunctional Uterine Bleeding, Polymenorrhoea, Men-
orrhagia, Dysmenorrhoea and Metropathia Haemorrhag-
ica:* 1 tablet three times daily for 10 days; bleeding
usually stops within 48 hours. Withdrawal bleeding
resembling true menstruation occurs a few days after the
end of treatment. One tablet twice daily, from days 19 to
26 of the two subsequent cycles, should be given to
prevent recurrence of the condition.

Endometriosis: 1 tablet three times daily for a minimum
treatment period of six months. The dosage should be
increased to 4 or 5 tablets a day if spotting occurs. The
initial dosage should be resumed when bleeding or
spotting stops.

Postponement of menstruation: 1 tablet three times
daily, starting three days before the expected onset of
menstruation. Menstruation usually follows within three
days of finishing the treatment.

Pre-menstrual syndrome: 1 tablet daily from days 16 to
25 of the menstrual cycle.

High dosage

For disseminated breast carcinoma the starting dose is 8
tablets (40 mg) per day increasing to 12 tablets (60 mg)
if no regression is noted.

Contra-indications, warnings, etc

Contra-indications: Pregnancy, disturbance of liver
function, history during pregnancy of idiopathic jaundice,
severe pruritus, herpes, undiagnosed irregular vaginal
bleeding.

Side-effects: These rarely occur at the usual dosage
levels of 15 mg per day. Mild nausea has been reported.
High dosage treatment, even over long periods, is well
tolerated; transitory digestive upsets and jaundice have
rarely been reported.

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SYNTEX PHARMACEUTICALS LIMITED

If menstrual bleeding should fail to follow a course of UTOVLAN, the possibility of pregnancy must be ruled out before a further course is given.

Pharmaceutical precautions No special precautions.

Legal category POM.

Package quantities Cans of 100 and 1,000

Further information Nil.

Product licence number 0286/5007.

** Trade Mark*



VED-S* TABLETS

Presentation Brown mottled tablets embossed ved-S. Each tablet contains:

glycyrrhizinized liquorice	380 mg
minium hydroxide gel	100 mg
gnesium carbonate	200 mg
dium bicarbonate	100 mg

es Action and indications: For treatment of peptic ulcer and other allied conditions.

The main active constituent of Caved-S is deglycyrrhizinized liquorice, which has peptic ulcer healing and ismolytic activity and is free from deoxycortone like ions (i.e. does not alter serum levels of sodium, assium or chloride). Deglycyrrhizinized liquorice narily enhances the defence mechanism of the cosa by increasing the number of mucus secreting ls. The cell proliferation rate is also increased. The ismolytic activity and the action of the added antacids, viates gastric distress.

Usage and administration Oral administration. The lets should be taken between meals.

ult dose for gastric ulcer: 2 tablets three times a day.

ult dose for duodenal ulcer: Increase to 2 tablets six es a day when necessary.

phyllactic dose: 1 tablet three times a day for gastric er, 2 tablets three times a day for duodenal ulcer.

ildren's dosage 10-14 years: Half adult dose.

The tablets should be lightly chewed and swallowed ; in exceptional cases of objection to taste the tablets ould be broken into a few pieces and then swallowed h a drink of water. No additional antacids need be en.

ntra-indications, warnings, etc Rare cases of d diarrhoea can occur. No other side-effects have an reported.

idy of teratology and embryotoxicity of Caved-S in bits: Summary: No significant differences between ated and control groups were established in any of the ameters analysed. No skeletal or soft-tissue changes re found. The overall results of this study would icate that the compound failed to induce teratological ormalities in the conceptus of the animals studied. e administration of the compound (Caved-S) during s 6-18 of pregnancy did not produce signs of bryotoxicity and no teratogenic potential was dem-strated. However, Caved-S, like all drugs, should be en with caution during pregnancy.

idy of 13 weeks' subacute oral toxicity of Caved-S in gs: Summary: The oral administration of Caved-S for weeks at dose levels of 2,000, 1,000 and 500 mg/kg dy weight appears to be well tolerated by beagle dogs. significant differences were noted in parameters

analysed, either during compound administration or during four-week withdrawal from the dosing schedule.

Treatment of overdosage: No cases of overdosage have been reported. If excessive amounts are taken gastric lavage and supportive symptomatic treatment are recommended.

Pharmaceutical precautions *Storage:* Protect from excessive heat and moisture.

Legal category GSL.

Package quantities Containers of 60, 240 and 600 tablets.

Further information Nil.

Product licence number 0424/5000.

CEDOCARD* -5

Presentation Round white tablets, embossed 'CC' reverse side scored, containing 5 mg isosorbide dinitrate.

Uses For the treatment and prevention of angina pectoris and for the long term management of coronary insufficiency.

Cedocard-5 is a coronary vasodilator having a marked anti-anginal effect when administered sublingually as well as orally.

The mode of action depends on the reduced work load following vasodilation and reduced venous return.

Dosage and administration *Sublingual administration:* Adult dose: For treatment of acute attack of angina pectoris - 1 tablet as required.

Oral administration: Adult dose: For prophylaxis of angina pectoris 1-2 tablets three or four times a day as required.

To prevent nocturnal attacks of angina pectoris - 1-2 tablets before retiring to sleep.

Onset of action sublingually - one to two minutes and duration of up to two hours.

Onset of action orally - 20/30 minutes and duration of four to six hours.

No recommended dose for children.

Contra-indications, warnings, etc Development of tolerance to this drug and cross tolerance to other nitrates and nitrites.

Adverse reaction: Cutaneous vasodilation with flushing, transient episodes of dizziness and weakness, and other signs of cerebral ischaemia, may occur with postural hypotension.

Treatment of overdosage: In rare cases of overdosage, gastric lavage is indicated. Passive exercise of the extremities of the recumbent patient will promote venous return.

Pharmaceutical precautions *Storage:* Protect from heat and moisture.

Legal category P.

Package quantities Containers of 60 and 180.

Further information The high solubility of Cedocard-5 facilitates rapid dissolution after sublingual administration resulting in quick relief from an acute anginal attack. The unique formulation enables the same tablet to be swallowed, when a more prolonged action is obtained.

Cedocard-5 is more stable than trinitrin offering greater reliability.

Cedocard-5 may be prescribed in combination with beta-blocking agents.

Product licence number 0424/5001.

CEDOCARD-10*

Presentation Round, rose coloured tablets, scored on one side and imprinted with CC on the other side. Each tablet contains 10 mg isosorbide dinitrate.

Uses For the prophylaxis of angina pectoris.

Cedocard-10 relaxes vascular smooth muscle, dilates coronary vessels, reduces peripheral resistance and venous return, resulting in alteration of myocardial metabolism and reduction of myocardial oxygen demand.

Dosage and administration For oral administration.

Adult dose: 1–3 tablets four times daily. Onset of action 20–30 minutes and duration of four to six hours.

There is no recommended dose for children.

Contra-indications, warnings, etc

Contra-indications: A history of sensitivity to the drug.

Precautions: Tolerance and cross-tolerance to other nitrates may occur.

Adverse reactions: Transient headaches, these can usually be controlled by temporary dosage reduction.

Cutaneous vasodilation with flushing, transient episodes of dizziness and weakness, and other signs of cerebral ischaemia, may occur with postural hypotension.

Treatment of overdose: In rare cases of overdose, gastric lavage is indicated. Passive exercise of the extremities of the recumbent patient will promote venous return.

Pharmaceutical precautions *Storage:* Protect from heat and moisture.

Legal category P.

Package quantity Containers of 100 tablets.

Further information Nil.

Product licence number 0424/0015.

CEDOCARD-20*

Presentation Round, flat, bevel-edged blue tablets, scored on one side and imprinted CC on the other side, containing 20 mg isosorbide dinitrate per tablet.

Uses For the treatment of severe congestive heart failure. Cedocard-20 reduces elevated left ventricular filling pressure in patients with congestive heart failure, and lowers peripheral resistance, which leads to a

reduced after load; therefore, the heart has to perform less work to overcome the peripheral resistance.

For the prophylaxis of angina pectoris.

Dosage and administration Oral administration.

Severe congestive heart failure: After determination of peripheral resistance, arterial and pulmonary pressure and stroke volume, half a tablet of Cedocard-20 administered. On the basis of its effect on these parameters, an effective dose of Cedocard-20 is established. This dose can vary between $\frac{1}{2}$ and 2 tablets, and is then administered every 4 hours. Haemodynamic monitoring of the treatment should be carried out.

Angina prophylaxis: One half to 2 tablets three or four times daily.

No recommended dose for children.

Contra-indications, warnings, etc

Contra-indications: Hypotension, cardiac shock, known sensitivity to the drug.

Precautions: Treatment of severe congestive heart failure with Cedocard-20 should be checked haemodynamically, by measuring the intra-arterial pressure, pulmonary artery pressure, stroke volume, and peripheral resistance.

Adverse reactions: Transient headaches at the start of therapy; these can usually be controlled by temporary dosage reduction.

Treatment of overdose: In rare cases of overdose, gastric lavage is indicated. Passive exercise of the extremities of the recumbent patient will promote venous return.

Pharmaceutical precautions *Storage:* Protect from heat and moisture.

Legal category POM.

Package quantities Packs of 100 tablets.

Further information Nil.

Product licence number 0424/0008.

CEDOCARD RETARD* - 20

Presentation Round yellow sustained-release tablets embossed CC, SR and scored on reverse side, each containing 20 mg isosorbide dinitrate.

Uses For the prophylaxis of angina pectoris.

The active principle of Cedocard Retard-20 is isosorbide dinitrate which relaxes vascular smooth muscle and produces coronary vasodilation, reduction in peripheral resistance and venous return, alteration of myocardial metabolism, and reduction of the myocardial oxygen demand.

Dosage and administration For oral administration.

Adult dose: One tablet in the morning and 1 tablet before retiring to sleep. Onset of action 20–30 minutes and duration of action is 10–12 hours.

There is no recommended dose for children.

Contra-indications, warnings, etc

Contra-indication: A history of sensitivity to the drug.

Precautions: Tolerance and cross-tolerance to other nitrates may occur.

Adverse reactions: Cutaneous vasodilation with flushing, transient episodes of dizziness and weakness, and other signs of cerebral ischaemia, may occur with postural hypotension.

treatment of overdosage: In rare cases of overdosage, stric lavage is indicated. Passive exercise of the extremities of the recumbent patient will promote venous return.

Pharmaceutical precautions *Storage:* Protect from heat and moisture.

Legal category P.

Package quantities Containers of 60 tablets.

Further information Nil.

Product licence number 0424/0007.

EDOCARD* IV

Presentation Clear glass ampoules containing 10 mg isosorbide dinitrate in 10 ml of colourless isotonic saline solution.

Uses For the treatment of unresponsive congestive heart failure, particularly after myocardial infarction. Cedocard infusion reduces elevated left ventricular filling pressure in patients with congestive heart failure. For the control of refractory angina pectoris.

Dosage and administration Administration by intravenous infusion only.

Adult dose: The dosage must be determined individually. Doses of 2–10 mg per hour (33–167 mcg/min) are recommended.

There is no recommended dose for children.

Start the infusion with 2 mg/hour and increase progressively according to the evolution of haemodynamic parameters and the clinical condition of the patient. Gradually decrease the concentration of infusion and switch to oral or sublingual isosorbide dinitrate. There should be no abrupt interruption of the infusion except in severe hypotension. Continuous haemodynamic supervision during the infusion is required.

Preparation of solution for infusion: The contents of Edocard IV must be administered by infusion only.

Cedocard IV can be diluted with isotonic saline, 5–10% glucose solution or Krebs-Ringer solution.

Contra-indications, warnings, etc

Contra-indications: Hypotension, cardiogenic shock.

Precautions: Close supervision of the patient is necessary for safe and optimum treatment. Cedocard IV must be administered by infusion after dilution.

If PVC infusion bags (e.g. Travenol Vialflex, Boots Teriflex) and administration sets are used for Cedocard infusion, 15–30% of the drug can be lost by adsorption. There is no loss of active constituent from solution in glass or polyethylene apparatus.

It is recommended that Cedocard IV is administered using a syringe pump (glass or rigid plastic) with short sections of polyethylene tubing. Alternatively, a polyethylene infusion bag (e.g. Boots Polyfusor) may be used.

Should only PVC infusion bags be available, then it is important to carry out close haemodynamic monitoring of the patient; infusion rate should be modified according to required haemodynamic response. PVC bags of 500 ml volume should be used to minimise adsorption of isosorbide dinitrate.

Adverse reactions: Headache. In the case of an excessive reduction in blood pressure, phenomena indicating a reduced blood supply to the heart may appear.

Treatment of overdosage: If arterial systolic blood pressure drops below 90 mm. Hg, and if heart rate increases above 10% of its initial value, the infusion should be discontinued to allow a return to pretreatment levels. Passive exercise of the extremities of the recumbent patient will promote venous return.

Pharmaceutical precautions Protect from exposure to excessive heat. The Cedocard dilution for infusion is stable up to 24 hours.

Legal category POM.

Package quantities Packs of 10 ampoules.

Further information Nil.

Product licence number 0424/0012.

CEDURAN* TABLETS

Presentation Light khaki-coloured tablets, embossed 'CEDURAN' one side, scored reverse side. Each tablet contains:

Nitrofurantoin BP	100 mg
Deglycyrrhizinated liquorice	250 mg

Uses Ceduran has a powerful antibacterial action in the urine, with a broad spectrum that is effective against Gram-positive and Gram-negative bacteria with the exception of *Pseudomonas*. Orally administered Ceduran is absorbed quickly and excreted almost exclusively by the tubuli via the kidneys. The addition of deglycyrrhizinated liquorice does not affect the action of nitrofurantoin, but prevents the nausea, vomiting and gastro-intestinal disorders caused when nitrofurantoin is administered alone.

For the treatment of urinary tract infections.

Dosage and administration *Adults:* In acute urinary infections, 3–4 tablets daily.

In chronic urinary tract infections for prevention of relapse, 1–2 tablets daily.

Children: In acute urinary infections, 5–8 mg of nitrofurantoin per kg of body weight daily.

In chronic urinary tract infections, 2–4 mg of nitrofurantoin per kg of body weight daily. The tablets should be taken with food or milk.

Contra-indications, warnings, etc Insufficient renal function, prematurity, infants younger than one month, or of weight under 2,500 g.

Not recommended during the first trimester of pregnancy. In susceptible patients Ceduran may cause allergic symptoms such as erythema, rash, pruritis, pleuro-pneumonitis, eosinophilia and anaphylactoid reactions. Some reports have occurred of leucopenia, agranulocytosis (rare), polyneuritis, haemolytic anaemia with G6 PD deficiency and cholestatic icterus.

Treatment with Ceduran may colour the urine dark yellow or brown, which is caused by the presence of breakdown metabolites and is quite harmless.

Treatment of overdosage: Excessive intake would probably cause vomiting. Should overdosage occur, gastric lavage is recommended.

Pharmaceutical precautions *Storage:* Protect from excessive heat and moisture.

Legal category POM.

Package quantities 100 tablets foil packed.

Further information Nil.

Product licence number 0424/5002.

COLPERMIN*

Presentation A light blue/dark blue enteric coated hard gelatine capsule size 1, with a green band between cap and body. Each capsule contains 0.2 ml standardised peppermint oil BP.

Uses For the treatment of symptoms of discomfort and of abdominal colic and distension experienced by patients with irritable bowel syndrome.

The enteric coating of the capsule delays release of the peppermint oil until it reaches the distal small bowel. The oil exerts a local effect of colonic relaxation and a fall of intracolonic pressure.

Dosage and administration For oral administration.

Adult dose: One capsule three times a day, preferably before meals and taken with a small quantity of water. The capsules should *not* be taken immediately after food.

The dose may be increased to two capsules, three times a day when discomfort is more severe.

The capsules should be taken until symptoms resolve, usually within one or two weeks. At times when symptoms are more persistent, the capsules can be continued for longer periods of between 2 to 3 months.

There is no experience in the use of these capsules in children under the age of 15 years.

Contra-indications, warnings, etc

Precautions: The capsules should not be broken or chewed because this would release the peppermint oil prematurely, possibly causing local irritation of the mouth and oesophagus.

Patients who already suffer from heartburn, sometimes experience an exacerbation of these symptoms when taking the capsule. Treatment should be discontinued in these patients.

Colpermin, as with all drugs should be given with caution during pregnancy.

Adverse effects: Heartburn; sensitivity reactions to menthol, which are rare, and include erythematous skin rash, headache, bradycardia, muscle tremor and ataxia.

Treatment of overdosage: If capsules have been recently ingested, the stomach should be emptied by gastric lavage. Observation should be carried out with symptomatic treatment if necessary.

Pharmaceutical precautions Store in a cool place. Avoid direct sunlight.

Legal category P.

Package quantities Containers of 100 capsules.

Further information Nil.

Product licence number 0424/0009.

NIFEREX*

Presentation Niferex is a non-ionic polysaccharide iron complex.

Tablets, brown, each containing the equivalent 50 mg elemental iron.

Elixir, brown, flavoured, containing the equivalent 100 mg elemental iron per 5 ml teaspoonful.

Uses Haemopoietic. For the prophylaxis and treatment of uncomplicated iron-deficiency anaemia.

Dosage and administration *Prophylactic dose:*

Adults: 1 tablet or 2½ ml elixir daily.

Therapeutic dose: *Adults:* 2 tablets or 5 ml elixir once twice daily.

Children 6–12 years: 5 ml elixir daily.

Children 2–6 years: 2½ ml elixir daily.

Infants: 1 drop elixir (paediatric) per 1 lb body weight three times a day (one drop contains approximately 0.6 mg elemental iron).

Contra-indications, warnings, etc No specific contra-indications, but obviously Niferex should not be given to patients with known iron overload. In common with all oral iron preparations Niferex should be given with caution where there is peptic ulceration.

Treatment of overdosage: Gastric lavage is recommended. Previous case reports of overdose have not resulted in serious adverse effects.

Pharmaceutical precautions Niferex Tablets should be kept in a sealed container and dispensed in moisture-proof containers. Niferex elixir can be diluted with distilled water or sorbitol to almost any concentration without stability problems, as long as the pH is maintained above 5.

Legal category P.

Package quantities *Tablets:* Plastic container of 10 tablets.

Elixir: Bottle of 240 ml.

Paediatric elixir: Dropper bottle of 30 ml.

Further information Niferex is a highly water-soluble polysaccharide-iron complex which is stable in the range pH 4.5–11.0, and disassociates only after leaving the stomach. The iron is released over a period of one hour circumventing the nausea associated with sudden doses of free iron. In elixir form, the complex remains in solution and does not precipitate in gastric or duodenal fluid.

Niferex provides a good haemopoietic response with almost complete absence of side-effects normally associated with oral iron therapy. Acute toxicity studies have shown a safety factor at least 13 times greater than ferrous sulphate.

Product licence numbers

Tablets 5046/5000

Elixir 5046/5001

*Trade Mark

Pharm Limited

5 East Street

Landford Forum

Dorset

AFADOL*

Presentation Yellow tablet, bisected. Each tablet contains:

racetamol BP 500 mg
aspirine BP 30 mg

Uses For analgesia without sedation mild to moderate in associated with muscular disorders, tension, headaches, dysmenorrhoea, colds, arthritis and rheumatism.

Dosage and administration *Adult dose:* 2 tablets every three to four hours. As necessary.

Children age 5–12 years: 1 tablet.

Contra-indications, warnings, etc Nil.

Pharmaceutical precautions Store in cool dry place.

Legal category P.

Package quantities 100.

Further information Nil.

Product licence number 0551/5001.

EFFERCITRATE* TABLETS

Presentation White, circular, flat, effervescent tablets with a slightly rough surface, weighing about 2.7 g, 12 mm in diameter and having the odour of lemon and lime.

Each tablet contains the equivalent of 1.5 g of potassium citrate BP and 250 mg citric acid BP in a pleasantly flavoured effervescent base.

Uses Effercitrate tablets provide a convenient and reliable method to administer potassium citrate to increase the alkali reserve and render the urine more alkaline when treating urinary tract infections. They may also be used to prevent crystalluria during treatment with sulfonamides. Effercitrate Tablets do not have the uric acid increasing effect of bicarbonate on gastric secretion and are less purgative than potassium tartrate.

Dosage and administration *Adults and children over 12 years of age:* Two tablets in a tumblerful of water up to three times daily.

Children Age 1–6 years: One tablet in a tumblerful of water up to three times daily.

Not recommended for children under 1 year.

Sufficient should be given in all cases to render and maintain the urine alkaline.

Contra-indications, warnings, etc A mild diuresis usually follows treatment with Potassium Citrate.

Each tablet contains 13.9 mmol potassium. Care should be taken to prevent hyperkalaemia particularly in patients with impaired renal function.

Side-effects: In common with other potassium salts Effercitrate may give rise to gastric irritation and the tablets must always be taken well diluted with water. Gastric effects may be minimized by giving doses with or after meals.

Overdosage: Hyperkalaemia. Below 6.5 mmol per litre poisoning is minimal, moderate up to 8 mmol per litre and severe above 8 mmol per litre. Absolute toxicity is governed by pH and sodium levels. Hyperkalaemia symptoms, may be transiently controlled with calcium gluconate, glucose or glucose and insulin, sodium bicarbonate or hypertonic sodium infusions, cationic exchange resins, or haemo and peritoneal dialysis. Patients who are digitalized may experience acute digitalis intoxication during potassium removal.

Pharmaceutical precautions Store in a cool dry place. Effercitrate tablets are hygroscopic and should be dispensed in the original containers which include a desiccant, and should be kept closed.

Legal category P.

Package quantities Tubes contain 12 tablets.

Further information Each Effercitrate tablet contains the equivalent of the Potassium Citrate and Citric acid content of 5 ml Potassium Citrate Mixture BPC 1973.

Product licence number 0051/0002.

VERACUR* GEL

Presentation Clear, water-miscible gel in a tube. Veracur Gel contains 1.5% v/v of Solution of Formaldehyde BP.

Uses Treatment of warts, particularly plantar warts (verrucae).

Dosage and administration To be applied directly on to the wart (verruca) and covered with a plaster, twice a day. Remove the outer dead layers with an emery board or pumice stone as the treatment progresses.

Contra-indications, warnings, etc If required protect surrounding skin with a thin film of Vaseline petroleum jelly before application.

For external use only.

Not to be applied to broken skin.

Pharmaceutical precautions Store in cool dry place.

Legal category GSL.

Package quantities 15 g.

Further information Nil.

Product licence number 0551/5000.

*Trade Mark

ALBAMYCIN T*

Presentation Capsules (blue/grey) containing 125 mg novobiocin as novobiocin sodium and 125 mg tetracycline as tetracycline hydrochloride.

Yellow-orange granules for reconstitution as paediatric suspension, each 5 ml containing 62.5 mg novobiocin as novobiocin calcium and 62.5 mg tetracycline as tetracycline base.

Uses Antibacterial. Acute and chronic infections of the upper and lower respiratory tract, pyoderma, acne, urinary tract infections caused by organisms sensitive to the antibiotic combination.

Dosage and administration Oral.

Adults: 2 capsules every 12 hours. In severe infections 2 capsules every eight or six hours.

Children: Dosage is based upon 7.5 mg novobiocin plus 7.5 mg tetracycline/kg/day given in 2 divided doses. In severe infection the dose may be doubled.

Paediatric suspension: 0-6 months: 1.25-2.5 ml every 12 hours.

6 months to 2 years: 2.5-5 ml every 12 hours.

3-9 years: 5-10 ml every 12 hours.

The paediatric suspension should be reconstituted by adding 83 ml purified water slowly to the granules and shaking to promote suspension.

Contra-indications, warnings, etc

Contra-indications: Sensitivity to either antibiotic. Since novobiocin may interfere with the conjugation of bilirubin, administration to neonates is not recommended.

Side-effects: Nausea, urticaria, maculopapular rash, transient leucopenia and other blood dyscrasias have been reported. Tooth discoloration in children may occur if high dosages have been given in the neonatal period or early childhood or during the last trimester of the mother's pregnancy.

Overdosage: No action is deemed necessary. In the event of renal impairment being present, tetracycline will accumulate in the serum and dialysis is suggested in order to avoid possible liver damage.

Pharmaceutical precautions Albamycin T should be stored at a temperature not exceeding 30°C. Only purified water should be used to reconstitute the paediatric granules. A degree of frothing may be experienced on reconstitution.

After reconstitution Albamycin T Paediatric may be stored for one week without significant loss of potency.

Where further dilution is required use purified water.

Legal category POM.

Package quantities Albamycin T Capsules in bottles of 16 and 100.

Albamycin T Paediatric as dry granules for reconstitution to make 100 ml.

Further information Albamycin T is of particular value in mixed infections. The antibacterial actions novobiocin and tetracycline are dissimilar and this assists in the prevention of the rapid emergence resistant strains of susceptible bacteria.

Product licence numbers

Capsules 0032/5005

Granules 0032/5004

AMBAXIN* ▼

Presentation White to off-white rod-shaped score tablets with parallel sides and rounded ends, contain 400 mg bacampicillin hydrochloride, one side prin Upjohn, other side 130 on either side of the score.

Uses Antibacterial. Ambaxin is indicated in the treatment of infections due to susceptible strains of following: Gram-positive organisms - Streptococci (including *S. faecalis*), pneumococci, non-penicillina producing staphylococci, *Clostridia* spp. and *L. monocytogenes*. Gram-negative organisms - *H. influenzae meningococci*, *N. gonorrhoea*, *E. coli*, *P. mirabilis* and *Shigella* and *Salmonella*.

The indications for Ambaxin include the following: sinusitis, tonsillitis, peritonitis, acute and chronic bronchitis, pneumonia, skin and soft tissue infections, urinary infections, gonorrhoea, otitis media, pleurisy, acute endometritis, post-operative infections and paratyphoid fever. In vitro studies should be performed to determine causative organisms and their susceptibility to Ambaxin. Therapy may be initiated prior to obtaining results of susceptibility testing.

Penetration into the cerebrospinal fluid and brain occurs only when the meninges are inflamed.

Ampicillin, 10 mcg discs, should be used to determine the in vitro susceptibility of organisms to Ambaxin.

Ambaxin has no appreciable antibacterial activity in vivo but is rapidly hydrolysed to ampicillin in vivo, thus antibacterial spectrum is the same as that of ampicillin.

Cross-resistance with cephalosporins and penicillin may occur.

Dosage and administration The usual dosage for adults is one 400 mg tablet two or three times a day. Dosage may be doubled in severe infections or when infection is caused by less sensitive pathogens. The dosage for children over 5 years is one half a 400 mg tablet (200 mg) three times daily.

The dose for uncomplicated gonorrhoea is 1600 mg plus 1 gram probenecid in a single dose.

Contra-indications, warnings, etc

Contra-indications: A history of previous hypersensitivity to any of the penicillins is a contra-indication.

Warnings and precautions: The possibility of superinfection with mycotic organisms or bacterial pathogens should be kept in mind during therapy. Particular care should be taken in the treatment of atopic individuals. The risk of skin reaction is particularly high in patients with a history of allergic reactions.

in infectious mononucleosis or lymphatic leukaemia. with other potent antibiotics, periodic assessment of organ system function, including renal, hepatic and haematopoietic, should be made during prolonged therapy. Safety for use in pregnancy has not been established.

Side-effects: Ambaxin is well tolerated. Since bacampicillin is hydrolysed to ampicillin in-vivo, the possibility of countering those side-effects associated with ampicillin should be considered. Side-effects are generally mild, and of the usual penicillin type. Interruption of treatment is not usually necessary. The incidence of diarrhoea as a side-effect is lower than that seen with ampicillin.

Dosage: Since Ambaxin is a penicillin, problems of overdosage are unlikely to be encountered.

Pharmaceutical precautions Store at room temperature (15–25°C).

Legal category POM.

Package quantities 100 tablets in glass bottles.

Further information Ambaxin is more rapidly absorbed than equimolar amounts of ampicillin, and achieves three times the serum levels of ampicillin in 1/2 to 1 hour, thereby increasing its penetration into tissues of body fluids such as sinus mucosa and sputum, achieving concentrations greatly exceeding MIC's of susceptible pathogens. Ambaxin may be given without regard to time of food intake.

Product licence number 0032/0070.

COLESTID*

Presentation Light yellow, tasteless and odourless granules consisting of colestipol hydrochloride with 2% colloidal silicone dioxide.

Uses Ion-exchange resin which lowers plasma cholesterol levels through binding with bile acid in the intestinal lumen.

Colestid is indicated as adjunctive therapy to diet in the management of patients with elevated cholesterol levels. It has been shown to have no significant effect on glyceride levels.

Although Colestid is effective in all types of hypercholesterolaemia, it is medically most appropriate in patients with Fredrickson's type II hyperlipoproteinemia.

In patients with xanthomas, the skin lesions have been reported to regress on Colestid therapy.

Dosage and administration Colestid should be mixed with water or other fluids before ingesting.

The recommended total daily adult dosage of Colestid is 15–30 grams. This may be taken in divided doses two to four times daily.

Patients should take other drugs at least one hour before or one hour after Colestid to minimise possible interference with their absorption.

Preparation: To prepare Colestid, add the contents of a packet or scoop to 100 ml or more of the preferred vehicle (water, orange, tomato, or other fruit juices, milk) and mix thoroughly until dispersed. Alternatively, Colestid may be added to soups or pulpy fruits with a high water content or to carbonated beverages.

Contra-indications, warnings, etc

Contra-indications: Colestipol is contra-indicated in individuals who have previously demonstrated hypersensitivity to its use.

Warnings: To avoid accidental inhalation or oesophageal distress, Colestid should not be taken in its dry form.

Safety for use in pregnant women or in children has not been established.

Precautions: In man, Colestid may interfere with the absorption of certain drugs (e.g. digitalis and its alkaloids, tetracycline hydrochloride, chlorothiazide and penicillin G). Colestid has been shown not to interfere with the absorption of clindamycin, clofibrate, aspirin, tolbutamide, warfarin and methyl dopa. The clinical response to concomitant medication should be closely monitored and appropriate adjustments made.

Side-effects: The most common adverse reactions reported with Colestid have been of a functional gastrointestinal nature. The most frequent is constipation, which is usually mild, transient and responsive to the usual adjunctive measures.

Transient and modest elevation of SGOT and of alkaline phosphatase have been observed. No medical significance is attached to these observed changes.

Overdosage: No toxic effects due to overdosage have been reported.

Pharmaceutical precautions None.

Legal category POM.

Package quantities Box containing 30 x 5 gram foil sachets. Also 250 gram bottles.

Further information Colestid is not absorbed; its action is limited to the lumen of the gastro-intestinal tract, and it is passed in the faeces. It binds bile acids in the intestinal lumen and causes them to be excreted in the faeces together with the polymer.

When the enterohepatic circulation of bile acids is interrupted, cholesterol conversion to bile acids is enhanced and plasma cholesterol levels are thereby lowered. In addition, Colestid may also reduce plasma and tissue cholesterol levels by decreasing the intestinal bile acid concentration below that required for maximum cholesterol absorption.

Product licence numbers

Foil Sachet 0032/0055

Bottle Pack 0032/0057

CYTOSAR*

Presentation Off-white, freeze-dried cake of 100 mg cytosine arabinoside (cytarabine) in a rubber-capped vial.

Uses Cytotoxic. For induction of remission in acute myeloid leukaemia in adults and for other acute leukaemias of adults and children.

Dosage and administration By intravenous infusion or injection, and subcutaneous injection. The accompanying 5 ml ampoule containing water for injection and 0.9% w/v benzyl alcohol should be used for preparing a solution of cytarabine in the vial. Such solution contains 20 mg/ml cytarabine.

The physician is reminded that in practice Cytosar has been administered in combination with a variety of other cytotoxic agents using a number of different dosage schedules, and reference to the current literature before commencing treatment is recommended.

Dosage recommendations may be converted from those in terms of bodyweight to those related to surface

area by means of nomograms such as are presented in Documenta Geigy.

1. *Remission induction: Adults:* (a) Continuous treatment:

- (i) Rapid injection – 2 mg/kg/day is a judicious starting dose. Administer for 10 days. Obtain daily blood counts. If no antileukaemic effect is noted and there is no apparent toxicity, increase to 4 mg/kg/day and maintain until therapeutic response or toxicity is evident. Almost all patients can be carried to toxicity with these doses.
- (ii) 0.5–1.0 mg/kg/day may be given in an infusion of up to 24 hours duration. Results from one-hour infusions have been satisfactory in the majority of patients. After 10 days this initial daily dose may be increased to 2 mg/kg/day subject to toxicity. Continue to toxicity or until remission occurs.

(b) Intermittent treatment:

3–5 mg/kg/day is administered intravenously on each of five consecutive days. After a two to nine-day rest period, a further course is given. Continue until response or toxicity occurs.

The first evidence of marrow improvement has been reported to occur 7–64 days (mean 28 days) after the beginning of therapy.

In general, if a patient shows neither toxicity nor remission after a fair trial, the cautious administration of higher doses is warranted. As a rule patients have been seen to tolerate higher doses when given by rapid intravenous injection as compared with slow infusion. This difference is due to the rapid metabolism of Cytosar and the consequent short duration of action of the high dose.

Children: Children appear to tolerate higher doses than adults and, where dose ranges are quoted, the children should receive the higher dose and the adults the lower.

2. *Maintenance therapy:* Remissions which have been induced by cytarabine, or by other drugs, may be maintained by intravenous or subcutaneous injection of 1 mg/kg once or twice weekly.

Contra-indications, warnings, etc

Contra-indications: Therapy with Cytosar should not be considered in patients with pre-existing drug-induced bone marrow suppression, unless the clinician feels that such management offers the most hopeful alternative for the patient. Cytosar should not be used in the management of non-malignant disease, except for immunosuppression.

Warning: Cytosar is a potent bone marrow suppressant. Therapy should be started cautiously in patients with pre-existing drug-induced bone marrow suppression. Patients receiving this drug must be under close medical supervision and, during induction therapy, should have leucocyte and platelet counts performed daily. Bone marrow examinations should be performed frequently after blasts have disappeared from the peripheral blood. Facilities should be available for management of complications, possibly fatal, of bone marrow suppression (infection resulting from granulocytopenia and other impaired body defences, and haemorrhage secondary to thrombocytopenia). One case of anaphylaxis that resulted in acute cardiopulmonary arrest and required resuscitation has been reported. This occurred immediately after the intravenous administration of Cytosar.

Severe and at times fatal CNS, GI and pulmonary toxicity (different from that seen with conventional

therapy regimens of Cytosar) has been reported following some experimental Cytosar dose schedules. The reactions include reversible corneal toxicity; cerebellar and cerebellar dysfunction, usually reversible; severe gastrointestinal ulceration, including pneumatosis cystoides intestinalis, leading to peritonitis; sepsis and liver abscess; and pulmonary oedema. Cytosar is known to be teratogenic in some animal species. The use of Cytosar in women who are, or who may become, pregnant should be undertaken only after due consideration of the potential benefits and hazards.

This product should not normally be administered to patients who are pregnant or to mothers who are breastfeeding.

Cytosar has been shown to be carcinogenic in animals. The possibility of a similar effect should be borne in mind when designing the long-term management of the patient.

Precautions: Patients receiving Cytosar (cytarabine) must be monitored closely. Frequent platelet and leucocyte counts are mandatory. Suspend or modify therapy when drug-induced marrow depression has resulted in a platelet count under 50,000 or a polymorphonuclear count under 1,000 per mm³. Counts of formed elements in the peripheral blood may continue to fall after the drug is stopped and reach lowest values after drug-free intervals of five to seven days. If indicated, restart therapy when definite signs of marrow recovery appear (e.g. successive bone marrow studies). Patients whose drug is withheld until 'normal' peripheral blood values are attained may escape from control.

When intravenous doses are given quickly, patients are frequently nauseated and may vomit for several hours afterwards. This problem tends to be less severe when the drug is infused.

The human liver apparently detoxifies a substantial fraction of an administered dose. Use the drug with caution and at reduced dose in patients whose liver function is poor.

Periodical checks of bone marrow, liver and kidney functions should be performed in patients receiving Cytosar.

The safety of this drug for use in infants is not established.

Like other cytotoxic drugs, Cytosar may induce hyperuricaemia secondary to rapid lysis of neoplastic cells. The clinician should monitor the patient's blood uric acid level and be prepared to use such supportive and pharmacological measures as may be necessary to control this problem.

Side-effects: Adverse reactions seen with cytarabine treatment have included those seen with cytotoxic agents having an effect on bone marrow, such as leucopenia, thrombocytopenia, anaemia, bone marrow suppression and megaloblastosis. Other side-effects have included: nausea, vomiting, diarrhoea, oral ulceration, hepatic dysfunction. Occasional adverse experiences have been reported as follows: renal dysfunction, anorexia, sepsis, gastro-intestinal haemorrhage, irritation or sepsis at site of injection, neuritis or neurotoxicity, rash, freckling, oesophagitis, skin and mucosal bleeding, chest pain, joint pain and reduction in reticulocytes.

A Cytosar syndrome has been described. It is characterised by fever, myalgia, bone pain, occasionally chest pain, maculopapular rash, conjunctivitis and malaise. It usually occurs 6–12 hours following drug administration. Corticosteroids have been shown to be beneficial in treating or preventing this syndrome. If the symptoms of

se syndrome are serious enough to warrant treatment, corticosteroids should be contemplated as well as continuation of therapy with Cytosar.

verdosage: Cessation of therapy, followed by management of ensuing bone marrow depression including whole blood or platelet transfusion and antibiotics as quired.

harmaceutical precautions Reconstituted solutions should be stored at room temperature and used within 48 hours.

Discard any solution in which a slight haze develops.

Legal category POM.

Package quantities Cytosar is supplied as a vial of sterile powder 100 mg cytosine arabinoside in company with an ampoule containing 5 ml diluent (water for injection plus 0.9% w/v benzyl alcohol).

Further information Published work indicates that cytosar is effective in the indications for which it is commended. However, a greater treatment success has been achieved in certain studies by the combination of Cytosar with other agents. The literature should be referred to in determining whether this latter course of action should be considered.

Product licence number 0032/5037.

ALACIN C*

Presentation Hard-filled gelatine capsules (maroon/white) containing 150 mg clindamycin (as clindamycin hydrochloride).

Hard-filled gelatine capsules (lavender/white) containing 75 mg clindamycin (as clindamycin hydrochloride).

Pink, sucrose-based granules for paediatric suspension, with pineapple flavour. Each 5 ml reconstituted suspension contains 75 mg clindamycin (as clindamycin hydrochloride).

Uses Antibacterial. Serious infections caused by susceptible Gram-positive organisms, staphylococci (both penicillinase and non-penicillinase producing), streptococci (except *Strep. faecalis*), and pneumococci. It is also indicated in serious infections caused by susceptible aerobic pathogens.

Clindamycin does not penetrate the blood/brain barrier in therapeutically effective quantities.

Dosage and administration Oral. Absorption of clindamycin C is not appreciably modified by the presence of food.

Capsules: *Adults:* Moderately severe infection, 150–400 mg every six hours. Severe infection, 300–450 mg every six hours. Dalacin C Capsules should always be taken with a glass of water.

Paediatric: To each 100 ml bottle of granules add 74 ml water and shake.

Children: 3–6 mg/kg every six hours depending on the severity of the infection.

In children under one year or weighing 10 kg or less the minimum recommended dose is 2.5 ml (37.5 mg) every eight hours.

The following paediatric dose regime is recommended as a guide:

Moderately severe infection: 0–11 months: 3.5–9.0 kg: 2.5 ml every eight hours.

1–3 years: 10–15 kg: 2.5 ml every six hours.

4–7 years: 16–25 kg: 5 ml every six hours.

8–12 years: 26–38 kg: 7.5 ml every six hours.

Severe infection: 0–11 months: 3.5–9.0 kg: 2.5 ml every six hours.

1–3 years: 10–15 kg: 5 ml every six hours.

4–7 years: 16–25 kg: 7.5 ml every six hours.

8–12 years: 26–38 kg: 10 ml every six hours.

Adults: *Moderately severe infection:* 10 ml every six hours. *Severe infection:* 20 ml every six hours.

Note: In cases of β -haemolytic streptococcal infection, treatment with Dalacin C should continue for at least 10 days to diminish the likelihood of subsequent rheumatic fever or glomerulonephritis.

Contra-indications, warnings, etc

Contra-indications: Dalacin C is contra-indicated in patients previously found to be hypersensitive to this antibiotic. Although cross-sensitisation to lincomycin has not been demonstrated, it is recommended that Dalacin C is not used in patients who have demonstrated lincomycin sensitivity.

Warnings: Dalacin C should only be used in the treatment of serious infections. In considering the use of the product the practitioner should bear in mind the type of infection and the potential hazard of the diarrhoea which may develop since cases of colitis have been reported. The appearance of marked diarrhoea should be regarded as an indication that the product should be discontinued immediately.

Studies indicate a toxin(s) produced by *Clostridia* (especially *Clostridium difficile*) is the principal direct cause of antibiotic-associated colitis. These studies also indicate that this toxigenic *Clostridium* is usually sensitive in-vitro to vancomycin. When 125 mg to 500 mg of vancomycin is administered orally four times a day, there is a rapid observed disappearance of the toxin from faecal samples and a coincident clinical recovery from the diarrhoea.

Precautions: Care should be observed in the use of Dalacin C in atopic individuals, e.g. asthma and allergy.

Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore it should be used with caution in patients receiving such agents.

Periodic liver function tests and blood counts should be carried out during prolonged therapy. Such monitoring is also recommended in neonates and infants. Safety and appropriate dosage in infants less than one month old have not been established.

The dosage of Dalacin C may require reduction in patients with renal or hepatic impairment due to prolongation of the serum half-life of the antibiotic.

Safety for use in pregnancy has not yet been established.

Overdosage: In cases of overdosage that may have led to adverse reactions, therapy should be discontinued and the usual emergency treatment, including corticosteroids, adrenaline and antihistamines, instituted. The serum biological half-life of clindamycin is 2.4 hours. Clindamycin cannot be readily removed from the blood by dialysis or peritoneal dialysis.

Side-effects: In general Dalacin C is well tolerated. Side-effects referable to the gastro-intestinal tract include abdominal discomfort, loose stools or diarrhoea or colitis (see 'Warnings'), nausea or occasional vomiting. Hyper-

sensitivity reactions are rare, even in patients sensitive to penicillins. A low incidence of skin rash has been observed. Dalacin C has been shown to be free from major toxicity; no direct relationship to ototoxicity, nephrotoxicity, neurotoxicity, liver disease or haematopoietic damage has been established.

Pharmaceutical precautions Dalacin C Paediatric Granules are stable at room temperature (18–25°C) for at least 24 months.

Following reconstitution the paediatric suspension is stable for up to two weeks at room temperature.

Where further dilution is required use purified water.

Legal category POM.

Package quantities 75 mg capsules in bottles of 16 and 100. 150 mg capsules in bottles of 16, 100 and 500. Paediatric granules to make 100 ml suspension.

Further information Rapid absorption gives peak serum levels within 45 minutes and such levels exceed the *in vitro* minimum inhibitory concentrations for most sensitive bacteria.

Clindamycin demonstrates cross-resistance with lincomycin. When tested by *in vitro* methods, some staphylococcal strains originally resistant to erythromycin rapidly developed resistance to clindamycin.

Product licence numbers

Dalacin C Capsules 75 mg	0032/5006
Dalacin C Capsules 150 mg	0032/5007
Dalacin C Paediatric	0032/0023

DALACIN C* PHOSPHATE STERILE SOLUTION

Presentation Clear colourless sterile solution of clindamycin phosphate containing the equivalent of 150 mg clindamycin base per ml.

Uses Antibacterial. Dalacin C Phosphate is indicated in serious infections caused by susceptible Gram-positive organisms, *staphylococci* (both penicillinase and non-penicillinase-producing), *streptococci* (except *S. faecalis*), and *pneumococci*. It is also indicated in serious infections caused by susceptible anaerobic pathogens, such as, *Bacteroides* spp., *Fusobacterium* spp., *Propionibacterium*, *Peptostreptococcus* spp. and microaerophilic streptococci.

Clindamycin does not penetrate the blood/brain barrier in therapeutically effective quantities.

Dosage and administration Dalacin C Phosphate must be diluted prior to IV administration (see Package Insert) and should be infused over at least 10–60 minutes.

Adults: Parenteral (IM or IV administration).

Serious infections: 600 mg–1.2 g/day in two, three or four equal doses.

More severe infections: 1.2–2.7 g/day in two, three or four equal doses.

Single IM injections of greater than 600 mg are not recommended nor administration of more than 1.2 g in a single one-hour infusion.

For more serious infections, these doses may have to be increased. In life-threatening situations doses as high as 4.8 g daily have been given intravenously to adults.

Alternatively, the drug may be administered in the form of a single rapid infusion of the first dose followed by continuous IV infusion.

For details of dilution and infusion rates see package insert.

Children (over 1 month of age): Parenteral (IM or IV administration).

Serious infections: 15–25 mg/kg/day in three or four equal doses.

More severe infections: 25–40 mg/kg/day in three or four equal doses.

In severe infections it is recommended that children be given no less than 300 mg/day regardless of body weight.

Note: In cases of β -haemolytic streptococcal infections treatment should continue for at least 10 days.

Contra-indications, warnings, etc

Contra-indications: Dalacin C Phosphate is contra-indicated in patients previously found to be hypersensitive to preparations containing clindamycin. Although cross-sensitisation to lincomycin has not been demonstrated, it is recommended that Dalacin C Phosphate should not be used in patients who have demonstrated lincomycin sensitivity.

Warnings: Dalacin C Phosphate should only be used in the treatment of serious infections. In considering the use of this product the practitioner should bear in mind the type of infection and the potential hazard of the diarrhoea that may develop since cases of colitis have been reported. The appearance of marked diarrhoea should be regarded as an indication that the drug should be discontinued immediately.

Studies indicate a toxin(s) produced by *Clostridi*, (especially *Clostridium difficile*) is the principal direct cause of antibiotic-associated colitis. These studies also indicate that this toxigenic *Clostridium* is usually sensitive *in vitro* to vancomycin. When 125 mg to 500 mg of vancomycin is administered orally four times a day, there is a rapid observed disappearance of the toxin from faecal samples and a coincident clinical recovery from the diarrhoea.

Precautions: Care should be observed in the use of Dalacin C Phosphate in atopic individuals, e.g. asthma and allergy.

Periodic liver function tests and blood counts should be carried out during prolonged therapy. Such monitoring is also recommended in neonates and infants. Safety and appropriate dosage in infants less than one month old have not been established.

The dosage of Dalacin C Phosphate may require reduction in patients with renal or hepatic impairment due to prolongation of the serum half-life of the drug.

Safety for use in pregnancy has not yet been established.

Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore, it should be used with caution in patients receiving such agents.

Side-effects: In general Dalacin C Phosphate is well tolerated. Side-effects referable to the gastro-intestinal tract include abdominal discomfort, loose stools, diarrhoea or colitis (see Warnings), nausea or occasional vomiting. Hypersensitivity reactions are rare, even in patients sensitive to penicillins though a few cases of anaphylactoid reactions have been reported. A low incidence of skin rash has been observed.

Jaundice and abnormalities in liver function tests have been observed during clindamycin therapy. Transient neutropenia (leukopenia) and eosinophilia have been

orted, and occasional reports of agranulocytosis and myelocytopenia have been made.

ain, induration and sterile abscess have been reported after intramuscular injection and thrombophlebitis afteravenous infusion. Reactions can be minimised or avoided by giving deep IM injections and avoiding prolonged use of indwelling intravenous catheters.

Dosage: In cases of overdosage that may have led to adverse reactions, therapy should be discontinued and the usual emergency treatment, including corticosteroids, adrenaline and antihistamines, instituted. The human biological half-life of clindamycin is 2.4 hours. Clindamycin cannot be readily removed from the blood by dialysis or peritoneal dialysis.

Pharmaceutical precautions In vitro compatibility studies monitored for 24 hours at room temperature show a concentration no greater than 6 mg/ml have demonstrated no inactivation or physical incompatibility with the use of Dalacin C Phosphate in IV solutions containing sodium chloride, glucose or potassium usually used clinically.

The following drugs are physically incompatible with Dalacin C Phosphate: ampicillin, diphenylhydantoin, bitarates, aminophylline, calcium gluconate and magnesium sulphate.

Compatibility or incompatibility with other drugs besides the ones already mentioned has not been determined.

Store at room temperature. Avoid refrigeration.

Pharmaceutical category POM.

Package quantities 5 × 2 ml and 5 × 4 ml ampoules.

Further information Biologically inactive clindamycin phosphate is rapidly converted to active clindamycin following injection.

By the end of short-term intravenous infusion, peak serum levels of active clindamycin are reached. Biologically inactive clindamycin phosphate disappears rapidly from the serum; the average disappearance half-life is six minutes. However, the serum disappearance half-life of active clindamycin is about three hours in adults and two and a half hours in children.

Clindamycin demonstrates cross-resistance with lincomycin. When tested by in vitro methods some staphylococcal strains originally resistant to erythromycin rapidly developed resistance to clindamycin.

Product licence number 0032/0042.

EPO-MEDRONE®

Presentation White, sterile aqueous suspension for injection containing 40 mg per ml methylprednisolone acetate.

Uses Corticosteroid (glucocorticoid), Depo-Medrone is indicated in conditions requiring a glucocorticoid effect, e.g. anti-inflammatory, anti-allergic, anti-rheumatic.

Dosage and administration Depo-Medrone should not be mixed with any other suspending agent or solution. Depo-Medrone may be used by any of the following routes: intramuscular, intra-articular, peritendinous, intrabursal, peribursal, intralesional, into the tendon sheath and rectal.

Intramuscular – for sustained systemic effect:

Allergic conditions (hay fever, asthma, rhinitis, drug reactions), 80–120 mg (2–3 ml).

Dermatological conditions (atopic, contact and seborrhoeic dermatitis), 40–120 mg (1–3 ml).

Collagen diseases (rheumatoid arthritis, SLE), 40–120 mg (1–3 ml) per week.

Adrenogenital syndrome, 40 mg (1 ml) every two weeks.

Note: Depo-Medrone is not intended for the prophylaxis of hay fever or other seasonal allergies and should be administered only when symptoms are present.

The frequency of intramuscular injections should be determined by the duration of clinical response.

On average the effect of a single 2 ml (80 mg) injection may be expected to last approximately two weeks.

In the case of seasonal allergic rhinitis a single injection is frequently sufficient. If necessary, however, a second injection may be given after two to three weeks.

Intra-articular: Rheumatoid arthritis, osteoarthritis. The dose of Depo-Medrone depends upon the size of the joint and the severity of the condition. Repeated injections, if needed, may be given at intervals of one to five or more weeks depending upon the degree of relief obtained from the initial injection. A suggested dosage guide is: large joint (knee, ankle, shoulder), 20–80 mg (0.5–2 ml); medium joint (elbow, wrist), 10–40 mg (0.25–1 ml); small joint (metacarpophalangeal, interphalangeal, sternoclavicular, acromioclavicular), 4–10 mg (0.1–0.25 ml).

Intrabursal: Subdeltoid bursitis, prepatellar bursitis, olecranon bursitis. For administration directly into bursae, 4–30 mg (0.1–0.75 ml). In most acute cases, repeat injections are not needed.

Intralesional: Localised neurodermatitis, hypertrophic lichen planus, nummular eczema, necrobiosis lipoidica diabetorum, alopecia areata, discoid lupus erythematosus and insect bites. For administration directly into the lesion for local effect in dermatological conditions, 20–60 mg (0.5–1.5 ml). For large lesions, the dose may be distributed by repeated local injections of 20–40 mg (0.5–1 ml). One to four injections are usually employed. Care should be taken to avoid injection of sufficient material to cause blanching, since this may be followed by a small slough.

Periarticular: Epicondylitis. Infiltrate 4–30 mg (0.1–0.75 ml) into the affected area.

Into the tendon sheath: Tendinitis, tenosynovitis, epicondylitis. For administration directly into the tendon sheath, 4–30 mg (0.1–0.75 ml). In recurrent or chronic conditions, repeat injections may be necessary.

Rectal: Ulcerative colitis, 40–120 mg (1–3 ml). Administer in retention enemas or by continuous drip in 30–300 ml of water, three to seven times weekly for two or more weeks.

Special precautions should be observed when administering Depo-Medrone. Intramuscular injections should be made deeply into the gluteal muscles. The usual technique of aspirating prior to injection should be employed to avoid intravascular administration. Doses recommended for intramuscular injection must not be administered superficially or subcutaneously. Skin depression at the site of injection due to atrophic changes in the subcutaneous tissues has occasionally been reported following administration of corticosteroids. Intravenous injections should be carefully made using precise anatomical localisation. In the treatment of tendinitis care should be taken to inject Depo-Medrone into the tendon sheath rather than into the substance of the tendon.

Contra-indications, warnings, etc

Contra-indications: The usual contra-indications to the systemic or local use of corticosteroids should be observed. These include; latent, healed and active tuberculosis, peptic ulcer, acute psychoses, Cushing's syndrome, herpes simplex keratitis, vaccinia and varicella.

Warnings: Depo-Medrone *must not* be given by the intravenous route. Because of its inhibitory effect on fibroplasia, methylprednisolone may mask signs of infection and enhance dissemination of the infecting organism. Hence all patients receiving methylprednisolone should be watched for evidence of intercurrent infection. Should infection occur it must be brought under control by the use of appropriate antibacterial therapy, or administration of corticosteroids should be discontinued.

Injections of Depo-Medrone should be made only under aseptic conditions. At times of stress it may be necessary to increase the systemic dose when long-term therapy is involved.

Due to the absence of a true tendon sheath, the Achilles tendon should not be injected with Depo-Medrone.

Precautions: The presence of diabetes, osteoporosis, chronic psychotic reactions, predisposition to thrombophlebitis, hypertension, congestive heart failure, renal insufficiency and the presence of infection necessitate the carefully controlled use of methylprednisolone. While therapy with corticosteroids does not appear to be contra-indicated during pregnancy, caution is recommended, particularly during the first trimester. Also neonates of mothers who received such therapy during pregnancy should be observed for signs of hypoadrenalism and appropriate measures instituted if such signs exist.

Side-effects: Side-effects associated with the use of corticosteroids may be observed, including 'Cushing's syndrome, moon facies, supraclavicular pads of fat, hirsutism, striae and acne, hyperglycaemia, osteoporosis, peptic ulceration, hypertension, psychic disturbance, posterior subcapsular cataracts, suppression of growth in children, subcutaneous and cutaneous atrophy, sterile abscess, vertigo, weakness, myopathy, thrombo-embolism, pancreatitis, exophthalmos and headache.

Overdosage: No known antidote. Following overdosage the possibility of adrenal suppression should be guarded against by gradual diminution of dose levels over a period of time. In such event the patient may require to be supported during any further traumatic episode.

Pharmaceutical precautions Depo-Medrone should be protected from freezing.

Depo-Medrone should not be mixed with any other fluid.

Legal category POM.

Package quantities 1 ml, 2 ml and 5 ml rubber-capped vials packed singly and as 6-vial clinic packs, and a 2 ml pre-filled disposable syringe.

Further information Methylprednisolone, has achieved a clinically acceptable split between glucocorticoid effect and undesired mineralocorticoid effect. Methylprednisolone has five times the anti-inflammatory activity of hydrocortisone but has little tendency to cause salt and water retention. Depo-Medrone affords

advantages in treatment which include high concentration in low fluid volume, greater gastric tolerance avoidance of the GI tract and complete physician control of dosage.

Product licence numbers

2 ml syringe 0032/5015

Vials 0032/5038

DEPO-MEDRONE* WITH LIDOCAINE

Presentation White, sterile aqueous suspension injection containing 40 mg per ml methylprednisolone acetate and 10 mg per ml lidocaine hydrochloride.

Uses Corticosteroid (glucocorticoid). Depo-Medrone with Lidocaine is indicated in conditions requiring glucocorticoid effect: e.g. anti-inflammatory or an rheumatic. It is recommended for local use where a added anaesthetic effect would be considered advantageous.

Dosage and administration Depo-Medrone with Lidocaine should not be mixed with any other preparations as flocculation of the product may occur. Depo-Medrone with Lidocaine may be used by any of the following routes: intra-articular, peri-articular, intrabursal, and into the tendon sheath.

Intra-articular: Rheumatoid arthritis, osteoarthritis. The dose of Depo-Medrone with Lidocaine depends on the size of the joint and the severity of the condition. Repeated injections, if needed, may be given at intervals of one to five or more weeks depending upon the degree of relief obtained from the initial injection. A suggested dosage guide is: large joint (knee, ankle, shoulder) 0.1–2 ml (20–80 mg of steroid); medium joint (elbow, wrist) 0.25–1 ml (10–40 mg of steroid); small joint (metacarpophalangeal, interphalangeal, sternoclavicular, acromioclavicular) 0.1–0.25 ml (4–10 mg of steroid).

Peri-articular: Epicondylitis. Infiltrate 0.1–0.75 ml (4–30 mg of steroid) into the affected area.

Intrabursal: Subacromial bursitis, prepatellar bursitis, olecranon bursitis. For administration directly into bursa 0.1–0.75 ml (4–30 mg of steroid). In most acute cases repeat injections are not needed.

Into the tendon sheath: Tendinitis, tenosynovitis, epicondylitis. For administration directly into the tendon sheath, 0.1–0.75 ml (4–30 mg of steroid). In recurrent chronic conditions, repeat injections may be necessary.

For infants and children, the recommended dosage should be reduced, but dosage should be governed by the severity of the condition rather than by strict adherence to the ratio indicated by age or body weight.

Special precautions should be observed when administering Depo-Medrone with Lidocaine. Intrasyndov injections should be carefully made using precise anatomical localisation. In the treatment of tendinitis care should be taken to inject Depo-Medrone with Lidocaine into the tendon sheath rather than into the substance of the tendon.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to any of the components of the preparation. Depo-Medrone with Lidocaine should not be used in patients who exhibit heart block. The usual contra-indications to the systemic local use of corticosteroids should be observed. These include; latent, healed and active tuberculosis, peptic ulcer, acute psychoses, Cushing's syndrome, herpes simplex keratitis, vaccinia and varicella.

arnings: Depo-Medrone with Lidocaine must not be given by the intravenous or intrathecal route. Because of its inhibitory effect on fibroplasia, methylprednisolone may mask signs of infection and enhance dissemination of the infecting organism. Hence, all patients receiving methylprednisolone should be watched for evidence of recurrent infection. Should infection occur it must be sought under control by the use of appropriate antibacterial therapy, or administration of corticosteroids should be discontinued.

Injections of Depo-Medrone with Lidocaine should only be made under strict aseptic techniques.

Due to the absence of a true tendon sheath, the Achilles tendon should not be injected with Depo-Medrone with Lidocaine.

Precautions: The presence of diabetes, osteoporosis, manic or psychotic reactions, predisposition to thrombophlebitis, hypertension, congestive heart failure, renal insufficiency and the presence of infection necessitate a carefully controlled use of methylprednisolone. While therapy with corticosteroids does not appear to be contraindicated during pregnancy, caution is recommended, particularly during the first trimester. Also, neonates of mothers who received such therapy during pregnancy should be observed for signs of hypoadrenalism and appropriate measures instituted if such signs exist.

Retardation of linear growth has been noted in children receiving corticosteroids for 6 months or longer, the retardation being roughly proportional to the dose. Following cessation of therapy, the growth rate may be accelerated. For this reason the growth of children receiving prolonged steroid therapy should be observed carefully.

Side effects: Side effects associated with the use of corticosteroids may be observed, including Cushing's syndrome, moon facies, supraclavicular pads of fat, striae, acne, hyperglycaemia, osteoporosis, peptic ulceration, hypertension, psychic disturbance, posterior subcapsular cataracts, suppression of growth in children, subcutaneous and cutaneous atrophy, sterile abscess, vertigo, weakness, myopathy, thromboembolism, pancreatitis, exophthalmos and headache.

Overdosage: In general no positive action is required to be taken. The patient should, however, be observed closely for possible adverse reactions and appropriate steps taken.

Pharmaceutical precautions Depo-Medrone with lidocaine should be protected from freezing. Depo-Medrone with Lidocaine should not be mixed with any other fluid.

Legal category POM.

Package quantities 2 ml rubber-capped vials and 10 x 1 ml vial clinic packs.

Further information Methylprednisolone has achieved a clinically acceptable split between glucocorticoid effect and undesired mineralocorticoid effect. Methylprednisolone has five times the anti-inflammatory activity of hydrocortisone but has little tendency to cause salt and water retention. Depo-Medrone with lidocaine affords advantages in treatment which include high concentration in low fluid volume, greater gastric tolerance in avoidance of the GI tract and complete physician control of dosage.

Product licence number 0032/0076

DEPO-PROVERA*

Presentation White, sterile aqueous suspension containing 50 mg/ml medroxyprogesterone acetate.

Uses Progestogen.

For treatment of endometriosis.

Short-term antifertility agent when an oral contraceptive is contra-indicated or considered inappropriate in the following circumstances: (a) for wives of men undergoing vasectomy, for protection until the vasectomy becomes effective; (b) in women who are being immunised against rubella, to prevent pregnancy during the period of activity of the virus.

Dosage and administration Doses should be given intramuscularly deeply into the gluteal muscle.

Endometriosis: 50 mg i.m. once a week or 100 mg i.m. every two weeks for six months or longer.

Short term anti-fertility agent:

1. For menstruating women a single injection of 150 mg i.m. should be given during the first three to five days of the menstrual cycle.

2. For puerperal women the injection should ideally be given during the first week after delivery, but may be given at any time in the first six weeks post partum. (N.B. For wives of men undergoing vasectomy a second injection of 150 mg i.m. three months after the first injection may be necessary in a small proportion of patients where the husband's sperm count has not fallen to zero.)

Contra-indications, warnings, etc

Contra-indications: Depo-Provera is contra-indicated in thrombophlebitis or history of pulmonary embolism, and liver dysfunction or disease. It is also contra-indicated in known or suspected malignancy of breast or genital organs.

Warnings: Whether administered alone or in combination with oestrogen, Depo-Provera should not be employed in patients with abnormal uterine bleeding until a definite diagnosis has been established and the possibility of genital malignancy eliminated.

Precautions: Animal studies show that Depo-Provera possesses adrenocorticoid activity. While such activity has not been observed in human subjects, patients receiving large doses of Depo-Provera continuously and for long periods should be observed closely.

Some instances of female foetal masculinisation, clitoral hypertrophy, have been observed on large doses.

This product has not been approved for long-term use as a contraceptive.

In long-term studies in the Beagle dog, Depo-Provera causes mammary nodules, a small number of which become malignant. The relevance of the dog observations for humans has not yet been established.

Side-effects: Clinically Depo-Provera is well tolerated. No significant untoward effects have been reported.

Delay in return to normal menstrual cycling and transient infertility lasting up to 18 months or occasionally longer may be observed in patients who have been on continuous therapy with Depo-Provera over a prolonged period.

Depo-Provera frequently causes disruption of the normal menstrual cycle and irregular vaginal bleeding or spotting may be experienced. The frequency of occurrence of this bleeding usually decreases with subsequent injections and after one year on treatment many women have amenorrhoea.

Overdosage: No positive action is required to be taken.

Pharmaceutical precautions Store at room temperature and protect from freezing. Do not mix with other agents.

Legal category POM.

Package quantities 1 ml, 3 ml and 5 ml vials.

Further information Provera is a potent progestational agent with very low toxicity. Depo-Provera is ideally suited to the patient with endometriosis in whom oestrogen or androgen treatment may be considered to offer too many drawbacks on grounds of intolerance or masculinisation.

The contraceptive effect of 150 mg i.m. Depo-Provera lasts approximately 90 days.

A 150 mg per ml strength of Depo-Provera is also available in a 3.3 ml vial for alternative indications.

Product licence number 0032/0056.

DEPO-PROVERA* ▼

Presentation White sterile aqueous suspension. Each 1 ml contains 150 mg medroxyprogesterone acetate.

Uses Progestogen. A proportion of certain classes of malignant tumours have been shown to respond to hormone administration or ablative hormonal surgery. These classes include carcinoma of endometrium, carcinoma of kidney and carcinoma of breast. Depo-Provera has been shown to be effective as adjunctive therapy in carcinoma of endometrium, carcinoma of kidney and carcinoma of breast in post-menopausal women.

Dosage and administration Doses should be given intramuscularly, deep into the gluteal muscle.

Endometrial or renal carcinoma: The normal initial dose lies in the range 400–1,000 mg per week, but doses in excess of 1,000 mg per day have been used without serious adverse effects. If improvement is noted within a few weeks or months and the disease appears stabilised, it may be possible to maintain the improvement with as little as 400 mg per month.

Breast carcinoma: The recommended schedule is 500 mg/day for 28 days. The patient should then be placed on a maintenance schedule of 500 mg twice weekly as long as the patient is responding to treatment.

Progression of disease at any time during therapy indicates treatment with Depo-Provera should be terminated, although response to hormonal therapy may not be evident until after at least 8–10 weeks of therapy.

Where large doses are being administered consideration should be given to dividing the dose between two separate sites.

Contra-indications, warnings, etc

Contra-indications: Depo-Provera is contra-indicated in thrombophlebitis or a history of pulmonary embolism and liver dysfunction or disease.

Warning: In the treatment of carcinoma of breast occasional cases of hypercalcaemia have been reported.

Precautions: Animal studies show that Depo-Provera possesses adrenocortical activity. This has also been reported in man, therefore patients receiving large doses continuously and for long periods should be observed closely. The administration of large doses to pregnant women has resulted in the observation of some instances of female foetal masculinisation.

Side-effects: Depending on the volume injected, some patients may be expected to show undesirable sequelae at the site of injection such as residual lump, change colour of skin or sterile abscess. Other adverse reactions noted, particularly with large doses, have been:

Breast: In a few instances breast tenderness or galactorrhoea has occurred.

Psychic: An occasional patient has experienced nervousness, insomnia, somnolence, fatigue or dizziness.

Skin and mucous membranes: Sensitivity reactions ranging from pruritus, urticaria, angioneurotic oedema to generalised rash and anaphylaxis have occasional been reported. Acne, alopecia or hirsutism have been reported in a few cases.

Gastro-intestinal: Rarely nausea has been reported. Jaundice has been noted in a few instances.

Overdosage: No positive action is required to be taken.

Pharmaceutical precautions Store at room temperature and protect from freezing. Do not mix with other agents. Discard any remaining contents after use.

Legal category POM.

Package quantities 3.3 ml vial.

Further information Provera is a potent progestational agent with very low toxicity. A 50 mg/ml strength of Depo-Provera is also available in 1, 3 and 5 ml vials for alternative indications.

Product licence number 0032/0082.

HALCION* ▼

Presentation Blue flat oval tablets scored on one side and imprinted Upjohn 17 on the other side, each containing 0.25 mg triazolam.

Pale lavender flat oval tablets scored on one side and imprinted Upjohn 10 on the other, each containing 0.125 mg triazolam (for geriatric use).

Uses Halcion is a hypnotic which can be administered effectively for short-term and intermittent use in patients with recurring insomnia and poor sleeping habits. As with all hypnotics, long-term use is not recommended. Halcion may also be used in the treatment of insomnia associated with anxiety states and emotional distress.

Dosage and administration The usual dose for adults is 0.25 mg before retiring. The initial dose for geriatric patients is 0.125 mg and this may be increased to 0.25 mg if necessary.

Contra-indications, warnings, etc

Contra-indications: Halcion is contra-indicated in patients with known hypersensitivity to benzodiazepines.

Warnings: As with all medicaments of this type, avoidance of alcohol in patients receiving Halcion is recommended since the individual response cannot be foreseen. Similarly, during its period of activity, Halcion may modify patients' reactions (driving, operating machinery) to a varying extent depending on dosages and individual susceptibility.

Precautions: In elderly and/or debilitated patients, it is recommended that treatment with Halcion be initiated at 0.125 mg to decrease the possibility of development of over-sedation, dizziness, or impaired co-ordination. Halcion is to be combined with other drugs having

known hypnotic properties or CNS depressant effects, consideration should be given to potential additive effects.

As with other benzodiazepines, caution should be exercised if the patient is in a depressed state or reveals evidence of a latent depression since these conditions may be intensified by hypnotic agents.

The usual precautions should be observed in patients with impaired renal or hepatic function.

Safety for use during pregnancy has not yet been established.

Use in Nursing Mothers: Human studies have not been performed; however, studies in rats have indicated that Halcion and its metabolites are secreted in milk. Therefore administration to nursing mothers is not recommended.

Safety and effectiveness in patients under the age of 8 have not been established.

Side-effects: Drowsiness, dizziness, light-headedness, confusion and impaired co-ordination have occurred. The incidence and severity of these pharmacological effects are generally dose-related. Severe sedation and impaired co-ordination are indicative of drug intolerance or overdose.

Adverse reactions: Headache has occurred in some patients. Less frequent adverse reactions which have been reported are taste alterations and depression. Adverse reactions which have been reported rarely are pruritus, skin rash, blurred vision, hiccups, palpitations, epigastric discomfort, diarrhoea, and burning eyes. As with other benzodiazepines, occasional cases of anterograde amnesia have been reported. Abnormal psychological reactions to most benzodiazepines have been reported. Rare behavioural adverse effects include paradoxical aggressive outbursts, excitement and the uncovering of depression with suicidal tendencies.

Overdose: Manifestations of Halcion overdose include extensions of its pharmacological activity, namely somnolence and hypnosis. As in all cases of drug overdose, respiration, pulse, and blood pressure should be monitored and supported by general measures when necessary. Immediate gastric lavage should be performed. Intravenous fluids should be administered and an adequate airway maintained.

Experiments in animals have indicated that cardiovascular collapse can occur with massive intravenous doses of Halcion (over 100 mg/kg, > 20,000 times the maximum daily human dose). This could be reversed with positive mechanical respiration and the intravenous infusion of noradrenaline or metaraminol. Other animal experiments have suggested that haemodialysis and forced diuresis are probably of little value.

Pharmaceutical precautions Keep container tightly closed and protect from light.

Legal category POM.

Package quantities Bottles of 100 and 500.

Further information Halcion has a relatively short biological half-life as do its metabolites. It does not cause enzyme induction in man. The preponderance of data from sleep laboratory studies indicates that there would be no significant tolerance development, drug accumulation or withdrawal effects after cessation of treatment.

Product licence numbers

0.25 mg Tablet 0032/0058

0.125 Tablet 0032/0063

KAOPTECTATE*

Presentation Off-white suspension. Each 5 ml contains 1.03 g Kaolin BP in an aromatic and carminative vehicle.

Uses Antidiarrhoeal.

Diarrhoea of non-specific origin.

Dosage and administration Oral.

Adult: 30–120 ml after each bowel movement.

Children: 5 ml or more according to age after each bowel movement.

Contra-indications, warnings, etc

Contra-indications: Intestinal obstruction.

Warnings: None.

Precautions: None.

Side-effects: None.

Overdose: None.

Pharmaceutical precautions None.

Legal category GSL.

Package quantities Bottles of 500 ml.

Further information Nil.

Product licence number 0032/5040.

LINCOCIN*

Presentation Capsules (dark blue/light blue) containing 500 mg lincomycin as lincomycin hydrochloride.

Colourless sterile solution. Contains 300 mg per ml lincomycin as lincomycin hydrochloride.

Red syrup with raspberry flavour. Each 5 ml contains 250 mg lincomycin as lincomycin hydrochloride.

Uses Antibacterial.

Lincomycin is indicated in serious infections caused by susceptible Gram-positive organisms, staphylococci (both penicillinase and non-penicillinase producing), streptococci (except *Strep. faecalis*) and pneumococci. It is also indicated (given parenterally) in serious infections caused by susceptible anaerobic pathogens.

Lincomycin does not penetrate the blood/brain barrier in therapeutically effective quantities.

Dosage and administration Oral. Intramuscular. Intravenous.

Oral:

Capsules: Adults: Moderately severe infections, 1 capsule three times a day. Severe infection, 1 capsule four times a day.

Syrup 250: Children 1–6 months: 1.25–2.5 ml three times a day.

6 months to 2 years: 2.5–5 ml three times a day.

3–9 years: 2.5–5 ml four times a day.

10–12 years: 5–10 ml four times a day.

For optimal absorption, it is recommended that nothing be given by mouth except water for a period of one or two hours before and after oral administration.

Intramuscular: Sterile solution. Injections should be made deeply into the gluteal muscles.

Adults: Moderately severe infection, 600 mg (2 ml) every 24 hours. Severe infection, 600 mg (2 ml) every 12 hours or more often.

Children (over 1 month): Moderately severe infection,

10 mg/kg/every 24 hours. Severe infection, 10 mg/kg/every 12 hours or more often.

Intravenous: Sterile solution.

Adults: 600 mg (2 ml) every 8–12 hours. Administer as an infusion in 250 ml or more 5% glucose or normal saline over a period of not less than one hour.

Children (over 1 month): 10–20 mg/kg/day in 2 or 3 equal doses at 8- or 12-hour interval. Administer as an infusion as above.

Treatment for infections caused by β -haemolytic streptococci should be continued for at least 10 days to guard against subsequent rheumatic fever or glomerulonephritis.

Contra-indications, warnings, etc

Contra-indications: Patients with a history of sensitivity to lincomycin. Although cross-sensitisation to clindamycin (Dalacin C) has not been demonstrated, it is recommended that Lincocin is not used in patients who have exhibited sensitivity to clindamycin.

Warnings: Lincocin should only be used in the treatment of serious infections. In considering the use of the product the practitioner should bear in mind the type of infection and the potential hazard of the diarrhoea which may develop since cases of colitis have been reported. The appearance of marked diarrhoea should be regarded as an indication that the product should be discontinued immediately.

Studies indicate a toxin(s) produced by *Clostridia* (especially *Clostridium difficile*) is the principal direct cause of antibiotic-associated colitis. These studies also indicate that this toxigenic *Clostridium* is usually sensitive in vitro to vancomycin. When 125 mg to 500 mg of vancomycin is administered orally four times a day, there is a rapid observed disappearance of the toxin from faecal samples and a coincident clinical recovery from the diarrhoea.

Precautions: Pending further clinical experience Lincocin is not recommended in the newborn, in the prophylaxis of a recurrence of rheumatic fever, and in patients with pre-existing kidney, liver, endocrine or metabolic disease, unless special clinical circumstances so indicate. Lincomycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore it should be used with caution in patients receiving such agents. In the case of renal impairment, a reduced dosage regime should be used. During prolonged Lincocin therapy, periodic liver function studies and blood counts should be performed. Although there is no evidence of ill effects in either the mother or foetus, Lincocin should be used with customary caution in pregnant women.

The long-term use of lincomycin may give rise to an overgrowth of non-susceptible organisms, particularly yeasts.

Side-effects: Lincocin is well tolerated. With oral administration, gastro-intestinal side-effects have been encountered, such as loose stools or diarrhoea, or colitis (see 'Warnings'), nausea, vomiting and abdominal cramps. Other minor side-effects have been observed infrequently. Leucopenia (neutropenia), agranulocytosis and hypersensitivity reactions have been reported on rare occasions.

Overdosage: In cases of overdosage that may have led to adverse reactions therapy should be discontinued and the usual emergency treatment, including corticosteroids, adrenaline and antihistamines, instituted. The

serum biological half-life of lincomycin is 5.4 ± 1 hr. Lincomycin cannot be readily removed from the blood by dialysis or peritoneal dialysis.

Pharmaceutical precautions Storage temperature for capsules should not exceed 30°C. Lincocin Sterile Solution should be protected from light and freezing and stored at under 30°C.

Dilution of the Syrup 250 should be carried out using Syrup BP.

Legal category POM.

Package quantities Capsules in bottles of 12 and 100.

Syrup 250, Bottles of 100 ml.

Sterile solution 2 ml and 10 x 2 ml ampoules.

Further information Lincomycin exhibits cross-resistance with clindamycin. When tested by in vitro methods, some staphylococcal strains originally resistant to erythromycin rapidly developed resistance to lincomycin.

Product licence numbers

Capsules 0032/5008

Solution 0032/5009

Syrup 0032/5010

LONITEN* ▼

Presentation Round white biconvex tablets with the dosage strength imprinted on one side and scored on the other with a U on either side of the score.

Each tablet contains 2.5 mg, 5 mg or 10 mg minoxidil.

Uses Loniten is indicated for the treatment of severe hypertension.

It should not be used as the sole agent to initiate therapy. It is a peripheral vasodilator and should be given in conjunction with a diuretic, to control salt and water retention, and a beta-adrenergic blocking agent, or appropriate substitute, to control reflex tachycardia.

Dosage and administration *Adults and patients over*

12 years of age: An initial daily dose of 5 mg, which may be given as a single or divided dosage is recommended. This dose may first be increased to 10 mg daily and subsequent increases should be by increments of 10 mg in the daily dose. Dosage adjustments should be made at intervals of not less than three days, until optimum control of blood pressure is achieved. It is seldom necessary to exceed 50 mg per day although in exceptional circumstances, doses up to 100 mg per day have been used. Twice-daily dosage is satisfactory. Where diastolic pressure reduction of less than 30 mm Hg is required, once-daily dosing has been reported as effective.

Dosage requirements may be lower in dialysis patients.

Children: For patients of 12 years of age or under, the initial dose should be 0.2 mg per kilogram given as a single or divided daily dosage. Incremental increases of 0.1–0.2 mg per kilogram in the daily dose are recommended at intervals of not less than three days until optimum blood pressure control has been achieved or the maximum daily dose of 1.0 mg/kg has been reached.

Rapid reduction of blood pressure: Rapid reduction of blood pressure can be achieved using continuous blood pressure monitoring and incremental doses of 5 mg every six hours.

Concomitant antihypertensive therapy: It is recommended that, where possible, antihypertensive therapy, other than a beta-adrenergic blocking agent and a diuretic, be discontinued before Loniten treatment is started. It is recognised that some antihypertensive agents should not be abruptly discontinued. These drugs could be gradually discontinued during the first week of Loniten treatment.

Loniten causes sodium retention and if used alone can result in several hundred milli-equivalents of salt being retained together with a corresponding volume of water. Therefore, in all patients who are not on dialysis, sodium must be given in conjunction with a diuretic in sufficient dosage to maintain salt and water balance. Examples of the daily dosages of diuretics commonly used when starting therapy with Loniten include:

1. Hydrochlorothiazide (100 mg) – or other thiazides of equivalent effective dosage.
2. Chlorthalidone (100 mg).
3. Furosemide (80 mg).

If excessive water retention results in a weight gain of more than 3 pounds when a thiazide or chlorthalidone is being used, diuretic therapy should be supplemented with spironolactone or changed to furosemide, the dosage of which may be increased in accordance with the patient's requirements. Diuretic dosage in children could be proportionally less in relation to weight.

Patients will require a sympathetic nervous system depressant to limit a Loniten-induced rise in heart rate. The preferred agent is a beta-blocker equivalent to an adult propranolol dosage of 80–160 mg/day. Higher doses may be required when pre-treated patients have an increase in heart rate exceeding 20 beats per minute when simultaneous introduction causes an increase exceeding 10 beats per minute. When beta-blockers are contra-indicated, alternatives such as methyldopa may be used instead and should be started 24 hours prior to Loniten.

Contra-indications, warnings, etc

Contra-indications: Loniten is contra-indicated in patients with a pheochromocytoma.

Warnings: If used alone, Loniten can cause a significant retention of salt and water leading to positive physical signs such as oedema, and to clinical deterioration of some patients with heart failure. Diuretic treatment alone, or in combination with restricted salt intake is, therefore, necessary for all patients taking Loniten.

Patients who have had myocardial infarction should not be treated with Loniten after a stable post-infarction state has been established.

The physician should bear in mind that if not controlled by sympathetic suppressants, the rise in cardiac rate and output that follows the use of potent vasodilators may induce anginal symptoms in patients with undiagnosed coronary artery disease, or may aggravate pre-existing angina pectoris.

The effect of Loniten may be additive to concurrent antihypertensive agents. The interaction of Loniten with sympathetic-blocking agents such as guanethidine or ethanidine may produce excessive blood pressure reduction and/or orthostasis.

Precautions: The safety of Loniten in pregnancy remains to be established.

Hypertrichosis occurs in most patients treated with Loniten and all patients should be warned of this possibility before starting therapy. Spontaneous reversal

to the pre-treatment state can be expected one to three months after cessation of therapy.

Soon after starting Loniten therapy approximately 60% of patients exhibit ECG alterations in the direction and magnitude of their T waves. Large changes may encroach on the ST Segment, unaccompanied by evidence of ischaemia. These asymptomatic changes usually disappear with continuing Loniten treatment. The ECG reverts to the pre-treatment state if Loniten is discontinued.

Pericardial effusion has been detected in patients treated with a Loniten-containing regime. A cause and effect relationship has not been established. Most effusions have either been present before Loniten was given, or occurred among uraemic patients. However, it is suggested that Loniten-treated patients should be periodically monitored for signs or symptoms of pericardial effusion and appropriate therapy instituted if necessary.

Salt and water retention in excess of 2 to 3 pounds may diminish the effectiveness of Loniten. Patients should therefore, be carefully instructed about compliance with diuretic therapy and a detailed record of body weight should be maintained.

Side-effects: Most patients receiving Loniten experience a diminution of pre-existing side-effects attributable to their disease or previous therapy. New events or side-effects likely to increase include peripheral oedema, associated with or independent of weight gain; increases in heart rate; hypertrichosis; and a temporary rise in creatinine and blood urea nitrogen. Gastro-intestinal intolerance, rash and breast tenderness are infrequently reported side-effects of Loniten therapy.

Overdosage: If exaggerated hypotension is encountered, it is most likely to occur in association with residual sympathetic nervous system blockade (guanethidine-like effects or alpha-adrenergic blockade). Recommended treatment is intravenous administration of normal saline. Sympathomimetic drugs, such as nor-adrenaline or adrenaline, should be avoided because of their excessive cardiac-stimulating action. Phenylephrine, angiotensin II and vasopressin, which reverse the effect of Loniten, should be used only if inadequate perfusion of a vital organ is evident.

Pharmaceutical precautions None.

Legal category POM.

Package quantities 2.5 mg, 5 mg, and 10 mg Loniten tablets supplied as bottles of 100.

Further information Loniten is a potent vasodilator which probably exerts its action after binding to the smooth muscle of the blood vessel wall. At least 90% of an oral dose is rapidly absorbed and the average plasma half-life in man is 4.2 hours. The clinical duration of action is up to 72 hours. Approximately 90% of administered drug is metabolised and excreted in the urine within 24 hours. Drug-related materials can be removed by dialysis.

Product licence numbers

2.5 mg	0032/0064
5 mg	0032/0065
10 mg	0032/0066

MEDRONE*

Presentation Oval double-scored white tablet 4 mg methylprednisolone; oval double-scored pink tablet

2 mg methylprednisolone; oval double-scored white tablet marked 'Upjohn 73' 16 mg methylprednisolone.

Uses Anti-inflammatory agent.

Medrone is indicated for conditions requiring glucocorticoid activity, including collagen diseases, allergic diseases, certain dermatological conditions, acute and chronic ocular inflammatory diseases, certain leukaemias and lymphatic neoplastic diseases, ulcerative colitis, nephrosis, and various metabolic diseases responsive to corticosteroid treatment.

Dosage and administration Oral.

The dosage recommendations shown in the table are suggested initial daily doses and are intended as guides. The average total daily dose recommended should be given in 4 equally divided doses and given with meals and a snack at bedtime (excepting in alternate-day therapy when the minimum effective daily dose is doubled and given every other day at 8.00 a.m.)

The initial suppressive dose level is continued until a satisfactory clinical response is obtained, a period usually of three to seven days in the cases of rheumatic diseases (except for acute rheumatic carditis), allergic conditions affecting the skin or respiratory tract, and ocular inflammatory diseases. If a satisfactory response is not obtained in seven days, re-evaluation of the case to confirm the original diagnosis should be made. As soon as a satisfactory clinical response is obtained, the daily dose should be reduced gradually, either to termination of treatment in the case of acute conditions (e.g. seasonal asthma, exfoliative dermatitis, acute ocular inflammations) or to the minimal effective maintenance dose level in the case of chronic conditions (e.g. rheumatoid arthritis, systemic lupus erythematosus, bronchial asthma, atopic dermatitis). In chronic conditions, and in rheumatoid arthritis especially, it is important that the reduction in dosage from initial to maintenance dose levels be accomplished slowly. Decrements of not more than 2 mg at intervals of 7–10 days are suggested. In rheumatoid arthritis, maintenance steroid therapy should be at the lowest possible level.

In general, dosage for children should be based upon clinical response and is at the discretion of the clinician.

In alternate-day therapy, the minimum daily corticoid requirement is doubled and administered as a single dose every other day at 8.00 a.m.

Contra-indications, warnings, etc

Contra-indications: Medrone is contra-indicated in patients with latent, healed and active tuberculosis, Cushing's syndrome, peptic ulcer, acute psychoses, herpes simplex keratitis, vaccinia and varicella.

Warnings: Because of its inhibitory effect on fibroplasia, Medrone may mask signs of infection and enhance dissemination of the infecting organism. All patients should be watched for such intercurrent infection, which must be brought under control by use of appropriate antibacterial measures. As a general rule the administration of the corticosteroid should not be discontinued suddenly, but tailed off over a period. In certain situations involving intercurrent infection the corticosteroid dosage may require to be stepped up to counter the effects of shock.

Precautions: The presence of diabetes, osteoporosis, chronic psychotic reactions, predisposition to thrombophlebitis, hypertension, congestive heart failure and renal insufficiency necessitate the carefully controlled use of methylprednisolone. While therapy with cortico-

steroids during pregnancy does not appear to be contraindicated, caution is recommended, particularly during the first trimester. Neonates of mothers who have received such therapy during pregnancy should be observed for signs of hypoadrenalism and appropriate measures instituted if such signs are present.

Medrone should be used with caution in young children as corticosteroids are known to interfere with normal growth pattern.

Side-effects: Side-effects associated with the use of corticosteroids may be observed, including Cushing's syndrome, moon facies, supraclavicular pads of fat, hirsutism, striae and acne, hyperglycaemia, osteoporosis, peptic ulceration, hypertension, psychic disturbance, posterior subcapsular cataracts, suppression of growth in children, subcutaneous and cutaneous

<i>Indications</i>	<i>Recommended initial daily dosage</i>
<i>Collagen diseases</i>	
Rheumatoid arthritis	
Severe	12–16 mg
Moderately severe	8–12 mg
Moderate	4–8 mg
Children	4–8 mg
Systemic lupus erythematosus	20–96 mg
Acute rheumatic fever	1.1 mg per kg of body weight per day until ESR normal for one week
<i>Allergic diseases</i>	
Severe seasonal asthma	16–40 mg
Severe pollinosis	16–40 mg
Exfoliative dermatitis	16–40 mg
Contact dermatitis	16–40 mg
Severe intrinsic asthma	12–40 mg
Intractable allergic rhinitis	12–40 mg
Generalised atopic dermatitis	12–40 mg
Generalised infantile eczema	8–12 mg
<i>Ocular inflammatory diseases (of the posterior segment)</i>	
Acute	12–40 mg
Chronic	12–40 mg
<i>Haematological disorders</i>	
Acute granulocytic leukaemia	16–96 mg
Acute monocytic leukaemia	16–96 mg
Chronic lymphocytic leukaemia	16–96 mg
Thrombocytopenia	16–96 mg
Haemolytic anaemia	16–96 mg
	In some cases, doses of the order of 300 mg have been employed to establish control
<i>Miscellaneous diseases</i>	
Adrenogenital syndrome	4–12 mg
Ulcerative colitis	16–60 mg
Nephrosis	20–60 mg (for 10–14 days or until diuresis ensues)
Refractory congestive heart failure or cirrhosis of the liver with ascites	16–24 mg Medrone must be administered in conjunction with an effective diuretic

atrophy, sterile abscess, vertigo, weakness, myopathy, thrombo-embolism, pancreatitis, exophthalmos and headache.

Overdosage: Administration of Medrone should not be discontinued abruptly but tapered off over a period of time. Appropriate action should be taken to alleviate the symptoms produced by any side-effect that may become apparent. It may be necessary to support the patient with corticosteroids during any further period of trauma occurring within two years of overdosage.

Pharmaceutical precautions No special precautions are required.

Legal category POM.

Package quantities 2 and 4 mg tablets in bottles of 30 and 100.

16 mg tablets in bottles of 14.

Further information Medrone has achieved a clinically acceptable split between glucocorticoid effect and undesired mineralocorticoid effect. Weight for weight, methylprednisolone has five times the anti-inflammatory activity of hydrocortisone but has little tendency to cause salt and water retention. The 16 mg tablet gives opportunity for use of alternate-day therapy in long-term use in chronic conditions.

Medrone Tablets 2 mg	0032/5017
Medrone Tablets 4 mg	0032/5018
Medrone Tablets 16 mg	0032/0024

MEDRONE* ACNE LOTION

Presentation A pale yellow emulsion containing the following active ingredients (% w/v):

Methylprednisolone acetate	0.25%
Sulphur (from colloidal sulphur)	5%
Aluminium chlorhydroxide complex	10%

Uses For topical application in the treatment of acne vulgaris, rosacea and seborrhoeic dermatitis.

Dosage and administration Apply sparingly once or twice a day. Shake well before use.

Contra-indications, warnings, etc

Contra-indications: Contra-indications, warnings and precautions are those which normally apply to topical corticosteroids.

Warnings: Contact with the eyes should be avoided. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Side-effects: Medrone Acne Lotion is designed to produce a drying effect on the skin. Should excessive drying or peeling of the skin occur, the frequency of application should be reduced. Other less frequently occurring side-effects include erythema, itching, burning, hyperpigmentation and occasional hypersensitivity or allergic reactions.

Overdosage: Unlikely to produce serious toxicity unless taken in very large amounts. Ingestion of 30 grams of aluminium chlorhydroxide complex has produced serious toxicity and an emetic should be considered, together with supportive therapy in such cases of massive ingestion.

Pharmaceutical precautions Protect from freezing. The lotion should not be diluted and should be dispensed in the original container.

Legal category POM.

Package quantities 25 ml and 75 ml polythene bottles.

Further information If infection is present the companion product Neo-Medrone Acne Lotion (which contains neomycin) is available.

Product licence number 0032/0041.

NEO-CORTEF* EYE/EAR DROPS NEO-CORTEF* EYE/EAR OINTMENT

Presentation White, sterile aqueous suspension containing hydrocortisone acetate 15 mg (1.5%) and neomycin sulphate 5 mg (0.5%) per ml. Yellow soft ointment containing hydrocortisone acetate 15 mg (1.5%) and neomycin sulphate 5 mg (0.5%) per gram.

Uses Inflammatory and infective ear and eye conditions susceptible to the action of the neomycin/hydrocortisone combination.

Such conditions include:

Eye: Phlyctenular keratoconjunctivitis, non-specific superficial keratitis, blepharitis, acne rosacea keratitis, allergic conjunctivitis, deep keratitis, sclerokeratitis, episcleritis, post-operative keratitis, post-operative and post-traumatic uveitis.

Ear: Otitis externa.

Dosage and administration *Drops:* Eye: 1 or 2 drops three or more times daily.

Ear: 1 or 2 drops in the external ear canal three or more times daily.

Ointment: Applications should be made one or more times daily.

Contra-indications, warnings, etc

Contra-indications: The presence of tuberculous, fungal and acute purulent infections of the eye, viral infections of the eye such as herpes simplex, vaccinia and varicella, and history of sensitivity to neomycin.

Warnings: Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in the first trimester of pregnancy, i.e. in large amounts or for prolonged periods. In infants, long-term continuous topical corticosteroid therapy, with or without occlusion, should be avoided due to possible adrenal suppression.

Precautions: Because of its inhibitory effect on fibroplasia, hydrocortisone may mask signs of infection and enhance dissemination of an infecting organism.

Side-effects: An incidence of sensitivity to neomycin has been reported in topical applications containing this antibiotic.

Overdosage: Unlikely to produce any serious toxic effects if ingested.

Pharmaceutical precautions None.

Legal category POM.

Package quantities Neo-Cortef Eye/Ear Drops supplied as 5 ml and 10 ml plastic squeeze bottles with applicator tip.

Neo-Cortef Eye/Ear Ointment is supplied in tubes of 3.9 g with applicator tip.

Further information Nil.

Product licence numbers

Neo-Cortef Eye/Ear Drops 0032/5026
Neo-Cortef Eye/Ear Ointment 0032/5027

NEO-CORTEF* OINTMENT AND LOTION

Presentation *Ointment*: Off-white, greasy-based ointment containing 10 mg (1%) or 25 mg (2.5%) hydrocortisone acetate and 5 mg (0.5%) neomycin sulphate per gram.

Lotion: Milky-white lotion containing 10 mg (1%) hydrocortisone acetate and 5 mg (0.5%) neomycin sulphate per millilitre.

Uses Anti-inflammatory and antibacterial.

Neo-Cortef Ointment and Lotion are indicated for infected dermatoses and allergic skin conditions complicated by infections caused by organisms susceptible to the action of neomycin.

Dosage and administration *Topical application*: Apply a small amount one to three times daily.

Contra-indications, warnings, etc

Contra-indications: The presence of tuberculous, fungal or viral infections such as herpes simplex, vaccinia and varicella, and a history of sensitivity to neomycin.

Warnings: In infants, long-term continuous topical corticosteroid therapy, with or without occlusion, should be avoided due to the risk of possible adrenal suppression. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in the first trimester of pregnancy, i.e. in large amounts or for prolonged periods.

Precautions: Because of its inhibitory effect on fibroplasia, hydrocortisone may mask signs of infection and enhance dissemination of an infecting organism.

Side-effects: An incidence of sensitivity to neomycin has been reported in topical applications containing this antibiotic.

Overdosage: Unlikely to produce any serious toxic effects if ingested.

Pharmaceutical precautions Store at room temperature.

Legal category POM.

Package quantities Neo-Cortef Ointment 1% in tubes of 5 g and 20 g, 2.5% in tubes of 20 g.

Neo-Cortef Lotion 1% in 15 ml plastic squeeze bottles.

Further information Nil.

Product licence numbers

Neo-Cortef Ointment 1% 0032/5030
Neo-Cortef Ointment 2.5% 0032/5031
Neo-Cortef Lotion 1% 0032/5029

NEO-MEDRONE* ACNE LOTION

Presentation Pale yellow lotion containing suspension of methylprednisolone acetate 2.5 mg, neomycin

sulphate 2.5 mg, sulphur 50 mg, aluminium chlor hydroxide complex 100 mg per ml of aqueous base.

Uses Neo-Medrone Acne Lotion is indicated for the treatment of acne vulgaris, rosacea and seborrhoeic dermatitis.

Dosage and administration Topical application to the affected area sparingly once or twice a day. Shake well before using.

Contra-indications, warnings, etc

Contra-indications: Contra-indications, warnings and precautions are those which normally apply to topical corticosteroids, and the product is contra-indicated in patients with a history of sensitivity to neomycin.

Warnings: Contact with the eyes should be avoided. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Side-effects: Neo-Medrone Acne Lotion is designed to produce a drying effect on the skin. Should excessive drying or peeling of the skin occur, the frequency of application should be reduced. Other less frequently occurring side-effects include erythema, itching, burning, hyperpigmentation and occasional hypersensitivity or allergic reactions.

Overdosage: Unlikely to produce serious toxicity unless taken in very large amounts. Ingestion of 30 grams of aluminium chlorhydroxide complex has produced serious toxicity and an emetic should be considered, together with supportive therapy in such cases of massive ingestion.

Pharmaceutical precautions Store at room temperature. Protect from freezing.

Legal category POM.

Package quantities 25 ml and 75 ml plastic squeeze bottles.

Further information Neo-Medrone Acne Lotion should be used as an adjunct to usual skin cleansing or dietary recommendations.

Product licence number 0032/5032.

ORTHOXICOL* SYRUP

Presentation Syrup containing Orthoxine (methoxyphenamine hydrochloride) 338 mg, codeine phosphate 219 mg and sodium citrate 6.5 g per 100 ml. The rec syrup has a characteristic cherry flavour.

Uses Cough syrup.

Indicated in cough associated with the common cold bronchitis, bronchial asthma, tracheitis and laryngitis.

Dosage and administration Oral.

Adults and Children over 12 years: 5–10 ml every three to four hours as required.

Children: 6–12 years: 2.5–5 ml repeated every four hours as required

Contra-indications, warnings, etc

Contra-indications: A history of sensitisation to codeine or an adverse reaction to Orthoxine.

Warnings: The stated dose should not be exceeded.

Precautions: Whilst the dose of Orthoxine given is low, the usual precautions to the use of systemic sympathomimetic therapy should be observed.

Side-effects: In the occasional patient some dryness of the mouth and drowsiness may be experienced.

Overdosage: Dosage should be stopped and appropriate action taken to combat codeine overdosage.

Pharmaceutical precautions Store at room temperature.

Where dilution is required use Syrup BP.

Legal category P.

Package quantities Bottles of 500 ml.

Further information Orthoxicol Syrup depresses the cough reflex, liquefies tenacious mucus and affords some bronchodilatation.

Product licence number 0032/5041.

ORTHOXINE* HYDROCHLORIDE

Presentation White, scored tablet marked 'U' on opposite side, each tablet containing methoxyphenamine hydrochloride 100 mg.

Uses Sympathomimetic bronchodilator. Indicated in bronchial asthma, allergic rhinitis, acute urticaria, gastrointestinal allergy, allergic headaches and nocturnal leg cramps.

Dosage and administration Oral.

Adults: 50–100 mg every three to four hours.

Children: 25–50 mg every four to six hours.

Contra-indications, warnings, etc

Contra-indications: A history of adverse reaction to Orthoxine.

Warnings: The stated dose should not be exceeded.

Precautions: Use with caution in patients with hypertension, hyperthyroidism, acute coronary disease, cardiac decompensation and diabetes mellitus.

Adverse reaction: The sympathomimetic amines in general have vasopressor and cardio-acceleratory activity and may also produce psychomotor stimulation with associated insomnia and anxiety. Orthoxine, at normal daily dose levels, up to 500 mg, is relatively free from these effects.

Side-effects: Drowsiness, mouth dryness, nausea and dizziness have been reported.

Overdosage: Dosage should be stopped and action to counter symptoms of sympathomimetic overstimulation instituted if needed.

Pharmaceutical precautions None.

Legal category P.

Package quantities Bottles of 100.

Further information Onset of bronchodilatation occurs about 30 minutes after an initial dose and FEV₁ usually improves over the course of the next four to six hours.

Product licence number 0032/5042.

PROSTIN E2* STERILE SOLUTIONS

Presentation Colourless sterile solutions in ampoules containing 1 mg/ml or 10 mg/ml dinoprostone, Prostaglandin E₂, in ethanol.

Uses Oxytocic agent.

Indications for Prostin E2 are: induction of labour, foetal death in utero, therapeutic termination of pregnancy, missed abortion and hydatidiform mole.

Presentation:

1. 0.75 ml ampoule of a 1 mg/ml solution of dinoprostone in ethanol – for induction of labour and foetal death in utero (intravenous).

2. 0.5 ml ampoule of a 10 mg/ml solution of dinoprostone in ethanol – for therapeutic termination of pregnancy, missed abortion and hydatidiform mole (intravenous).

3. 0.5 ml ampoule of a 10 mg/ml solution of dinoprostone in ethanol (plus a 50 ml vial of saline diluent) – for therapeutic termination of pregnancy (extra-amniotic).

Dosage and administration Prostin E2 Sterile Solution may be administered by two routes, intravenous or extra-amniotic, depending on dose form and indication as shown above. *In each case the ampoule contents must be diluted before use and full instructions on method of dilution and dosage are given on the package insert which should be consulted prior to initiation of therapy.* The following is a guide to dosage:

1. *Prostin E2 1 mg/ml solution (in ethanol). Intravenous for induction of labour:* Dilute with normal saline or 5% dextrose according to the package insert to produce a 1.5 mcg/ml solution. The 1.5 mcg/ml solution is infused at 0.25 mcg/minute for 30 minutes and then maintained or increased. Cases of foetal death in utero may require higher doses. An initial rate of 0.5 mcg/minute may be used with stepwise increases, at intervals of not less than one hour.

2. *Prostin E2 10 mg/ml solution (in ethanol). Intravenous for therapeutic termination of pregnancy, missed abortion and hydatidiform mole:* Dilute with normal saline or 5% dextrose according to package insert to produce a 5 mcg/ml solution. The 5 mcg/ml solution is infused at 2.5 mcg/minute for 30 minutes and then maintained or increased to 5 mcg/minute. The rate should be maintained for at least four hours before increasing further.

3. *Prostin E2 10 mg/ml solution (in ethanol). Extra-amniotic for therapeutic termination of pregnancy:* Dilute with the 50 ml of diluent provided according to the package insert to produce a 100 mcg/ml solution. The 100 mcg/ml solution is instilled via a 12–14 French-gauge Foley catheter. Initial instillation is 1 ml, then, dependent on uterine response, 1 or 2 ml usually at two-hour intervals.

Contra-indications, warnings, etc

Contra-indications: There are no absolute contra-indications to the use of Prostin E2. However, its use is not recommended in the following circumstances:

1. Where the patient is sensitive to prostaglandins.
2. For patients in whom oxytocic drugs are generally contra-indicated or where prolonged contractions of the uterus are considered inappropriate, such as: cases with a history of Caesarean section or major uterine surgery; cases in which major degrees of cephalopelvic disproportion may be present; cases in which foetal malpresentation is present; cases in which there is clinical

suspicion or definite evidence of pre-existing foetal distress; cases in which there is a history of difficult labour and/or traumatic delivery; grand multiparae with six or more previous term pregnancies; cases with a history of pelvic inflammatory disease.

3. In therapeutic termination of pregnancy where known pelvic infection exists, unless adequate prior treatment has been instituted.

4. The extra-amniotic route should not be employed in the presence of cervicitis or vaginal infections.

Warnings: There is some evidence in animals of a low order of teratogenicity, therefore, if abortion does not occur or is suspected to be incomplete as a result of prostaglandin therapy, the appropriate treatment for complete evacuation of the uterus should be instituted in all instances.

Since prostaglandins may potentiate the effect of oxytocin it is recommended that the use of these drugs simultaneously or in sequence be carefully monitored.

The products are available only to hospitals and clinics with specialised obstetric units and should only be used where 24-hour resident medical cover is provided.

Precautions: Caution should be exercised in the administration of Prostin E2 in patients with: (i) glaucoma or raised intra-ocular pressure; (ii) asthma or a history of asthma.

In addition, in labour induction, cephalopelvic relationships should be carefully evaluated before use of Prostin E2. During use, uterine activity, foetal status and the progression of cervical dilatation should be carefully monitored to detect possible evidence of undesired responses, e.g. hypertonus, sustained uterine contractions or foetal distress. In cases where there is a known history of hypertonic uterine contractility or tetanic uterine contractions, it is recommended that uterine activity and the state of the foetus should be continuously monitored throughout labour. The possibility of uterine rupture should be borne in mind where high-tone myometrial contractions are sustained.

Side-effects: Clinical studies have not revealed any life-threatening adverse reactions. The incidence of side-effects is directly dose-related.

Nausea, vomiting and diarrhoea have been reported as commonly encountered at dose levels required to induce therapeutic termination of pregnancy by the intravenous route; however, these side-effects are markedly less frequent with doses used by either the extra-amniotic route for therapeutic termination of pregnancy, or intravenously for induction of labour. Transient vasovagal symptoms, including flushing, shivering, headache and dizziness, have been recorded. On intravenous use of Prostin E2 local tissue irritation and erythema have occurred.

No evidence of thrombophlebitis has been recorded and local tissue erythema at the infusion site has disappeared within two to five hours after infusion. A temporary pyrexia and elevated WBC are not unusual, but both have reverted after termination of infusion. In extra-amniotic therapy the possibility of local infection must be considered and appropriate therapy initiated if necessary.

Overdosage: Treatment of overdosage must be, at this time, symptomatic, as clinical studies with prostaglandin antagonists have not progressed to the point where recommendations may be made. However, the following guidelines are recommended.

If evidence of excessive uterine activity or side-effects

appear, the rate of infusion should be decreased discontinued.

In cases of massive overdosage resulting in extreme uterine hypertonus appropriate obstetric procedures are indicated.

Pharmaceutical precautions Prostin E2 Sterile Solutions (in ethanol) must be refrigerated at 4°C. The should be diluted before use only with the diluent stated. Diluted solutions should be used within 24 hours (48 hours for extra-amniotic).

Legal category POM.

Package quantities

1. Pack containing 1 × 0.75 ml ampoule of Prostin E2 Sterile Solution 1 mg/ml (IV induction).

2. Pack containing 1 × 0.5 ml ampoule of Prostin E2 Sterile Solution 10 mg/ml (IV termination).

3. Pack containing 1 × 0.5 ml ampoule of Prostin E2 Sterile Solution 10 mg/ml plus 50 ml diluent (E termination).

Further information Oral Prostin E2 Tablets are also available for the induction of labour.

Product licence numbers

0.75 ml ampoule (1 mg/ml i.v.)	0032/0020
0.5 ml ampoule (10 mg/ml i.v.)	0032/0021
0.5 ml ampoule (10 mg/ml e.a.)	0032/0026

PROSTIN E2* TABLETS

Presentation Prostin E2 tablets are presented as white, roughly rectangular tablets embossed on one side to resemble the letter 'U'. Each tablet contains 0.5 mg dinoprostone.

Uses Oxytocic agent. Prostin E2 tablets are indicated for the induction of labour when there are no foetal or maternal contra-indications.

Dosage and administration The dosage of Prostin E2 must be adapted to the patient's response and should always be maintained at the lowest level which will produce satisfactory uterine response. All doses should be taken with a small glass of water.

An initial dose of 0.5 mg (1 tablet) should be given. Thereafter, doses should be given hourly. The usual dose will be 0.5 mg (1 tablet), but if uterine activity is inadequate, 1 mg (2 tablets) may be given hourly until such time as adequate uterine activity is established. Thereafter it may be possible to reduce the dosage to 0.5 mg (1 tablet) hourly. It is recommended that a total single dose of 1.5 mg (3 tablets) not be exceeded.

Contra-indications, warnings, etc

Contra-indications: There are no absolute contra-indications to the use of Prostin E2. However, its use is not recommended in the following circumstances:

1. Where the patient is sensitive to prostaglandins.
2. For patients in whom oxytocic drugs are generally contra-indicated or where prolonged contractions of the uterus are considered inappropriate, such as:

Cases with a history of Caesarean section or major uterine surgery;

Cases in which major degrees of cephalopelvic disproportion may be present;

Cases in which there is clinical suspicion or definite evidence of pre-existing foetal distress;

Cases in which there is a history of difficult labour and/or traumatic delivery;

Grand multiparae with six or more previous term pregnancies.

3. Cases with a history of pelvic inflammatory disease.

Warnings: Since it has been found that prostaglandins may potentiate the effect of oxytocin, it is recommended that these drugs should not be used together, and, if used in sequence, that the patient's uterine activity should be carefully monitored.

The product is available only to hospitals, and clinics with specialised obstetric units and should only be used where 24-hour resident medical cover is provided.

Precautions: Caution should be exercised in the administration of Prostin E2 tablets for the induction of labour in patients with: (i) glaucoma or raised intra-ocular pressure; (ii) asthma or a history of asthma. In addition, labour induction, cephalopelvic relationships should be carefully evaluated before use of Prostin E2. During use, uterine activity, foetal status, and the progression of cervical dilatation should be carefully monitored to detect possible evidence of undesired responses, e.g. hypertonus, sustained uterine contractions, or foetal stress. In cases where there is a known history of hypertonic uterine contractility or tetanic uterine contractions, it is recommended that uterine activity and the state of the foetus should be continuously monitored throughout labour. The possibility of uterine rupture should be borne in mind where high-tone myometrial contractions are sustained.

Side-effects: Clinical studies have not revealed any life-threatening adverse reactions. The incidence of side-effects is directly dose-related. Nausea, vomiting and diarrhoea have been noted following oral administration of Prostin E2, but have seldom been severe enough to necessitate discontinuation of medication.

Verdosage: Uterine hypertonus or unduly severe uterine contractions have rarely been encountered, but might be anticipated to result from overdosage. In the rare instance where temporary discontinuation of therapy is not effective in reversing foetal distress or uterine hypertonus, prompt delivery is indicated. Treatment of overdosage must be, at this time, symptomatic, since clinical studies with prostaglandin antagonists have not progressed to the point where recommendations may be made. It is currently believed that vomiting produced by overdosage may act as a self-limiting factor in protecting the patient.

Pharmaceutical precautions Prostin E2 tablets have a shelf-life of two years when stored at 4°C. Store in a refrigerator. The tablets should be used within three months of opening the bottle.

Legal category POM.

Package quantities Prostin E2 tablets are packed in bottles of 10.

Further information The exact mode of action of the prostaglandins is not yet completely understood. Prostin E2 has been shown to have a local action on isolated uterine musculature and clinically its main action is oxytocic. However, unlike other oxytocics, Prostin E2 exhibits the capacity of the prostaglandins to influence uterine activity at any stage of gestation. Prostin E2 does not exhibit an antidiuretic effect. Other Prostin E2 dose forms are available for induction of labour and foetal death in utero (intravenous route), therapeutic termination of pregnancy (intravenous and extra-amniotic

routes), missed abortion and hydatidiform mole (intravenous route).

Product licence number 0032/0040.

PROSTIN E2* VAGINAL TABLETS

Presentation Prostin E2 Vaginal Tablets are presented as white biconvex capsule-shaped tablets debossed with 'UPJOHN' and '715' on one side. Each tablet contains 3 mg dinoprostone.

Uses Oxytocic. Prostin E2 Vaginal Tablets are indicated for the induction of labour, especially in patients with favourable induction features, when there are no foetal or maternal contra-indications.

Dosage and administration One tablet (3 mg) to be inserted high into the posterior fornix. A second tablet may be inserted after six to eight hours if labour is not established. Maximum dose 6 mg.

Contra-indications, warnings, etc

Contra-indications: There are no absolute contra-indications to the use of Prostin E2. However, its use is not recommended in the following circumstances.

1. For patients in whom oxytocic drugs are generally contra-indicated or where prolonged contractions of the uterus are considered inappropriate such as:

Cases with a history of Caesarian section or major uterine surgery;

Cases in which major degrees of cephalopelvic disproportion may be present;

Cases in which there is clinical suspicion or definite evidence of pre-existing foetal distress;

Cases in which there is a history of difficult labour and/or traumatic delivery;

Grand multiparae with six or more previous term pregnancies.

2. Patients with ruptured membranes.

3. Patients with known hypersensitivity to prostaglandin.

Warning: Since it has been found that prostaglandins may potentiate the effect of oxytocin, it is recommended that, if these drugs are used together or in sequence, the patient's uterine activity should be carefully monitored.

The product is available only to hospitals and clinics with specialised obstetric units.

Precautions: Caution should be exercised in the administration of Prostin E2 Vaginal Tablets for the induction of labour in patients with:

(i) glaucoma or raised intra-ocular pressure;

(ii) asthma or a history of asthma.

In addition, in labour induction, cephalopelvic relationships should be carefully evaluated before use of Prostin E2. During use, uterine activity, foetal status, and the progression of cervical dilatation should be carefully monitored to detect possible evidence of undesired responses, e.g. hypertonus, sustained uterine contractions, or foetal distress. In cases where there is a known history of hypertonic uterine contractility or tetanic uterine contractions, it is recommended that uterine activity and the state of the foetus should be continuously monitored throughout labour. The possibility of uterine rupture should be borne in mind where high-tone myometrial contractions are sustained. Animal studies lasting several weeks at high doses have shown that prostaglandins of the E and F series can induce

proliferation of bone. Such effects have also been noted in newborn infants who have received prostaglandin E₁ during prolonged treatment. There is no evidence that short-term administration of Prostin E2 Vaginal Tablets can cause similar bone effects.

Side Effects: Very occasional nausea and vomiting. Uterine hypertonus or unduly severe uterine contractions have rarely been encountered.

Overdosage: Treatment of overdosage must be, at this time, symptomatic, since clinical studies with prostaglandin antagonists have not progressed to the point where recommendations may be made.

Pharmaceutical precautions Prostin E2 Vaginal Tablets have a shelf-life of 24 months when stored in a refrigerator at 4°C. The tablets should be used within 1 month of opening the bottle.

Legal category POM.

Package quantities Prostin E2 Vaginal Tablets are packed in bottles of 4.

Further information Unlike other oxytocics, Prostin E2 exhibits the capacity of the prostaglandins to influence uterine activity at any stage of gestation. Other Prostin E2 dosage forms are available for induction of labour (oral and i.v. routes), foetal death in utero (i.v. route), therapeutic termination of pregnancy (i.v. and extra-amniotic routes), missed abortion and hydatidiform mole (i.v. route).

Product licence number 0032/0074.

PROSTIN F2 alpha* STERILE SOLUTIONS

Presentation Colourless, sterile aqueous solution containing 5 mg per ml dinoprost (Prostaglandin F₂ alpha). Dinoprost is presented as the tromethamine (THAM) salt.

1. Prostin F2 alpha Sterile Solution 5 mg/ml, 1.5 ml ampoule (intravenous).
2. Prostin F2 alpha Sterile Solution 5 mg/ml, 4 ml and 8 ml ampoules (intra-amniotic).
3. Prostin F2 alpha Sterile Solution 5 mg/ml, 5 ml ampoule (intravenous).

Uses Oxytocic agent. Prostin F2 alpha is indicated for induction of labour, foetal death in utero, therapeutic termination of pregnancy, missed abortion and hydatidiform mole.

Dosage and administration Prostin F2 alpha may be administered by the intravenous and intra-amniotic routes as follows:

1. Intravenous: for induction of labour and foetal death in utero.
2. Intra-amniotic: for therapeutic termination of pregnancy during the second trimester.
3. Intravenous: for therapeutic termination of pregnancy, missed abortion and hydatidiform mole.

For each route of administration except the intra-amniotic route, the ampoule contents must be diluted before use and full instructions on method of dilution and dosage are given on the package insert which should be consulted prior to initiation of therapy. The dose of Prostin F2 alpha used normally depends not only upon the indication but also on patient response. Increase in

dosage above that recommended is possible but may produce excessive uterine activity and be governed by the unacceptable appearance of dose-related side effects, such as nausea and vomiting.

The following is a guide to dosage:

1. *Prostin F2 alpha 5 mg/ml (1.5 ml ampoule) intra venous for induction of labour and foetal death in utero*: 15 mcg/ml solution is infused at 2.5 mcg/minute for at least 30 minutes and then maintained or increased. Case of foetal death in utero may require higher doses than those given above. An initial rate of 5 mcg/minute may be used with step-wise increases, at intervals of not less than one hour.
2. *Prostin F2 alpha 5 mg/ml (4 and 8 ml ampoules intra-amniotic for therapeutic termination of pregnancy*: 8 ml of undiluted solution (40 mg initial dose) should be withdrawn from the ampoule(s) and should be injected slowly into the amniotic sac.
3. *Prostin F2 alpha 5 mg/ml (5 ml ampoule) intra venous for therapeutic termination of pregnancy, missed abortion and hydatidiform mole*: 50 mcg/ml solution is infused at 25 mcg/minute for at least 30 minutes and then maintained or increased to 50 mcg/minute. This rate should be maintained for at least four hours before increasing further.

Contra-indications, warnings, etc

Contra-indications: There are no absolute contra-indications to the use of Prostin F2 alpha. However, its use is not recommended in the following circumstances:

1. Where the patient is sensitive to prostaglandins.
2. For patients in whom oxytocic drugs are generally contra-indicated or where prolonged contractions of the uterus are considered inappropriate, such as: cases with a history of Caesarean section or major uterine surgery cases in which major degree of cephalopelvic disproportion may be present; cases in which foetal malpresentation is present; cases in which there is clinical suspicion or definite evidence of pre-existing foetal distress; cases in which there is a history of difficult labour and/or traumatic delivery; grand multiparae with six or more previous term pregnancies; cases with a history of pelvic inflammatory disease.
3. In therapeutic termination of pregnancy where known pelvic infection exists, unless adequate prior treatment has been instituted.
4. The intra-amniotic route should not be employed in patients with a history of Caesarean section or prior major uterine surgery.

Warnings: There has been some evidence in animals of a low order of teratogenic activity, therefore, if abortion does not occur or is suspected to be incomplete as a result of prostaglandin therapy, the appropriate treatment for complete evacuation of the pregnant uterus should be instituted in all instances. Since it has been found that prostaglandins may potentiate the effect of oxytocin, it is recommended that these drugs should not be used together, and if used in sequence, that the patient's uterine activity should be carefully monitored.

The products are available only to hospitals and clinics with specialised obstetric units and should only be used where 24-hour resident medical cover is provided.

Precautions: Caution should be exercised in the administration of Prostin F2 alpha for induction of labour or therapeutic termination of pregnancy in patients with (i) glaucoma or raised intra-ocular pressure; (ii) asthma or history of asthma. In addition, in labour induction

uld be carefully evaluated
During infusion, uterine
progression of cervical
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Product licence numbers

1.5 ml ampoule	0032/0037
4 and 8 ml ampoules	0032/0051 (intra-amniotic)
5 ml ampoule	0032/0038

PROSTIN VR* STERILE SOLUTION ▼

Presentation Ampoule containing 0.5 mg alprostadil in 1 ml dehydrated ethanol.

Uses Prostin VR is indicated to temporarily maintain the patency of the ductus arteriosus until corrective or palliative surgery can be performed in infants who have congenital defects and who depend upon the patent ductus for survival. Such congenital heart defects include pulmonary atresia, pulmonary stenosis, tricuspid atresia, tetralogy of Fallot, interruption of the aortic arch, coarctation of the aorta, aortic stenosis, aortic atresia, mitral atresia, or transposition of the great vessels with or without other defects.

Dosage and administration For administration by intravenous drip or constant-rate infusion pump.

In infants with lesions restricting pulmonary blood flow (blood is flowing through the ductus arteriosus from the aorta to the pulmonary artery), Prostin VR may be administered by continuous infusion through an umbilical artery catheter placed at or just above the junction of the descending aorta and the ductus arteriosus, or intravenously. Adverse effects have occurred with both routes of administration, but the types of reactions are different. A higher incidence of flushing has been associated with intra-arterial than with intravenous administration.

Infusion should begin with 0.1 micrograms alprostadil per kilogram of body weight per minute. If the aorta can not be catheterised via the umbilical artery, the infusion may be given through a catheter advanced from the periphery into a larger vein.

In infants with lesions restricting systemic blood flow (blood is flowing through the ductus arteriosus from the pulmonary artery to the aorta), Prostin VR may be administered by continuous infusion through an umbilical artery catheter passed across the ductus arteriosus and into the pulmonary artery proximal to the ductus arteriosus, or intravenously. Infusion should begin with 0.1 micrograms alprostadil per kilogram of body weight per minute. If the pulmonary artery can not be catheterised via the umbilical artery, the infusion may be given through a catheter advanced from the periphery into a large vein.

When an effect is achieved, decrease the infusion to the lowest possible dose while maintaining the desired effects.

Dilution Instructions: To prepare infusion solutions, dilute 1 ml of Prostin VR Sterile Solution with sterile 0.9% Sodium Chloride Intravenous Infusion or sterile 5% Dextrose Intravenous Infusion. Dilute to volumes appropriate for the delivery system available. Prepare fresh infusion solutions every 24 hours. Discard any solution more than 24 hours old.

Examples: Dissolve 1 ml Prostin VR Sterile Solution (500 micrograms alprostadil) in 25 to 100 ml sterile 0.9% Sodium Chloride Intravenous Infusion or sterile 5% Dextrose Intravenous Infusion to provide a solution containing 500 micrograms alprostadil. The infusion rate can be calculated as follows:

Infusion rate (ml/hr) =

$$\frac{\text{Vol. containing 500 mcg alprostadil} \times \text{body weight (kg)}}{83.3}$$

With an infusion pump limited to discrete infusion rates, infuse 2 or 4 ml per hour. Calculate the volume of 0.9% saline or 5% dextrose to add to 1 ml Prostin VR Sterile Solution to deliver 0.1 micrograms alprostadil per kilogram of body weight per minute at the chosen pump rate as follows:

$$\text{Volume of saline or dextrose needed (ml)} = \frac{\text{Pump rate (ml/hour)} \times 83.3}{\text{body weight (kg)}} - 1$$

The infusion solution may be mixed conveniently in a graduated mixing chamber inserted between the IV bottle and the pump.

Change the dosage from 0.1 micrograms per kilogram of body weight per minute to 0.05 micrograms per kilogram of body weight per minute by reducing the pump rate to one-half the original rate.

PARTICULAR CARE SHOULD BE TAKEN IN CALCULATING AND PREPARING DILUTIONS OF PROSTIN VR

Contra-indications, warnings, etc

Contra-indications: None.

Warnings: Only the recommended Prostin VR dosages should be administered and only by medically trained personnel in hospitals or other facilities with immediately available intensive care.

Approximately 10–12% of neonates with congenital heart defects treated with Prostin VR Sterile Solution (alprostadil) experienced apnoea. Apnoea is most often seen in neonates weighing less than 2 kg at birth and usually appears during the first hour of drug infusion. Therefore, Prostin VR Sterile Solution should be used where ventilatory assistance is immediately available.

Precautions: Prostin VR Sterile Solution (alprostadil) should be infused for the shortest time and at the lowest dose which will produce the desired effects. The risk of long-term infusion of Prostin VR should be weighed against the possible benefits that critically ill infants may derive from its administration.

Cortical proliferation of the long bones has followed long-term infusions of alprostadil in infants and dogs. The proliferation in infants regressed after withdrawal of the drug.

Use Prostin VR Sterile Solution (alprostadil) cautiously in neonates with histories of bleeding tendencies.

Care should be taken to avoid the use of Prostin VR Sterile Solution in neonates with respiratory distress syndrome (hyaline membrane disease), which sometimes can be confused with cyanotic heart disease. If full diagnostic facilities are not immediately available, cyanosis (pO_2 less than 40 mmHg) and restricted pulmonary blood flow apparent on an X-ray are good indicators of congenital heart defects.

In all infants, commencing when infusion starts, intermittently monitor arterial pressure by umbilical artery catheter, auscultation, or with a Doppler transducer. Should arterial pressure fall significantly, decrease the rate of infusion immediately.

A weakening of the wall of the ductus arteriosus and pulmonary artery has been reported, particularly during prolonged administration.

Side-effects and Adverse reactions: The most frequent

adverse reactions observed with Prostin VR are related to its known pharmacological effects. These include flushing, bradycardia, hypotension, tachycardia, cardiac arrest, oedema, apnoea, diarrhoea, fever, convulsions disseminated intravascular coagulation, and hypokalaemia.

Overdosage: The effects of Prostin VR abate quickly when infusion is stopped.

Pharmaceutical precautions Prostin VR must be stored in a refrigerator. See dilution instructions for shelf-life of diluted solutions.

Legal category POM.

Package quantities Pack containing 5 × 1 ml ampoules Prostin VR Sterile Solution.

Further information Alprostadil (formerly known as prostaglandin E_2) dilates the ductus arteriosus in neonates, probably by relaxing smooth muscle in other parts of the vascular system, and can thus lower blood pressure.

Product licence number 0032/0083.

PROVERA*

Presentation White compressed tablets scored or one face, embossed 286 on either side of score, and marked U on other face, containing 5 mg medroxyprogesterone acetate.

Uses Progestogen.

Indicated for secondary amenorrhoea and for functional uterine bleeding.

Dosage and administration Oral.

Secondary Amenorrhoea: 2.5–10 mg daily for 5–10 days beginning on the assumed or calculated sixteenth to twenty-first day of the cycle. Repeat treatment for three consecutive cycles. In amenorrhoea associated with a poorly developed proliferative endometrium, conventional oestrogen therapy may be employed in conjunction with medroxyprogesterone acetate in doses of 5–10 mg for 10 days.

Functional uterine bleeding: 2.5–10 mg daily for 5–10 days commencing on the assumed or calculated sixteenth to twenty-first day of the cycle. Treatment should be given for two consecutive cycles. When bleeding occurs from a poorly developed proliferative endometrium, conventional oestrogen therapy may be employed in conjunction with medroxyprogesterone acetate, in doses of 5–10 mg for 10 days.

Contra-indications, warnings, etc

Contra-indications: None applicable.

Precautions: Whether administered alone or in conjunction with oestrogens, Provera should not be employed in patients with abnormal uterine bleeding until a definite diagnosis has been established and the possibility of genital malignancy eliminated.

Side-effects: No significant untoward effects or intolerance have been reported.

Overdosage: In animals Provera has been shown to be capable of exerting an adreno-corticoid effect but this has not been reported in the human, following usual dosages. The oral administration of Provera at a rate of 100 mg per day has been shown to have no effect on adrenal function.

Pharmaceutical precautions None.

Legal category POM.

Package quantities Bottles of 100.

Further information Provera is a highly active gestational agent. During its years of clinical use no significant toxicity has been recorded and it appears to be free of androgenic and oestrogenic effects.

Product licence number 0032/5035.

OVERA 100 mg*

Presentation White tablets marked 'U' on one side and '467' on the other, containing 100 mg medroxyprogesterone acetate.

Uses Progestogen.

Indicated for the treatment of certain hormone-dependent neoplasms, such as endometrial carcinoma and oestrogenoma.

Dosage and administration Oral.

100–400 mg daily continued for up to three months in order to assess response.

Intra-indications, warnings, etc

Contra-indications: Provera 100 mg is not recommended for primary or total therapy for carcinoma unless surgery or radiotherapy is not feasible.

Warnings: None applicable.

Precautions: In animals Provera has been shown to be capable of exerting an adreno-corticoid effect, but this has not been reported in the human, following usual dosages. The oral administration of Provera at a rate of 0 mg per day has been shown to have no effect on renal function.

Side-effects: Provera 100 mg appears to be devoid of androgenic effects. Masculinisation of the female foetus has not been demonstrated in animals but, despite extensive studies, the only changes reported in humans have been of minor significance (clitoral hypertrophy) and have reverted to normal in a few weeks.

Overdosage: No action required other than cessation of therapy (see 'Precautions').

Pharmaceutical precautions None.

Legal category POM.

Package quantities Bottles of 100.

Further information Provera 100 mg has achieved considerable success in the hormonal management of gynaecological malignancy. The overall picture is that of a selective remission has been obtained in about 25% of cases.

Product licence number 0032/5036.

SOLU-CORTEF*

Presentation White, freeze-dried powder of hydrocortisone sodium succinate, equivalent to 100 mg hydrocortisone, in rubber-capped vials.

Uses Anti-inflammatory agent.

Indicated for acute adrenocortical insufficiency, bilateral adrenalectomy, severe shock, acute hypersensitivity reactions, overwhelming infections with severe toxicity, systemic lupus erythematosus in relapse, aspiration

pneumonitis and other conditions requiring the metabolic and anti-inflammatory actions of hydrocortisone.

Dosage and administration Intravenous injection, intravenous infusion or intramuscular injection.

Preparation of solutions for intravenous or intramuscular use:

For intravenous and intramuscular injection add 2 ml sterile water for injection from accompanying ampoule to the vial, shake and withdraw for use.

For intravenous infusion, prepare a primary solution as above and then add to 100–1,000 ml (not less than 100 ml) of 5% dextrose in water, or isotonic saline or 5% dextrose in isotonic saline solution, if patient is not on sodium restriction.

When reconstituted as directed, the pH of solution will range from 7.0 to 8.0.

Dosage usually ranges from 100 mg to 500 mg, depending on the severity of the condition, and should be administered by intravenous injection over a period of one to several minutes.

In infants and children dose may be reduced but should not be less than 25 mg daily.

In critically ill patients, particularly in shock, it has been recommended that a dose of 1 g administered intravenously over several minutes be given, followed by 500 mg every four to eight hours for three to five days if necessary.

Contra-indications, warnings, etc

Contra-indications: The usual contra-indications to the use of systemic corticosteroids apply (excepting in the case of treatment of bilateral adrenalectomy) and include latent, healed and active tuberculosis, herpes simplex, chronic nephritis, acute psychosis, Cushing's syndrome, peptic ulcer and predisposition to thrombophlebitis.

Warnings: Due to its inhibitory effect on fibroplasia hydrocortisone may mask signs of infection, and enhance dissemination of the infecting organism.

Precautions: The existence of congestive heart failure, hypertension, diabetes, osteoporosis, or chronic psychotic reactions necessitate caution in the administration of Solu-Cortef.

Injection into the deltoid muscle should be avoided because of a high incidence of subcutaneous atrophy.

Side-effects: Since Solu-Cortef is normally employed on a short-term basis it is unlikely that side-effects will occur; however, the possibility of side-effects attributable to corticosteroid therapy should be recognised.

Overdosage: No known antidote. Following overdosage the possibility of adrenal suppression should be guarded against by gradual diminution of dose levels over a period of time. In such event the patient may require to be supported during any further traumatic episode.

Pharmaceutical precautions Store at room temperature. No diluents, other than referred to, are recommended.

Legal category POM.

Package quantities Solu-Cortef is supplied as: 100 mg vial with an ampoule containing 2 ml of water for injection.

Further information In the treatment of shock, massive, pharmacological, doses of corticosteroid of the order of equivalents of 1 g hydrocortisone are accepted therapy. It is considered that the corticosteroid assists in resensitising the capillary bed, thus helping to prevent blood stagnation and the onset of irreversible shock.

Product licence number
100 mg vial 0032/5019.

SOLU-MEDRONE*

Presentation Mix-O-Vials of 40 mg and 125 mg methylprednisolone (as the sodium succinate). Each Mix-O-Vial consists of adjoining compartments of lyophilised powder and solvent. Also 500 mg, 1 g and 2 g vials of methylprednisolone (as the sodium succinate) with solvent.

Uses Medrone is a potent corticosteroid with an anti-inflammatory activity at least five times that of hydrocortisone. An enhanced separation of glucocorticoid and mineralocorticoid effect results in a reduced incidence of sodium and water retention.

Solu-Medrone is indicated for any condition in which rapid and intense corticosteroid effect is required such as:

1. Hypersensitivity reactions.
2. Severe shock, i.e. haemorrhagic, septic, surgical, traumatic, or cardiogenic.
3. Overwhelming infection with severe toxæmia.
4. Acute adrenal insufficiency.
5. Suppression of graft rejection reactions following transplantation.
6. Cerebral oedema.
7. The treatment of certain emergency situations in advanced cancer patients such as acute dyspnoea due to pulmonary or mediastinal metastases or the obstruction of other hollow viscera.

Dosage and administration Solu-Medrone may be administered intravenously or intramuscularly, the preferred method for emergency use being intravenous injection given over a suitable time interval (see 'Precautions'). For intravenous infusion the initially prepared solution may be diluted with 5% dextrose, isotonic saline or dextrose saline. Dosage should be varied according to the severity of the condition. In general not less than 0.5 mg/kg/day. In the treatment of shock and graft rejection reactions a dose of up to 30 mg/kg may be required for limited periods. For detailed recommendations on dosage see Package Insert.

Contra-indications, warnings, etc

Contra-indications: Like all corticosteroids Solu-Medrone is contra-indicated in herpes simplex keratitis, acute psychoses, and latent, healed or active tuberculosis. Relative contra-indications include active or latent peptic ulcer, Cushing's syndrome, diverticulitis, osteoporosis, renal insufficiency, thromboembolic tendencies, diabetes mellitus, hypertension, local or systemic infection including viral, fungal and other exanthematous diseases. Pregnancy is included as a relative contra-indication.

Warnings and precautions: There have been a few reports of cardiovascular collapse associated with the rapid intravenous administration of large doses of Solu-Medrone (greater than 500 mg) in organ transplant recipients. The cause and relation to other medications (e.g. diuretics) are not known at this time, but physicians and surgeons should be alert to this possibility. When administering Solu-Medrone in high doses intravenously, it should be given over a period of 10–20 minutes. It should be remembered that prolonged high-dose corticosteroid therapy can cause serious corticosteroid-induced side-effects, and high dose therapy

should, in general, be continued only until the patient condition has stabilised: usually not beyond 48–hours.

Solu-Medrone should not be used for the treatment of cardiogenic shock if the central venous pressure is under 10 cm water.

In the treatment of acute adrenal insufficiency sodium-retaining corticosteroid, in addition to Solu-Medrone, will be needed.

When used to treat cerebral oedema due to brain trauma, gastro-intestinal bleeding may occur and the stool guaiac tests may be diagnostically helpful. Prompt lactic peptic ulcer therapy (i.e. antacids, etc) should be considered.

Injection into the deltoid muscle should be avoided because of a high incidence of subcutaneous atrophy.

The normal precautions to the use of system corticosteroids should be observed.

Adverse reactions and side-effects: Under normal circumstances Solu-Medrone therapy would be considered as short-term. However, the possibility of side-effects and adverse reactions common to corticosteroids must be considered, particularly when high-dose therapy is being used.

Overdosage: No known antidote. Following overdosage the possibility of adrenal suppression should be guarded against by gradual diminution of dose levels over period of time. In such event the patient may require be supported during any further traumatic episode.

Pharmaceutical precautions Mix-O-Vials should be protected from freezing. Prepared solutions should be used within 48 hours. No special requirement for syringe or infusion solution containers.

Legal category POM.

Package quantities Mix-O-Vials of 40 mg/1 ml, and 125 mg/2 ml.

Vials of 500 mg, 1 g and 2 g plus solvent.

Further information The following instructions for the use of the Mix-O-Vials should be observed. Remove the protective cap from the Mix-O-Vial. Give a half-turn to the piston and press it down as far as possible to allow the diluent to pass into the lower powder chamber. Shake well until solution is complete. Sterilise the surface of the rubber piston. Hold the vial up at 45° and insert the syringe needle through the centre of the piston and withdraw the required quantity of solution.

Product licence numbers

40 mg/1 ml	0032/0033
125 mg/2 ml	0032/0034
500 mg/8 ml	0032/0035
1 g/16 ml	0032/0039
2 g/32 ml	0032/0073

TOLANASE*

Presentation White, scored, convex tablets marked 'UPJOHN 70' on the opposite side, containing 100 mg tolazamide.

White, scored, convex tablet marked 'UPJOHN 11' on other side, containing 250 mg tolazamide.

Uses Sulphonylurea.

Indicated in maturity-onset diabetes of mild to moderate severity.

Dosage and administration Oral.

100–250 mg daily, or up to 1 g daily in divided doses necessary. It is doubtful whether doses greater than 1 g daily will result in improved control. (For dose inversion from other oral hypoglycaemic agents see literature.)

Depending on the results of urinary glucose tests and blood sugar determinations the daily dose should be either raised or lowered by amounts of one tablet (100 mg or 250 mg) at weekly intervals.

Contra-indications, warnings, etc

Contra-indications: Tolanase is not indicated in juvenile labile (brittle) diabetes, or in patients with infections those undergoing surgery or trauma. It is contra-indicated in patients with ketosis, acidosis or in coma, and who have a history of such.

Since Tolanase has not been studied extensively in diabetes complicated by pregnancy or in diabetics with liver, kidney or endocrine disease, it is not recommended in these instances.

Warnings: The appearance of significant acetonuria in a patient transferred from insulin to tolazamide makes a return to insulin therapy mandatory.

Side-effects: The most commonly encountered symptoms are gastro-intestinal (1.8%), including nausea, anorexia, diarrhoea. Other minor occurrences, such as dizziness, weakness, insomnia, lethargy, have been reported. A disulfiram-like action after taking alcohol has not been reported.

Overdosage: Action should be taken to counteract the ensuing hypoglycaemic period. No known antidote.

Pharmaceutical precautions Store at room temperature.

Legal category POM.

Package quantities Tolanase is supplied as tablets containing 100 mg or 250 mg tolazamide in bottles of 10 and 500.

Further information The half-life of seven hours makes Tolanase an ideal agent for a single or twice-daily dose regime.

Product licence numbers

Tablets 100 mg 0032/5043

Tablets 250 mg 0032/5044

TROBICIN*

Description Vial containing spectinomycin dihydrochloride pentahydrate equivalent to spectinomycin 3 g. Also ampoule of diluent containing benzyl alcohol 9%. When reconstituted with diluent each vial yields 1 ml containing the equivalent of 400 mg spectinomycin per millilitre.

Uses Antibiotic for intramuscular injection in the treatment of gonorrhoea.

Dosage and administration For adults a single dose as follows:

Males: 2 g by deep intramuscular injection.

Females: 4 g by deep intramuscular injection.

The dose may be divided between two injection sites.

Contra-indications, warnings, etc

Contra-indications: Trobicin is not indicated for the treatment of syphilis.

Warnings: Antibiotics used in high doses for short periods of time to treat gonorrhoea may mask or delay the symptoms of incubating syphilis. Since the treatment of acute syphilis demands prolonged therapy with any effective antibiotic, patients being treated for gonorrhoea should be closely observed clinically for a period of four to six weeks. Appropriate serological follow-up for at least four months should be instituted if a diagnosis of syphilis is suspected.

Safety for use in pregnancy has not been established.

Side-effects: During clinical trials no anaphylactic reactions or other serious side-effects were encountered. However, the usual precautions should be observed with atopic individuals. The following minor side-effects have been observed: dizziness, nausea, chills-fever, urticaria and (rarely) mild to moderate discomfort at the injection site.

Overdosage: Overdosage is unlikely to be a problem in practice.

Pharmaceutical precautions Shake vial vigorously immediately after adding diluent and before withdrawing dose. Dilution of the reconstituted suspension should not be necessary. Prepared suspension should be stored at room temperature and used within 24 hours. Otherwise no special storage precautions.

Legal category POM.

Package quantities 1 × 2 g vial plus diluent.

Further information Trobicin bears no structural or antigenic relationship to the penicillins. It is an inhibitor of protein synthesis in the bacterial cell, the site of action being the 30 S ribosomal subunit. Trobicin is rapidly absorbed after intramuscular injection, a single 2 g dose producing peak serum concentrations averaging 103 mcg/ml at one hour. Serum concentrations inhibitory to most gonococcal strains persist for up to eight hours. Up to 100% of the administered dose is excreted in the urine within 48 hours in a biologically active form.

Product licence number 0032/0032.

*Trade Mark

Wander Pharmaceuticals
(A Division of Sandoz Products Ltd)
98 The Centre
Feltham
Middlesex TW13 4EP

WANDER

CAFERGOT* SUPPOSITORIES

Presentation Off-white suppositories weighing 1.98 g. Each suppository contains 2 mg Ergotamine Tartrate PhEur and 100 mg Caffeine PhEur.

Uses Cafergot contains a combination of ergotamine and caffeine specially developed for the treatment of the acute migraine attack. Ergotamine aborts attacks of migraine and related vascular headaches by a direct vasoconstrictor effect on distended extra-cranial arteries. Concomitant administration of caffeine enhances the absorption of ergotamine.

Cafergot Suppositories are specially valuable for patients who have nausea and vomiting early in the attack and cannot retain or absorb anything taken by mouth. To be fully effective the suppositories must be used as early as possible in the attack.

Indications: Migraine. Migraine variants.

Dosage and administration One suppository should be administered at the first warning of an attack. This dose is normally sufficient, but if relief is not obtained additional doses may be taken up to a maximum of 3 suppositories. Subsequently, the total dose found effective in a previous attack should be administered immediately prodromal symptoms are experienced. Maximum dosage is 3 suppositories per day and 5 in any one week.

Contra-indications, warnings, etc

Contra-indications: Pregnancy, peripheral vascular disorders, coronary disease, impaired hepatic or renal function, sepsis, obliterative vascular disease, severe hypertension, breast feeding.

Precautions: Concomitant use of erythromycin and ergotamine should be avoided.

Overdosage: Treatment should be directed to the elimination of ingested material by aspiration and gastric lavage. Arterial spasm may be corrected by the administration of a vasodilator. General supportive measures should be applied with particular reference to the respiratory and cardiovascular systems.

Side-effects: Drowsiness, nausea, vomiting and occasionally weakness in the legs and muscle pain may occur; numbness and tingling of the extremities can be indicative of peripheral vascular disturbance and treatment must be stopped immediately if signs of circulatory impairment appear. Failure to observe this precaution can lead to the development of ergotism.

Pharmaceutical precautions Keep in a cool place.

Legal category POM.

Package quantities Boxes of 6 and 30.

Further information Cafergot suppositories no longer contain total alkaloids of belladonna or isobutylallylbar-

bituric acid. Cafergot suppositories without these constituents are supplied in packs marked 'Revised Formulation'.

Product licence number 0101/5001.

CAFERGOT* TABLETS

Presentation Very pale pink, round, coated tablet: 9.5–10 mm diameter, 5.4 to 5.6 mm thick, weighing 370 mg. Branded 'WANDER' on one face. Each tablet contains 1 mg Ergotamine Tartrate PhEur, 100 mg Caffeine PhEur.

Uses Properties: Cafergot contains a combination of ergotamine and caffeine specially developed for the treatment of the acute migraine attack. Ergotamine aborts attacks of migraine and related vascular headaches by a direct vasoconstrictor effect on distended extracranial arteries. Concomitant administration of caffeine enhances the absorption of ergotamine. To be fully effective the tablets must be taken as early as possible in the attack.

Indications: Migraine. Migraine variants.

Dosage and administration Two tablets should be taken at the first warning of an attack. This dose is normally sufficient, but if relief is not obtained within an hour a further tablet should be taken, repeated if necessary at half-hourly intervals up to a maximum of 6 tablets. Subsequently, the total dose found effective in a previous attack should be taken immediately prodromal symptoms are experienced. Maximum dosage is 6 tablets per day and 10 in any one week.

Contra-indications, warnings, etc

Contra-indications: Pregnancy, peripheral vascular disorders, coronary disease, impaired hepatic or renal function, sepsis, obliterative vascular disease, severe hypertension and breast feeding.

Precautions: Concomitant use of erythromycin and ergotamine should be avoided.

Overdosage: Treatment should be directed to the elimination of ingested material by aspiration and gastric lavage. Arterial spasm may be corrected by the administration of a vasodilator. General supportive measures should be applied with particular reference to the respiratory and cardiovascular systems.

Side-effects: Nausea, vomiting and occasionally weakness in the legs and muscle pain may occur, numbness and tingling of the extremities can be indicative of peripheral vascular disturbance and treatment must be stopped immediately if signs of circulatory impairment appear. Failure to observe this precaution may lead to the development of ergotism.

harmaceutical precautions None.

egal category POM.

ackage quantities Containers of 100.

urther information Nil.

roduct licence number 0101/5023.

ESERIL*

resentation Canary-yellow, coated, round, bi-concave tablets weighing 100 mg, 6 mm diameter, 3.4–3.9 mm thick, branded 'WANDER' one side. Each tablet contains 1.33 mg methysergide hydrogen maleate (equivalent to 1 mg methysergide base).

ses Deseril is a potent serotonin antagonist.

World-wide clinical trials indicate that Deseril will prevent, or reduce the frequency or severity of, headaches in 60–70% of patients.

indications:

1. Prophylactic treatment of migraine in patients, who, despite other attempts at control, experience attacks of such severity or regularity that their social or economic life is seriously disrupted. (*Note.* Deseril is not recommended for the treatment of the acute attack.)
2. Periodic migrainous neuralgia (Horton's syndrome).
3. To control the profuse diarrhoea associated with carcinoid disease.

dosage and administration *Prophylactic treatment of headache.* 1–2 tablets two or three times a day, with meals. The initial dose of 1 tablet should preferably be given at bedtime and dosage should be increased gradually to effective levels over an approximately two-week period, so that minimal effective doses are employed. It is wiser to settle for the smallest amount which will prevent 75% of the attacks than to increase the dose to a high level in an effort to prevent all headaches. From the outset, patients should understand that regular clinical supervision and periodic interruption in treatment are imperative so that side-effects can be recognised and minimised.

'carcinoid syndrome.' High oral doses are usually necessary. In most cases on record dosage ranged between 2 and 20 tablets daily.

Deseril is not recommended for the treatment of children.

Contra-indications, warnings, etc

Contra-indications: Pregnancy, peripheral vascular disease, phlebitis or cellulitis of the lower limbs, clinical arteriosclerosis, coronary artery disease, impaired hepatic, renal or renal tract function, valvular heart disease, severe hypertension, pulmonary or collagen disorders, states of cachexia or sepsis.

Warnings: *Note.* Continuous Deseril administration should not exceed six months without a drug-free interval of at least one month for reassessment. It is usually wise to decrease the dosage of the drug gradually or two or three weeks before complete withdrawal to prevent rebound headaches.

In patients undergoing treatment with Deseril, the dose of ergotamine required to control any acute attack may have to be reduced.

Precautions: Regular clinical supervision of patients under treatment with Deseril is essential. Particular

attention should be paid to complaints of urinary dysfunction, pain in the loin, flank or chest, and pain, coldness or numbness in the limbs. Patients should be regularly examined for the presence of cardiac murmurs, vascular bruits, pleural or pericardial friction rubs and abdominal or flank masses or tenderness. Treatment with Deseril should be stopped should any of these symptoms or signs occur. Caution is also advised during drug administration to patients with a past history of peptic ulceration. In carcinoid syndrome the risk of untoward side-effects due to the higher dosage must be weighed against the therapeutic requirements.

Overdosage: Treatment should be directed to elimination of the ingested material by aspiration and gastric lavage. General supportive measures should be applied. The patient should be carefully observed for peripheral vasospasm which may be treated by warmth, care being taken to protect ischaemic limbs. If there is evidence of impending tissue damage vasodilators may be used.

Side-effects:

1. **General:** The most commonly reported side-effects have been nausea, heartburn, abdominal discomfort, vomiting, dizziness, lassitude and drowsiness, particularly in the initial stages of treatment. These side-effects can often be minimised by taking the preparation with food. Tissue oedema, insomnia, leg cramps and weight gain have occurred, and very occasionally skin eruptions or loss of scalp hair. Psychic reactions have appeared in isolated instances. These effects regressed on reduction in dosage or withdrawal of medication.

2. Inflammatory fibroses:

(a) **Retroperitoneal fibrosis.** In a small percentage of patients, continuous long-term Deseril administration has been associated with abnormal development of fibrous tissue in the form of retroperitoneal fibrosis. This rare condition usually presents with symptoms of ureteric dysfunction. If, therefore, persistent loin or flank pain, oliguria or dysuria occur, pyelographic evidence of hydronephrosis and ureteric deviation or obstruction should be sought. In such patients, subjected to laparotomy, retroperitoneal fibrosis has been found. However, drug withdrawal alone is associated with clinical improvement over a few days to several weeks, and appreciation of this may avoid unnecessary surgical intervention.

(b) **Fibrosis in other areas.** There are isolated reports of similar fibrotic processes involving lungs, pleura, heart valves and major vessels. Examination of all patients prior to the institution of treatment is advisable and the development of signs or symptoms attributable to these effects should lead to immediate cessation of treatment. There is evidence which suggests that these fibrotic manifestations are reversible although less readily so than retroperitoneal fibrosis. On occasion pulmonary fibrosis has been localised to give, on radiography, a tumour-like appearance with or without obliteration of costophrenic angles and the development of pleural effusion. Appreciation of these effects should prevent unnecessary radical surgery.

3. **Vascular:** Vascular reactions, including arterial spasm, have been seen in some patients. Such occurrences are very rare. The following have all been described, although in some instances the role of Deseril is arguable: arterial spasm in a limb, causing coldness, numbness, pain or intermittent claudication; renal artery spasm giving rise

to transitory hypertension; mesenteric artery spasm causing abdominal pain; retinal artery spasm causing reversible loss of vision; coronary artery spasm causing angina and questionably resulting in myocardial infarction. Arterial spasm is rapidly reversible following drug withdrawal, and the development of significant sequelae is unlikely.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Containers of 100.

Further information Nil.

Product licence number 0101/5026.

GATINAR*

Presentation Gatinar is available as a clear, almost colourless to pale yellow syrup. Each 5 ml spoonful contains 3.35 g lactulose and 1.34 g of other sugars (lactose, galactose, tagatose and other keto-sugars).

Uses *Principal action:* Gatinar prevents the formation of hard stools and encourages normal bowel movement. Unlike traditional laxative preparations which act either on the innervation or musculature of the intestine or by bulk stimulus, Gatinar provides a natural substrate for the saccharolytic bacterial flora in the colon.

The active principle of Gatinar, lactulose, is a disaccharide which is not hydrolysed in the small intestine. Therefore it cannot be absorbed and is transported to the colon with water to retain the osmotic balance. In the colon, several species of bacteria can hydrolyse lactulose, to the monosaccharides galactose and fructose.

By encouraging this normal metabolic activity of the bacteria, the osmotic pressure of the colonic contents is doubled and more water is drawn into the bowel.

Further metabolism of the monosaccharides leads to the production of acetic and lactic acids and a lowering of colonic pH. This acidification of the colonic contents is considered to be the main reason for the effectiveness of Gatinar. In chronic portal-systemic encephalopathy it may be associated with the decrease in the relative concentration of free ammonia, the major agent involved in the cerebral disturbance.

Indications: Chronic constipation. Chronic portal-systemic encephalopathy.

Dosage and administration *Chronic constipation:* Because Gatinar acts naturally to encourage the normal activity of the bowel, it may be two or three days before the full benefit of the treatment is obtained. It is important, therefore, to follow the dosage regimen set out below.

Adults: Initially: Three to six 5 ml spoonfuls for the first two to three days of treatment. (Nine spoonfuls may be given in obstinate cases.)

Maintenance: Two to three 5 ml spoonfuls daily or according to the needs of the patient.

Children: Initially: two to five 5 ml spoonfuls for the first two or three days of treatment.

Maintenance: one to three 5 ml spoonfuls daily or according to the needs of the patient.

Chronic portal-systemic encephalopathy: Initial: Six to ten 5 ml spoonfuls three times daily according to the requirements of the patient for adequate acidification of the colonic contents.

Contra-indications, warnings, etc

Contra-indications: In common with other preparations used for the treatment of constipation, Gatinar should not be used in patients with gastro-intestinal obstruction.

Gatinar should not be given to patients with galactosaemia or intolerance to lactose.

Precautions: Gatinar should be used with caution during the first trimester of pregnancy.

Overdosage: No cases of intoxication due to deliberate or accidental overdosage with Gatinar have been reported to the Company.

Side-effects: Side-effects rarely occur after the administration of Gatinar. Mild, transient effects such as abdominal distention or cramps and flatulence, which subside after the initial stages of treatment, have occasionally been reported.

High doses may provoke nausea in some patients. This can be minimised by administration with water, fruit juice or with meals.

Pharmaceutical precautions Gatinar should be stored in a cool place.

Dilution of Gatinar is not recommended.

Legal category P.

Package quantities Bottles of 200 ml and 2 litres.

Further information Gatinar has an absolute calorific value of 18.7 kJ per 5 ml spoonful.

Product licence number 0101/0076.

SANOMIGRAN*

Presentation *0.5 mg Tablets:* Ivory/yellow, coated, bi-convex tablets of 5.5–5.6 mm diameter, weighing 90 mg. Printed WANDER on one face. Each tablet contains 725 mcg pizotifen hydrogen malate (equivalent to 500 mcg pizotifen base).

1.5 mg Tablets: Ivory/yellow, coated, bi-convex tablets of 9.0 mm diameter, weighing 280 mg. Printed SMG on one face. Each tablet contains 2.175 mg pizotifen hydrogen malate (equivalent to 1.5 mg pizotifen base).

Uses *Principal action:* Pharmacodynamic studies demonstrate that Sanomigran has a broad antagonistic activity against biogenic amines. Tests show powerful antiserotonergic and antitryptaminergic properties, marked antihistaminic effects and some antagonistic activity against kinins. Sanomigran also has a weak anticholinergic effect and useful sedative and antidepressant properties.

The well-documented prophylactic effect of Sanomigran against the migraine attack is associated with its ability to modify the humoral elements of the headache mechanism. The powerful antiserotonergic and antihistaminic properties inhibit the permeability-increasing effect of these amines on the affected cranial vessels, thereby checking transudation of plasmakinin and, as a result, maintaining the pain threshold of the receptors at 'normal' levels.

One of the first links in the chain of events leading to the migraine attack is a loss of tone in the extracranial arteries. A factor in this mechanism is the depletion of plasma serotonin. Sanomigran inhibits the re-uptake of serotonin by the blood platelets, thus maintaining plasma serotonin and preventing the loss of tone in the vessels. By this indirect effect Sanomigran provides a counter-

measure to the passive distension of the extracranial arteries and circumvents the migraine attack.

Indications: Prophylactic treatment of recurrent vascular headaches, including classical migraine, common migraine and cluster headache (periodic migrainous uralgia).

Dosage and administration Usually 1.5 mg daily which may be taken in one dose at night (one 1.5 mg tablet) or three times a day (three 0.5 mg tablets). The dosage can be adjusted to individual patient's requirements and may vary from 0.5 mg to 6 mg daily. Up to 6 mg may be given as a single daily dose.

Contra-indications, warnings, etc *Precautions:* Patients should be cautioned about the possibility of drowsiness and informed of its significance in the driving of vehicles and the operation of machinery. Although its anticholinergic activity is relatively weak, Sanomigran could probably not be administered in the presence of closed angle glaucoma or to patients with a predisposition to urinary retention. No adverse effects during pregnancy have been reported but Sanomigran should not be administered in pregnancy with due caution.

Overdosage: Symptoms of overdosage may include fatigue, drowsiness, dryness of the mouth, confusion, nausea, vomiting, dyspnoea, cyanosis, tachycardia, coma and respiratory paralysis. Treatment should be directed to the elimination of the drug by gastric lavage, diuresis. Severe hypotension must be corrected but it is noted that adrenaline may produce paradoxical effects. General surveillance measures are indicated.

Side-effects: The most commonly occurring side-effects are drowsiness, a gain in weight or an increased appetite. Other side-effects such as dizziness and nausea have been reported infrequently.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities 0.5 mg: containers of 100 tablets; 5 mg: Calendar packs of 28 tablets.

Further information Nil.

Product licence numbers

5 mg tablets 0101/0036

5 mg tablets 0101/0129

AVEGIL*

Presentation Tavegil is available as tablets and elixir.

Tablets: White, uncoated, round tablets, 7 mm in diameter, with bevelled edges, branded 'WANDER' on one side with a single break line and coded 'OT' on the other. Each tablet contains 1.34 mg clemastine hydrogen fumarate equivalent to 1 mg clemastine base.

Elixir: A clear, colourless liquid with an odour of peaches. Each 5 ml spoonful contains 670 mcg (0.67 mg) of clemastine hydrogen fumarate equivalent to 500 mcg (0.5 mg) of clemastine base.

Uses *Principal action:* Tavegil is a potent, specific antihistamine which is innately long-acting.

Indications: Allergic rhinitis, including hay fever and perennial rhinitis, vasomotor rhinitis. Allergic dermatoses, including pruritus, atopic eczema and contact dermatitis. Urticaria. Angioneurotic oedema. Drug allergy.

Dosage and administration *Tablets: Adults:* 1 tablet night and morning. In individual cases the dose may be increased to 6 tablets daily if necessary.

Children up to 12 years: $\frac{1}{2}$ –1 tablet night and morning according to age.

Elixir: Children up to 12 years: One or two 5 ml spoonfuls night and morning according to age.

Adults: Two 5 ml spoonfuls night and morning. In individual cases the dose may be increased to 12 spoonfuls daily if necessary. Tavegil Elixir is sugar-free and may be administered to diabetic patients.

Contra-indications, warnings, etc *Precautions:* Patients should be warned not to take charge of vehicles or machinery until the effect of Tavegil treatment on the individual is known. Tavegil may potentiate the effects of sedatives and alcohol. Tavegil should be given in pregnancy and breast feeding only if strictly indicated.

Overdosage: May give rise to confusion, nausea and vomiting. Treatment should be directed to the removal of ingested material by induced emesis or gastric lavage as appropriate.

Routine supportive measures are indicated to combat respiratory depression and hypotension.

Side-effects: Of the side-effects associated with antihistamine drugs, excessive sedation is the most common and troublesome. With Tavegil at normal dosage drowsiness is infrequent and when it occurs it is usually mild and transient. Very occasional miscellaneous side-effects such as weakness, dizziness, fatigue, dry mouth, palpitations, gastro-intestinal disturbance, heartburn and skin rash have occurred. In general, these adverse effects can be controlled by a diminution of dosage.

Pharmaceutical precautions Protect tablets from light. Tavegil Elixir may be diluted with Purified Water or Syrup BP. The diluted elixir should be used within 14 days.

Legal category P.

Package quantities *Tavegil Tablets:* Containers of 50 and 500.

Tavegil Elixir: Bottles of 150 ml and 2 litres.

Further information Tavegil Elixir has an absolute calorific value of 11 kcal per 5 ml spoonful.

Product licence numbers

Tavegil Tablets 0101/0033

Tavegil Elixir 0101/0058

TERONAC*

Presentation White, uncoated, bi-convex tablets of 8 mm diameter, each weighing 220 mg. Branded WANDER on one side, with a single break line and coded JC on the other. Each tablet contains 2 mg of mazindol base.

Uses *Principal action:* Teronac is an appetite suppressant with potent anorexic activity. It has a novel chemical structure.

It is unrelated to amphetamine and is not metabolised to an amphetamine derivative.

Indications: An aid to the establishment of a diet in the treatment of the overweight.

Teronac may be used in patients with stable heart disease, and in diabetic patients: (see Precautions).

Dosage and administration *Adults and children over 12 years of age:* 1 tablet after breakfast or as directed by the physician.

A treatment period of three months is recommended as an aid to the establishment of a controlled diet. The recommended dosage should not be exceeded in an attempt to increase the effect.

Contra-indications, warnings, etc

Contra-indications: Teronac should not be used during pregnancy, breast feeding or in patients with peptic ulcer, glaucoma, severe renal, hepatic or cardiac insufficiency, cardiac arrhythmias and severe hypertension.

Teronac does not inhibit monoamine oxidase (MAO) but potentiates the pressor effects of catecholamines. It can therefore be anticipated that Teronac will interact with the following: MAO inhibitors and antihypertensives of the adrenergic neurone blocking type, e.g. guanethidine and debrisoquine.

These medicinal agents should not be taken until one month has elapsed from the cessation of treatment with Teronac.

Precautions: Teronac should be used with caution in patients with coronary heart disease, severely agitated states, and in patients taking thyroid medication or psychostimulants.

Patients should be cautioned against taking cough and cold remedies containing sympathomimetic decongestants during treatment with Teronac and for one month after ceasing treatment, without first seeking the doctor's advice. This caution is also applicable to patients undergoing local anaesthesia for dental procedures with products containing adrenaline or other sympathomimetic haemostatics.

The response to insulin and oral antidiabetic agents may be affected in diabetic patients treated with Teronac and therefore dietary control and thus the metabolic status of the patient should be kept under observation during treatment and the dosage of insulin or oral antidiabetic agents adjusted if necessary.

Patients driving vehicles or operating machinery should be alerted to the possibility of impaired reactions.

Overdosage: Treatment should be directed to the removal of ingested material by induced emesis and gastric lavage as appropriate. Hyperactivity and anxiety are major factors of overdosage, excess CNS stimulation should be controlled if necessary with chlorpromazine. There is no reported use of forced acid diuresis, but it may be of theoretical value.

Side-effects: The most commonly occurring side-effects include constipation, dry mouth and insomnia. Less frequently nervousness, headache, dizziness, chills, skin rashes, reversible disturbances of micturition and sexual function may also occur. Mild tachycardia has occasionally been reported at higher dosage levels.

Pharmaceutical precautions Store in a dry place at a temperature not exceeding 21°C.

Legal category POM.

Package quantities Containers of 30 and 100 tablets.

Further information Weight loss is steady and consistent during treatment with Teronac. In contrast to treatment with amphetamine-like obesity preparations, tolerance to treatment does not develop and there is no rebound effect on mood or appetite on cessation of therapy.

Product licence number 0101/0079.

TREMONIL®

Presentation White, uncoated, bi-convex tablets 8 mm diameter, each weighing 155 mg. Break line one side, with 'WANDER' imprinted on the other side. Each tablet contains 5 mg of methixene hydrochloride.

Uses *Principal actions:* Tremonil is a parasympatholytic agent and has spasmolytic and antihistaminic properties.

Indications: Tremonil is indicated in the treatment of Parkinsonism of any aetiology: paralysis agitans, postencephalitic Parkinsonism, arteriosclerotic Parkinsonism, drug-induced Parkinsonism. It is more effective in controlling the tremors than in reducing the rigidity of this syndrome.

Tremonil is also indicated in the treatment of senile tremor.

Dosage and administration *Adults:* At the beginning of treatment the total daily dosage should be small and given in divided doses over the day. Treatment may be started with single doses of 2.5 mg ($\frac{1}{2}$ tablet), three times daily. The dose may then be slowly and gradually raised by small increments until the most effective dose is reached.

The optimum effective dose lies between 15 mg and 60 mg daily in divided dosage, depending upon the severity of symptoms initially and their response to treatment.

In elderly patients, the optimum maintenance dosage is often lower, e.g. 15–30 mg daily, than that required in younger subjects with comparable disease.

Children: There are no dosage recommendations for children.

Contra-indications, warnings, etc

Contra-indications: Prostatic hypertrophy and other conditions causing urinary retention; narrow angle glaucoma, cardiac arrhythmias, intestinal hypomotility, myasthenia gravis, acute intoxication with alcohol, hypnotics, analgesics or psychotropics.

Precautions: Autonomic disturbances occasionally occur during the initial stages of treatment and due caution should be observed in patients who have to drive or perform tasks requiring precision. If these do not disappear spontaneously as treatment proceeds, the dose should be lowered until the highest well-tolerated dose is reached. Treatment should be continued at this level for several days and then gradually increased.

Special care is needed in the adjustment of the dosage in patients with marked autonomic liability.

When changing treatment from another anti-Parkinson drug, the small starting dose of Tremonil should be substituted for a part of the dosage of the drug already in use. As the dose of Tremonil is increased, that of the drug for which it is being substituted should be reduced accordingly.

When adding Tremonil to another anti-Parkinson drug it is advisable to reduce slightly the dose of the latter for a few days. In this way the occurrence of undesirable side-effects due to the sudden increase in the total dose of parasympatholytic agents may be avoided.

When Tremonil is administered concurrently with phenothiazine tranquilisers to control extrapyramidal side-effects, the average total daily dose of Tremonil should be around 15 mg.

Tremonil should be given in the early stages of pregnancy and during breast feeding only if strictly indicated.

de-effects: Tremonil is generally well tolerated but signs of autonomic imbalance, e.g. dryness of mucous membranes, transient visual disturbances, tachycardia, lightheadedness and dizziness, may occur in some patients during the early stages of treatment. These symptoms tend to disappear spontaneously during treatment, but a temporary reduction in dosage may be required. See commendations under 'Dosage'.

Nausea, sensations of abdominal pressure, weakness and fatigue may occur half to one hour after a single dose of 10–15 mg.

Constipation and urinary retention have been noted.

Mental confusion may result from the use of synthetic anti-Parkinson drugs, especially when given in high dosage, or to elderly patients, and the possibility of this de-effect should be borne in mind, especially when several drugs are given concurrently.

If signs of mental confusion are observed the drug should be discontinued immediately.

verdosage: Toxic effects are anticholinergic in nature.

Gastric lavage. Routine supportive measures. Give fluids freely. Atropine antagonists such as neostigmine ethylsulphate may relieve the peripheral symptoms. Although physostigmine (1 to 4 mg i.v.) will antagonise the central effects, it is rarely indicated.

pharmaceutical precautions Nil.

legal category POM.

package quantities Containers of 100 tablets.

further information Nil.

product licence number 0101/5904.

RIOCOS*

presentation Clear, colourless syrup with a citrus flavour. Each 5 ml spoonful contains 5 mg Pholcodine hEur, 20 mg Pseudoephedrine Hydrochloride BP, 2 mg chlorpheniramine Maleate BP, 600 mg Glycerol PhEur, and 5.25 g Syrup BP.

Uses *Principal action:* Triocos is a cough suppressant and decongestant. Of the active ingredients, pholcodine has a specific depressant effect on the cough centre in the medulla, has a more potent action than codeine, causes less respiratory depression than morphine and is not implicated in undesirable gastro-intestinal side-effects such as constipation, anorexia or vomiting; it has also the advantage of being well tolerated by children. Pseudoephedrine hydrochloride is an effective nasal and bronchial decongestant. Chlorpheniramine maleate is a well-tried antihistamine beneficial in the management of nasal irritation and in associated allergic symptoms.

Indications: The relief of cough, particularly when associated with congestion of nasal and bronchial mucous membranes.

Dosage and administration *Adults:* Two to three 5 ml spoonfuls every six hours as required.

Children: 6–12 years: One to two 5 ml spoonfuls every six hours as required.

1–6 years: Half to one 5 ml spoonful every six hours as required.

Do not exceed three doses in 24 hours.

Contra-indications, warnings, etc *Precautions:* As pseudoephedrine is a sympathomimetic amine, Triocos should be given with caution to hypertensive patients,

patients suffering from heart failure or to patients with incipient or established urinary retention, and should not be given to those being treated with monoamine oxidase (MAO) inhibitors or antihypertensives. Caution is necessary in patients receiving beta-blockers.

Antihistamines may cause drowsiness and dulling of mental alertness. Patients undergoing treatment with Triocos are advised not to take charge of vehicles, or other means of transport or machinery where loss of attention may lead to accidents.

Care should be exercised when administering antihistamines to patients with epilepsy as convulsions may be precipitated, especially in children.

Side-effects: The side-effects are those attributed to the antihistamines generally and the commonest include drowsiness, nausea, vomiting, headache, blurred vision, anorexia and dryness of the mouth.

Overdosage: Severe respiratory depression can be reversed by i.v. naloxone treatment.

Pharmaceutical precautions Triocos may be diluted with Syrup BP. The diluted syrup should be used within 14 days.

Legal category P.

Package quantities Bottles of 100 ml and 1 litre.

Further information Sucrose content 3.5 g per 5 ml dose. Absolute calorific value 12.3 kJ/5 ml.

Product licence number 0101/0104.

TRIOGESIC*

Presentation *Tablets:* Pink, bi-convex, round tablets of 645 mg weight, 12 mm diameter with a single break line on one side, and 'TRIOGESIC' engraved on the other. Each tablet contains 12.5 mg Phenylpropanolamine Hydrochloride BP and 500 mg Paracetamol PhEur.

Elixir: A deep red, clear liquid with a taste and odour of cherries. Each 5 ml spoonful contains 3 mg Phenylpropanolamine Hydrochloride BP, 125 mg Paracetamol PhEur and 0.5 ml ethanol (96%).

Uses *Principal action:* Triogesic provides a decongestant in conjunction with an analgesic.

Indications: For decongestion and relief from pain in coryza, sinusitis and otitis media.

Dosage and administration *Tablets: Adults:* 1 or 2 tablets every four hours.

Children 6 years and over: Half a tablet every four hours.

Do not exceed 8 tablets (adults) or 4 tablets (children) in 24 hours.

Elixir: Adults: Four 5 ml spoonfuls every four hours.

Children 6 years and over: Two 5 ml spoonfuls every four hours.

Children 1 to 5 years: One to two 5 ml spoonfuls every four hours.

Do not exceed 8 doses (adults) or 4 doses (children) in 24 hours.

Contra-indications, warnings, etc

Contra-indications: Hypertension, glaucoma, urinary retention.

Precautions: Triogesic should not be administered to patients during, or for two weeks after completion of treatment with monoamine oxidase (MAO) inhibitors. Caution is necessary in patients receiving beta-blockers.

Overdosage: Treatment should be directed to the elimination of the ingested material by aspiration and gastric lavage, and general supportive measures provided. Paracetamol levels should be checked. The antidotes methionine or N-acetyl cysteine should be given if indicated by ingested dose, plasma levels and time since ingestion, to prevent liver damage.

Pharmaceutical precautions Triogesic Elixir may be diluted with Syrup BP and Purified Water BP. The diluted elixir should be used within 14 days.

Legal category P.

Package quantities *Triogesic Tablets:* Containers of 12, 30 and 250.

Triogesic Elixir: Bottles of 150 ml and 1 litre.

Further information Triogesic Elixir does not contain sucrose. Each 5 ml spoonful has an absolute calorific value of 22.1 kJ.

Product licence numbers

Triogesic Tablets 0101/5907
Triogesic Elixir 0101/5908

TRIOMINIC*

Presentation *Tablets:* Yellow, round, bi-convex tablets of 470 mg weight, 11.1 mm diameter, 4.7 mm thick. Impressed 'WANDER' on one side. Each tablet contains 25 mg Mepyramine Maleate BP, 25 mg pheniramine maleate and 50 mg Phenylpropanolamine Hydrochloride BP.

Syrup: Clear, orange-red syrup with citrus flavour. Each 5 ml spoonful contains 6.25 mg Mepyramine Maleate BP, 6.25 mg pheniramine maleate and 12.5 mg Phenylpropanolamine Hydrochloride BP.

Uses A combination of two antihistamines with a decongestant.

Indications: For symptomatic relief of hay fever, or other forms of rhinitis.

Dosage and administration *Tablets: Adults:* 1 tablet every six to eight hours, not exceeding 3 tablets in 24 hours. The tablets must be swallowed whole.

Syrup: Adults: Two 5 ml spoonfuls every four hours.

Children 6 years and over: One 5 ml spoonful every three to four hours.

Children under 6 years: Dosage in proportion (may be diluted with an equal volume of syrup or water).

The number of doses (adults and children) should not exceed 4 in 24 hours.

Contra-indications, warnings, etc

Contra-indications: Hypertension, glaucoma, urinary retention.

Precautions: Triominic should not be administered to patients during, or for two weeks after, treatment with monoamine oxidase (MAO) inhibitors. Caution is necessary in patients receiving beta-blockers. The usual precautions with antihistamines should be observed.

Overdosage: Treatment should be directed to the elimination of the ingested material by aspiration and gastric lavage. Measures should be taken to minimise excitation. Respiration may require assistance. General supportive measures are of importance.

Pharmaceutical precautions Triominic Tablets should be stored and dispensed in airtight containers.

The Syrup may be diluted with Syrup BP or Purified Water BP. The diluted syrup should be used within 14 days.

Legal category P.

Package quantities *Triominic Tablets:* Containers of 12, 50 and 250.

Triominic Syrup: Bottles of 150 ml and 1 litre.

Further information Triominic Syrup Contains 3.6 g sucrose per 5 ml spoonful with an absolute calorific value of 17.6 kJ.

Product licence numbers

Triominic Tablets 0101/5909
Triominic Syrup 0101/5910

TRIOPAED*

Presentation Clear, colourless liquid with a citrus flavour. Each 5 ml spoonful contains 4 mg Pholcodine PhEur, 750 mg Glycerol PhEur and 5.25 g Syrup BP.

Uses *Principal action:* Triopaed is a cough suppressant. The active ingredient, pholcodine has a specific depressant effect on the cough centre in the medulla. The central antitussive action of pholcodine is at least three times as powerful as that of codeine. Pholcodine is many times less toxic than codeine and is employed in much smaller doses. It causes less respiratory depression than morphine and is not implicated in gastro-intestinal side effects such as constipation, anorexia, vomiting etc.

Indications: Unproductive cough.

Dosage and administration *Children over 6 years:* One to two 5 ml spoonfuls every six hours as required.

2-6 years: One 5 ml spoonful every six hours as required.

Contra-indications, warnings, etc

Contra-indications: There are no known contra-indications to Triopaed apart from use in patients where suppression of cough reflex is inadvisable.

Side-effects: Pholcodine may occasionally cause nausea and drowsiness.

Overdosage: Gastric lavage and general supportive measures. Severe respiratory depression may be reversed by i.v. naloxone.

Pharmaceutical precautions Triopaed may be diluted with Syrup BP. The diluted Syrup should be used within 14 days of dispensing.

Legal category P.

Package quantities Bottles of 100 ml and 1 litre.

Further information Sucrose content 3.5 g per 5 ml dose. Absolute calorific value 15 kJ/5 ml.

Product licence number 0101/0109.

TRIOTUSSIC*

Presentation Opaque, orange suspension with orange flavour. Each 5 ml spoonful contains 12.5 mg Phenylpropanolamine Hydrochloride BP, 6.25 mg Mepyramine Maleate BP, 6.25 mg pheniramine maleate, 20 mg Noscapine PhEur, 90 mg terpin hydrate and 160 mg Paracetamol PhEur.

Uses *Indications:* Triotussic has been formulated to provide symptomatic relief of cough, pain and nasal congestion associated with the common cold.

Dosage and administration *Adults:* One to two 5 ml spoonfuls every three to four hours.

Children 6 years and over: Half to one 5 ml spoonful four times daily.

Children under 6 years: Dosage in proportion (may be diluted with Syrup BP).

The number of doses (adults and children) should not exceed 4 in 24 hours.

Contra-indications, warnings, etc

Contra-indications: Severe cardiovascular disorders, tachycardia, hypertension, glaucoma, urinary retention, prostatic enlargement, severe diabetes mellitus, hyrotoxicosis.

Precautions: Triotussic should not be administered to patients during, or for two weeks after, treatment with monoamine oxidase inhibitors (MAOIs) and antihypertensives. Caution is necessary in patients receiving beta-blockers. The usual precautions with antihistamines should be observed. The effects of alcohol and sedation may be potentiated and the effects of anticoagulants enhanced.

Overdosage: Treatment should be directed to the elimination of the ingested material by aspiration and gastric lavage. Respiration may require assistance. General supportive measures are of importance.

Pharmaceutical precautions Triotussic Suspension may be diluted with Syrup BP. The diluted syrup should be used within 14 days.

Legal category P.

Package quantities *Triotussic Suspension:* Bottles of 300 ml.

Further information Each 5 ml spoonful has an absolute calorific value of 17.35 kJ.

Product licence number 0101/5911.

ZADITEN* ▼

Presentation *1 mg capsules:* White, opaque, oblong, gelatine capsules, size 4 weighing 182 mg. Each capsule contains 1.38 mg ketotifen hydrogen fumarate (equivalent to 1 mg ketotifen base). Coded CS.

1 mg tablets: Off-white, uncoated, round, flat, bevelled tablets weighing 190 mg and 7 mm diameter. Single breakline one side and marked ZADITEN 1 on the other. Each tablet contains 1.38 mg ketotifen hydrogen fumarate (equivalent to 1 mg ketotifen base).

Elixir: Clear, colourless, strawberry flavoured elixir. Each 5 ml spoonful contains 1.38 mg ketotifen hydrogen fumarate (equivalent to 1 mg ketotifen base).

Uses *Principal action:* Zaditen possesses marked anti-anaphylactic properties and is effective in preventing asthmatic attacks.

Laboratory experiments indicate that this anti-anaphylactic activity may be due in the main to the inhibition of release of myotonic mediators from tissue mast cells and basophils, in particular SRS (slow reacting substance) and histamine, to the inhibition of SRS-induced broncho-spasms in vivo and to calcium antagonistic properties. In addition, Zaditen exerts a sustained

inhibitory effect on histamine reactions which can clearly be dissociated from its anti-anaphylactic properties.

Experimental investigations in asthmatic subjects have shown that Zaditen is as effective orally as a selective mast cell stabiliser administered by inhalation: antihistamines are ineffective in these tests.

The effectiveness of Zaditen in the prevention of bronchial asthma has been studied in long term clinical trials. Asthma attacks were reduced in number, severity and duration and in some cases the patients were completely freed from attacks. Progressive reduction of corticosteroids and/or bronchodilators was also possible.

The prophylactic activity of Zaditen may take several weeks to become fully established.

Zaditen will not abort established attacks of asthma.

Indications: Prophylactic treatment of bronchial asthma.

Dosage and administration *Adults:* 1 mg twice daily with food. If necessary the dose may be increased to 2 mg twice daily.

Children from two years: 1 mg twice daily with food. Patients known to be easily sedated should begin treatment with 0.5–1 mg at night for the first few days.

Contra-indications, warnings, etc

Contra-indications: A reversible fall in the thrombocyte count in patients receiving Zaditen concomitantly with oral antidiabetic agents has been observed in a few cases. This combination of drugs should therefore be avoided until this phenomenon has been satisfactorily explained.

Although there is no evidence of any teratogenic effect, recommendations for Zaditen in pregnancy or when breast feeding cannot be given.

Precautions: Post-marketing surveillance has shown, in the interim results, exacerbation of asthma in approximately 2 per 1000 patients. Since some of these asthmatic attacks might have been related to stopping existing treatment, it is important to continue such treatment for a minimum of two weeks after starting Zaditen. This applies especially to systemic corticosteroids and ACTH because of the possible existence of adrenocortical insufficiency in steroid-dependent patients: in such cases recovery of a normal pituitary-adrenal response to stress may take up to one year.

If intercurrent infection occurs Zaditen treatment must be supplemented by specific antimicrobial therapy.

During the first days of treatment with Zaditen reactions may be impaired. Patients should be warned not to take charge of vehicles or machinery until the effect of Zaditen treatment on the individual is known. Patients should be advised to avoid alcoholic drinks.

Zaditen may potentiate the effects of sedatives, hypnotics, antihistamines and alcohol.

Overdosage: The reported features of overdosage include confusion, drowsiness, nystagmus, headache and disorientation. One patient became unconscious and one developed convulsions. Bradycardia and respiratory depression should be watched for. Elimination of the drug with gastric lavage or emesis is recommended. Otherwise general supportive treatment is all that is required.

Side-effects: Drowsiness and, in isolated cases, dry mouth and slight dizziness may occur at the beginning of treatment, but usually disappear spontaneously after a few days.

Pharmaceutical precautions Protect from heat and

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WANDER PHARMACEUTICALS

moisture. Zaditen Elixir may be diluted with Syrup BP containing parahydroxybenzoate preservatives. Diluted elixir should be used within 14 days of preparation.

Legal category POM.

Package quantities *1 mg capsules*: Containers of 60 capsules.

1 mg tablets: Containers of 60 tablets.

Elixir 1 mg/5 ml: Bottles of 150 ml.

Further information Zaditen is currently being evaluated in other atopic conditions. Zaditen Elixir contains

1.5 g sucrose per 5 ml dose. Absolute calorific 13.1 kJals per 5 ml dose.

Product licence numbers

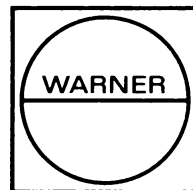
1 mg capsules 0101/0105

1 mg tablets 0101/0125

Elixir 1 mg/5 ml 0101/0137

**Trade Mark*

William R. Warner & Co. Limited
Mitchell House
Southampton Road
Eastleigh
Hampshire SO5 5RY



ANUGESIC* - HC CREAM

Presentation Buff-coloured cream with the characteristic odour of Balsam Peru. Each 100 g of cream contains:

Pramoxine Hydrochloride USP	1.00 g
Hydrocortisone Acetate Ph Eur	0.50 g
Benzyl Benzoate BP	1.20 g
Bismuth Oxide	0.875 g
Balsam Peru BPC 1973	1.85 g
Zinc Oxide Ph Eur	12.35 g
Resorcinol BP	0.875 g

Uses Anugesic-HC Cream provides antiseptic, astringent, emollient and decongestant properties. In addition the anti-inflammatory action of hydrocortisone helps to reduce swelling and hyperaemia. Pramoxine is a rapidly acting local anaesthetic. The cream may be used to provide lubrication for suppositories.

Anugesic-HC Cream is indicated for the comprehensive symptomatic treatment of severe and acute discomfort or pain associated with internal and external haemorrhoids, proctitis, cryptitis, anal fissures, pruritus ani and perianal sinuses. It is also indicated post-operatively in ano-rectal surgical procedures.

Dosage and administration *Adults:* Apply cream to the affected area at night, in the morning and after each evacuation.

Thoroughly cleanse the affected area, dry and apply cream by gently smoothing onto the affected area. For internal conditions use rectal nozzle provided and clean it after each use.

Not to be taken orally.

Children: Not recommended.

Contra-indications, warnings, etc

Contra-indications: Tubercular, fungal and most viral lesions including herpes simplex, vaccinia and varicella. History of sensitivity to any of the constituents.

Warnings: As with all products containing topical steroids the possibility of systemic absorption should be borne in mind. Prolonged or excessive use may produce systemic corticosteroid effects. During the first trimester of pregnancy long-term therapy with topical corticosteroids should be avoided.

Precautions: Following symptomatic relief definitive diagnosis should be established.

Side-effects: Rarely, sensitivity reactions.

Patients may occasionally experience transient burning on application, especially if the anoderm is not intact.

Overdosage: If swallowed, main toxic ingredient is resorcinol, which may cause shock, collapse, rash, convulsion and coma, but only if more than about 100 g Anugesic-HC Cream is swallowed.

Fever, nausea, vomiting, stomach cramps and diarrhoea may develop 3-12 hours after ingestion.

Pramoxine is relatively non-toxic and less sensitising than other local anaesthetics.

Hydrocortisone normally does not produce toxic effects in an acute single overdose.

Treatment of a large acute overdosage should include gastric lavage, purgation with magnesium sulphate and complete bed rest. If necessary, give oxygen, and general supportive measures. Methaemoglobinemia should be treated by intravenous methylene blue.

Pharmaceutical precautions Store at a temperature not exceeding 25°C.

Legal category POM.

Package quantity Tubes containing 15 g.

Further information Anugesic-HC Cream is prepared in a water-miscible base which provides intimate contact with the area to be treated without having to cross an anhydrous barrier. A cream is also more convenient to use being aesthetically more acceptable than ointments.

Product licence number 0019/5005.

ANUGESIC* - HC SUPPOSITORIES

Presentation Buff-coloured suppositories. Each 2.8 g suppository contains:

Pramoxine Hydrochloride USP	27 mg
Hydrocortisone Acetate Ph Eur	5 mg
Benzyl Benzoate BP	33 mg
Bismuth Oxide	24 mg
Bismuth Subgallate BP	59 mg
Balsam Peru BPC 1973	49 mg
Zinc Oxide Ph Eur	296 mg

Uses Anugesic-HC Suppositories provide antiseptic astringent, emollient and decongestant properties. In addition the anti-inflammatory action of hydrocortisone helps to reduce swelling and hyperaemia. Pramoxine is a rapidly acting local anaesthetic.

Anugesic-HC Suppositories are indicated for the comprehensive symptomatic treatment of severe and acute discomfort or pain associated with internal haemorrhoids, proctitis, cryptitis, anal fissures, pruritus ani and perianal sinuses. Also indicated post-operatively in ano-rectal surgical procedures.

Dosage and administration *Adults:* Remove wrapper and insert one suppository into the anus at night, in the morning and after each evacuation.

Not to be taken orally.

Children: Not recommended.

Contra-indications, warnings, etc

Contra-indications: Tubercular, fungal and most viral lesions including herpes simplex, vaccinia and varicella. History of sensitivity to any of the constituents.

Warnings: As with all products containing topical steroids the possibility of systemic absorption should be

borne in mind. Prolonged or excessive use may produce systemic corticosteroid effects. During the first trimester of pregnancy long-term therapy with topical corticosteroids should be avoided.

Precautions: Following symptomatic relief definite diagnosis should be established.

Side-effects: Rarely, sensitivity reactions.

Patients may occasionally experience transient burning on application, especially if the anoderm is not intact.

Overdosage: If swallowed, fever, nausea, vomiting, stomach cramps and diarrhoea may develop 3–12 hours after ingestion.

Pramoxine is relatively non-toxic and less sensitising than other local anaesthetics.

Hydrocortisone normally does not produce toxic effects in an acute single overdose.

Treatment of a large acute overdosage should include gastric lavage, purgation with magnesium sulphate and complete bed rest. If necessary, give oxygen, and general supportive measures. Methaemoglobinaemia should be treated by intravenous methylene blue.

Pharmaceutical precautions Store in a dry place, at a temperature not exceeding 25°C.

Legal category POM.

Package quantity Box of 12 suppositories.

Further information Nil.

Product licence number 0019/5006.

ANUSOL* CREAM & OINTMENT

Presentation *Anusol Cream:* A buff-coloured cream having the characteristic odour of Balsam Peru. Each 100 g of cream contains:

Bismuth Oxide	2.14 g
Balsam Peru BPC 1973	1.80 g
Zinc Oxide Ph Eur	10.75 g.

Anusol Ointment: A light buff coloured ointment having the characteristic odour of Balsam Peru. Each 100 g of ointment contains:

Bismuth Subgallate BP	2.25 g
Bismuth Oxide	0.875 g
Balsam Peru BPC 1973	1.875 g
Zinc Oxide Ph Eur	10.75 g.

Uses Anusol Cream and Anusol Ointment provide antiseptic, astringent and emollient properties which help to relieve discomfort associated with minor ano-rectal conditions. Anusol Cream also provides lubricating properties for use with suppositories. Indicated for the symptomatic relief of uncomplicated internal and external haemorrhoids, pruritus ani, proctitis and fissures. Also indicated post-operatively in ano-rectal surgical procedures and after incision of thrombosed or sclerosed ano-rectal veins.

Dosage and administration *Adults:* Apply to the affected area at night, in the morning and after each evacuation until the condition is controlled. Thoroughly cleanse the affected area, dry and apply cream or ointment. Anusol Ointment should be applied on a gauze dressing. Anusol Cream is prepared in a vanishing cream base and may be gently smoothed onto the affected area without the need to apply a gauze dressing. For internal conditions use rectal nozzle provided, and clean it after each use. Not to be taken orally.

Children: No dose recommended.

Contra-indications, warnings, etc

Contra-indications: History of sensitivity to any of the constituents.

Warnings: None applicable.

Precautions: None applicable.

Side-effects: Rarely, sensitivity reactions. Patients may occasionally experience transient burning on application especially if the anoderm is not intact.

Overdosage: Treatment of a large acute overdose should include gastric lavage, purgation with magnesium sulphate and complete bed rest. If necessary, apply oxygen and give general supportive measures.

Pharmaceutical precautions Store at a temperature not exceeding 25°C.

Legal category GSL.

Package quantities Anusol Cream: Tubes containing 23 g., Anusol Ointment: Tubes containing 25 g.

Further information The formula of Anusol Cream is similar to that of Anusol Ointment. The advantage of the cream preparation is that the water-miscible base gives intimate contact with the area to be treated and the medicaments do not have to cross an anhydrous barrier. A cream is also more convenient to use, being aesthetically more acceptable than ointments.

Product licence numbers

Anusol Cream 0019/0040.

Anusol Ointment 0019/5002.

ANUSOL* SUPPOSITORIES

Presentation Blue/grey suppositories. Each 2.8 g suppository contains:

Bismuth Subgallate BP	59 mg
Bismuth Oxide	24 mg
Balsam Peru BPC 1973	49 mg
Zinc Oxide Ph Eur	296 mg

Uses Anusol Suppositories provide antiseptic astringent and emollient properties which help to relieve discomforts associated with minor ano-rectal conditions.

Indicated for the symptomatic relief of uncomplicated internal haemorrhoids and proctitis. Also indicated post-operatively in ano-rectal surgical procedures and after incision of thrombosed or sclerosed ano-rectal veins.

Dosage and administration *Adults:* Remove wrapper and insert one suppository into the anus at night, in the morning and after each evacuation. Not to be taken orally.

Children: No dose recommended.

Contra-indications, warnings, etc

Contra-indications: History of sensitivity to any of the constituents.

Warnings: None applicable.

Precautions: None applicable.

Side-effects: Rarely, sensitivity reactions. Patients may occasionally experience transient burning on application, especially if the anoderm is not intact.

Overdosage: Treatment of a large acute overdose should include gastric lavage, purgation with magnesium sulphate and complete bed rest. If necessary, give oxygen and general supportive measures.

Pharmaceutical precautions Store at a temperature not exceeding 25°C.

Legal category GSL.

Packaging quantities Box of 12 or 24 suppositories.

Further information Nil.

Product licence number 0019/5001.

ANUSOL[®]-HC OINTMENT

Presentation A buff-coloured ointment having a characteristic odour of Balsam Peru. Each 100 g of ointment contains:

Hydrocortisone Acetate Ph Eur	0.25 g
Benzyl Benzoate BP	1.25 g
Bismuth Subgallate BP	2.25 g
Bismuth Oxide	0.875 g
Balsam Peru BPC 1973	1.875 g
Zinc Oxide Ph Eur	10.75 g
Resorcinol BP	0.875 g

Uses Anusol-HC Ointment provides antiseptic, astringent, emollient and decongestant properties which help to relieve discomforts associated with minor ano-rectal conditions. In addition the anti-inflammatory action of hydrocortisone helps reduce swelling and hyperaemia.

Indicated for the symptomatic relief of external and internal haemorrhoids, proctitis, cryptitis, anal fissures, pruritus ani and perianal sinuses. Also indicated post-operatively in ano-rectal surgical procedures.

Dosage and administration *Adults:* Apply ointment to the affected area at night, in the morning and after each evacuation.

Thoroughly cleanse the affected area, dry and apply ointment on a gauze dressing. For internal conditions use rectal nozzle provided and clean it after each use.

Not to be taken orally.

Children: Not recommended.

Contra-indications, warnings, etc

Contra-indications: Tubercular, fungal and most viral lesions including herpes simplex, vaccinia and varicella. History of sensitivity to any of the constituents.

Warnings: As with all products containing topical steroids the possibility of systemic absorption should be borne in mind. Prolonged or excessive use may produce systemic corticosteroid effects. During the first trimester of pregnancy long-term therapy with topical corticosteroids should be avoided.

Precautions: Following symptomatic relief definite diagnosis should be established.

Side-effects: Rarely, sensitivity reactions.

Patients may occasionally experience transient burning on application, especially if the anoderm is not intact.

Overdosage: If swallowed, main toxic ingredient is resorcinol, which may cause shock, collapse, rash, convulsion and coma, but only if more than about 100 g Anusol-HC Ointment is swallowed.

Fever, nausea, vomiting, stomach cramps and diarrhoea may develop 3–12 hours after ingestion.

Hydrocortisone normally does not produce toxic effects in an acute single overdose.

Treatment of a large acute overdose should include gastric lavage, purgation with magnesium sulphate and complete bed rest. If necessary, give oxygen, and general

supportive measures. Methaemoglobinaemia should be treated by intravenous methylene blue.

Pharmaceutical precautions Store at a temperature not exceeding 25°C.

Legal category POM.

Package quantities Tubes containing 15 g.

Further information Nil

Product licence number 0019/5004.

ANUSOL[®]-HC SUPPOSITORIES

Presentation Olive green suppositories. Each 2.8 g suppository contains:

Hydrocortisone Acetate Ph Eur	10 mg
Benzyl Benzoate BP	33 mg
Bismuth Subgallate BP	59 mg
Bismuth Oxide	24 mg
Balsam Peru BPC 1973	49 mg
Zinc Oxide Ph Eur	296 mg
Resorcinol BP	24 mg

Uses Anusol-HC Suppositories provide antiseptic, astringent, emollient and decongestant properties which help to relieve discomforts associated with minor ano-rectal conditions. In addition the anti-inflammatory action of hydrocortisone helps reduce swelling and hyperaemia.

Anusol-HC Suppositories are indicated for the symptomatic relief of internal haemorrhoids, proctitis, cryptitis, anal fissures, pruritus ani and perianal sinuses. Also indicated post-operatively in ano-rectal surgical procedures.

Dosage and administration *Adults:* Remove wrapper and insert one suppository into the anus at night, in the morning and after each evacuation.

Not to be taken orally.

Children: Not recommended.

Contra-indications, warnings, etc

Contra-indications: Tubercular, fungal and most viral lesions including herpes simplex, vaccinia and varicella. History of sensitivity to any of the constituents.

Warnings: As with all products containing topical steroids the possibility of systemic absorption should be borne in mind. Prolonged or excessive use may produce systemic corticosteroid effects. During the first trimester of pregnancy long-term therapy with topical corticosteroids should be avoided.

Precautions: Following symptomatic relief definite diagnosis should be established.

Side-effects: Rarely, sensitivity reactions.

Patients may occasionally experience transient burning on application, especially if the anoderm is not intact.

Overdosage: If swallowed, main toxic ingredient is resorcinol, which may cause shock, collapse, rash, convulsion and coma, but only if more than about 40 suppositories are ingested.

Fever, nausea, vomiting, stomach cramps and diarrhoea may develop 3–12 hours after ingestion.

Hydrocortisone normally does not produce toxic effects in an acute single overdose.

Treatment of a large acute overdose should include gastric lavage, purgation with magnesium sulphate and complete bed rest. If necessary, give oxygen, and general

supportive measures. Methaemoglobinaemia should be treated by intravenous methylene blue.

Pharmaceutical precautions Store at a temperature not exceeding 25°C.

Legal category POM.

Package quantities Box of 12 suppositories.

Further information Nil.

Product licence number 0019/5003.

CENTRAX*

Presentation Blue, slightly mottled, circular, biconvex tablets, having a single breakline on one face. Each tablet contains 10 mg prazepam.

Uses Centrax is indicated for the symptomatic relief of anxiety-tension states resulting from stressful circumstances, anxiety associated with anxiety neurosis and other psychoneuroses, and as an adjunct in other disease states in which anxiety is manifested.

Dosage and administration Oral

Adults: The usual dosage is 30 mg daily in divided doses. The dose should be adjusted within the range 10 mg to 60 mg daily in accordance with response of the patient.

Elderly: Half the normal adult dose may be sufficient for a therapeutic response in the elderly.

Children: None.

Contra-indications, warnings, etc

Contra-indications: Known sensitivity to benzodiazepines, acute pulmonary insufficiency.

Use in pregnancy: There is no evidence as to drug safety in human pregnancy, nor is there evidence from animal work that it is free from hazard. Do not use during pregnancy, especially during the first and last trimesters, unless there are compelling reasons.

Precautions: Chronic pulmonary insufficiency, and in renal or hepatic disease.

In labour: High single doses or repeated low doses have been reported to produce hypotonia, poor sucking and hypothermia in the neonate, and irregularities in the fetal heart. In view of their molecular size, prazepam and its metabolites are probably excreted in human milk, therefore Centrax should not be given to nursing mothers.

Caution must be exercised in patients with glaucoma or myasthenia gravis because of possible deleterious effects attributed to the benzodiazepines in such patients.

Warnings and adverse effects: As with other benzodiazepines drowsiness, sedation, blurring of vision, unsteadiness and ataxia have been reported. The effects occur following single as well as repeated dosage and may persist well into the following day. Performance at skilled tasks and alertness may be impaired. Patients should be warned of this hazard and advised not to drive or operate machinery during treatment. The effects are potentiated by alcohol, phenothiazines, narcotics, barbiturates, other CNS depressant drugs, MAO inhibitors, and other anti-depressants. The elderly are particularly liable to experience these symptoms together with confusion especially if organic brain symptoms are present. Therefore in elderly or debilitated patients, the initial dose should be small, and increments should be made gradually, in accordance with the response of the

patient, to preclude ataxia or excessive sedation. See also Dependence Potential and Withdrawal Symptom below. Abnormal psychological reactions to benzodiazepines have been reported. Rare behavioural adverse effects include paradoxical aggressive outbursts, excitement, confusion, and the uncovering of depression with suicidal tendencies. Other rare adverse effects include slight decreases in blood pressure, gastro-intestinal and visual disturbances, skin rashes, urinary retention, head ache, vertigo, change in libido, blood dyscrasias and jaundice.

Dependence potential and withdrawal symptoms: In general, the dependence potential of benzodiazepines is low but this increases when high doses are attained especially when given over long periods. This is particularly so in patients with a history of alcoholism or drug abuse, or in patients with marked personality disorders. Regular monitoring of treatment in such patients is essential and routine repeat prescriptions should be avoided. Treatment in all patients should be withdrawn gradually as symptoms such as depression, nervousness, rebound insomnia, irritability, sweating, and diarrhoea have been reported following abrupt cessation of treatment in patients receiving even normal therapeutic doses for short periods of time. Abrupt withdrawal following excessive dosage may produce confusion, toxic psychosis, convulsions, or a condition resembling delirium tremens.

Treatment of overdosage: Clinical features of benzodiazepine overdosage include impaired level of consciousness, dizziness, ataxia, slurred speech and respiratory depression. Gastric lavage or emesis is rarely necessary and the mainstay of management is general supportive therapy.

Pharmaceutical precautions No special precautions.

Legal category POM.

Package quantities Packs of 100 tablets.

Further information This is a long acting benzodiazepine. Repeated dosage will lead to accumulation of drug metabolites. The elderly and patients with impaired renal and/or hepatic function will be particularly susceptible to adverse effects listed above. Treatment should be kept to a minimum and given only under close medical supervision. Little is known regarding efficacy or safety of benzodiazepines in long term use. It is advisable to review treatment regularly, and to discontinue use as soon as possible.

Product licence number 0019/0054

CHOLEDYL*

Presentation Coated pink, bi-convex tablets with a debossed 'Choleydl 100' on one side, containing 100 mg Choline Theophyllinate BP.

Coated yellow, bi-convex tablets with a debossed 'Choleydl 200' on one side, containing 200 mg Choline Theophyllinate BP.

An amber-coloured, chocolate-flavoured, clear syrup. Each 5 ml spoonful contains Choline Theophyllinate BP 62.5 mg.

Uses For the relief and prophylaxis of bronchospasm in chronic bronchitis and asthma.

Dosage and administration *Tablets:* Oral administration.

Adults: 400–1,600 mg daily in divided doses. The usual adult dose is 100–400 mg four times daily.

Children (over 6 years): 3–4 × 100 mg tablets daily in divided doses. The 200 mg tablet should not be administered to children.

Syrup: Oral administration.

Children (3–6 years): One or two 5 ml spoonfuls three times daily.

Contra-indications, warnings, etc

Contra-indications: Use in patients with a known hypersensitivity to the xanthine group of drugs. An initial dose of 5 mg/kg may be increased slowly over three-day periods until an optimum clinical response is achieved. The peak serum theophylline level should not reach values greater than 20 mcg/ml. Use in children at more than six-hourly intervals.

Precautions and warnings: Caution should be exercised in its use in patients with cardiac disease. Care should be taken in its use in patients suffering from insomnia and in its concomitant use with β -adrenergic agonists, glucagon and the other xanthine drugs as these will potentiate the effect of theophylline. The incidence of toxic effects may be enhanced by the concomitant use of ephedrine. There is no evidence of safety of this drug in human pregnancy but it has been in wide use for many years without apparent ill consequences; animal studies have shown no hazard. Choleleryl syrup contains invert sugar syrup (3.7 ml/5 ml) and due care should be taken where it is prescribed for patients with diabetes mellitus.

Side-effects: Occasional gastro-intestinal upsets may occur.

Overdosage: Characterised by nausea, vomiting, gastro-intestinal irritation, unusual thirst, tachycardia, fall in BP and collapse.

Treatment: If more than about 1 g ingested: Gastric lavage. For fall in blood pressure, nurse in head-down position and give pressor drugs i.v. with general supportive measures.

Pharmaceutical precautions Choleleryl Syrup should be stored in a dry place at a temperature not exceeding 25°C, and protected from light.

Legal category P.

Package quantities *Tablets 100 mg:* Bottles containing 100 and 500 tablets.

Tablets 200 mg: Bottles containing 100 and 500 tablets.

Choleleryl Syrup: Bottles containing 200 ml and 1 litre.

Further information Nil.

Product licence numbers

Tablets 100 mg 0019/0049

Tablets 200 mg 0019/0050

Syrup 0019/0048

ESTROVIS*

Presentation Pink-coloured, bi-convex tablets having one side debossed with 'W' monogram, the other side debossed 'Estrovis 4'. Each tablet contains Quinestrol 4.0 mg.

Uses Quinestrol is a synthetic oestrogen which is stored to a considerable extent in body fat.

Estrovis is indicated both for the inhibition of lactation and the suppression of established lactation.

Dosage and administration *Adults:* Oral administration.

Inhibition: 1 tablet given within six hours of delivery. Symptoms of lactation may occasionally develop on the fourth to sixth day and should be treated expectantly. Only if these symptoms persist and prove troublesome should a second tablet of Estrovis be necessary.

Suppression: 1 tablet to be given immediately the decision to suppress lactation has been made, followed by a second tablet 48 hours later. In many cases one tablet only will suffice to suppress an already failing lactation.

When 2 tablets are given it is advisable to inform the patient that she may experience a heavier than normal period when her menses resume.

Contra-indications, warnings, etc

Contra-indications: Use in patients with a history of, or existent thromboembolic disorders, or with breast or genital cancer (known or suspected to be oestrogen dependent). Use in patients with existing thrombophlebitis or cerebrovascular disease or cardiovascular disease. Use in patients with undiagnosed, irregular vaginal bleeding. Use in pregnancy or suspected pregnancy and in patients with impaired liver function or with active liver disease.

Warnings and precautions: Use in patients suffering from epilepsy, or a history of migraine, asthma or cardiac dysfunction, may result in exacerbation of these disorders because of fluid retention. A decreased glucose tolerance may occur in diabetic patients on this treatment and their control must be carefully supervised. It is important that oestrogens or oestrogen/progestogen combinations should be used at the lowest possible dosage and for the shortest time period compatible with the requisite response.

Side-effects: Clinical studies have indicated an extremely low incidence of side-effects due to Estrovis: very rarely, nausea and vomiting have been reported.

Overdosage: Acute overdosage is seldom attended by any symptoms though there may be nausea and vomiting. Treatment is rarely required except symptomatically.

Pharmaceutical precautions Store in a cool dry place, not exceeding 25°C.

Legal category POM.

Package quantities Estrovis Tablets are supplied in packs of 2 or 20 designed so that the tablets may be dispensed one or two at a time.

Further information Nil.

Product licence number 0019/5009.

GELUSIL* SUSPENSION

Presentation A viscous white suspension, each 5 ml containing:

Magnesium Trisilicate Ph Eur	620 mg
Dried Aluminium Hydroxide Gel BP	310 mg

Uses Gelusil Suspension is a liquid antacid indicated for the relief of hyperacidity, indigestion and heartburn when occurring alone or in association with peptic ulcer.

Dosage and administration *Adults:* One to four 5 ml

spoonfuls of the liquid to be administered with water after meals or whenever symptoms arise.

Children (6–12 years): Half the adult dose.

Contra-indications, warnings, etc

Contra-indications: None known.

Warnings: None applicable.

Precautions: Prolonged or intensive therapy in patients with severe renal insufficiency may lead to hypermagnesaemia.

Side-effects: None is observed at the therapeutic dosage.

Overdosage: Symptoms are unlikely and treatment is rarely required.

Pharmaceutical	precautions	No	special
precautions.			

Legal category GSL.

Package quantities Gelusil Suspension is packed in clear glass bottles containing 200 ml.

Further information Nil.

Product licence number 0019/5012.

GELUSIL* TABLETS

Presentation A white bevel-edge tablet containing:

Magnesium Trisilicate Ph Eur	500 mg
Dried Aluminium Hydroxide Gel BP	250 mg

Uses Gelusil is an antacid indicated for the relief of gastric hyperacidity, indigestion and heartburn when occurring alone or in association with peptic ulcer.

Dosage and administration *Adults:* One or two tablets to be chewed or sucked after meals or whenever symptoms arise.

Children (6–12 years): Half the adult dose.

Contra-indications, warnings, etc

Contra-indications: None known.

Warnings: None applicable.

Precautions: Prolonged or intensive therapy in patients with severe renal insufficiency may lead to hypermagnesaemia.

Gelusil tablets contain 561 mg sugar per tablet and due care should be taken when it is prescribed for patients with diabetes mellitus.

Side-effects: None is observed at the therapeutic dosage.

Overdosage: Symptoms are unlikely and treatment is rarely required.

Pharmaceutical	precautions	No	special
precautions.			

Legal category GSL.

Package quantities Gelusil Tablets are packed in bottles containing 250 and 500 tablets and in foil-wrapped tubes of 20 and 50.

Further information Nil.

Product licence number 0019/5011.

LENTIZOL*

Presentation Capsules containing 50 mg Amitriptyline Hydrochloride BP – white pellets in a size 2 capsule with a pink body and a red cap.

Capsules containing 25 mg Amitriptyline Hydrochloride BP – white pellets in a size 3 all-pink capsule.

The pellets are prepared in a special sustained-release presentation which allows the active constituent to be released over a period of up to 12 hours.

Uses Symptoms of depressive illness especially when sedation is required.

Dosage and administration *Adults and adolescent over 16 years old:* – Oral administration.

Initially 50–100 mg as a single dose at night, increasing to 200 mg/day according to clinical response. Maintenance dose 50–100 mg at night.

Elderly

25–75 mg a day initially. The initial dose should be increased with caution under close supervision. Half the normal maintenance dose may be sufficient to produce a satisfactory clinical response.

Children (under 16 years)

Not recommended.

Use in pregnancy: Do not use during pregnancy especially during the first and last trimesters, unless there are compelling reasons. There is no, or inadequate evidence of safety of the drug in human pregnancy although it has been in wide use for many years without apparent ill-consequence. There is evidence of harmful effects in pregnancy in animals, when given in exceptionally high doses.

Contra-indications, warnings, etc

Contra-indications: Recent cardiac infarction and patients with any degree of heart block or disorders of cardiac rhythm. Patients with mania, severe liver disease or known hypersensitivity to dibenzazepines. Lentizol should not be given to mothers during breast feeding.

Precautions: The elderly are particularly liable to experience adverse reactions, especially agitation, confusion and postural hypotension (see Dosage).

Unless essential it is inadvisable to combine Lentizol with ECT.

Avoid if possible in patients with narrow angle glaucoma, symptoms suggestive of prostatic hypertrophy and a history of epilepsy. Lentizol should be used with caution in hyperthyroid patients.

Patients posing a high suicidal risk require close initial supervision.

Tricyclic anti-depressants potentiate the central nervous depressant action of alcohol.

Anaesthetics given during tri/tetracyclic anti-depressant therapy may increase the risk of arrhythmias and hypotension. If surgery is necessary, the anaesthetist should be informed that a patient is being so treated.

Drug interactions: Lentizol should not be administered concurrently or within 14 days of termination of treatment with MAO inhibitors. It should not be given with directly acting sympathomimetics, and should be used with caution when administered concurrently with anticholinergic drugs.

Lentizol may counteract the effect of adrenergic neurone blocking agents, and possibly clonidine, and therefore it would be advisable to review all anti-hypertensive therapy during treatment.

The action of Lentizol may be decreased by barbiturates, and potentiated by methyl phenidate.

Warnings: As improvement may not occur during the first 2–4 weeks of treatment, patients should be closely monitored during this period.

Amitriptyline may initially impair alertness. Patients could be warned of the possible hazard when driving or operating machinery.

Cardiac arrhythmias and severe hypotension are likely to occur with high dosage or in deliberate overdose. They may also occur in patients with pre-existing heart disease taking normal dosage.

Adverse effects: The following adverse effects, although not necessarily all reported with amitriptyline, have occurred with other tricyclic anti-depressants.

Amitriptyline may produce excessive perspiration and has some anticholinergic activity which may cause dryness of mouth, blurred vision, constipation, tachycardia and urinary retention. These symptoms are common but usually lessen on continuing therapy.

Other common adverse effects include postural hypotension, tremor and skin rashes. Interference with sexual function, nausea, anorexia and dizziness may also occur. Drowsiness may occur in some patients but this is usually controlled by reducing the dose. If necessary the dose may subsequently be gradually increased.

Serious adverse effects are rare; those reported include:

depression of the bone marrow, including agranulocytosis, cholestatic jaundice, hypomania, convulsions and peripheral neuropathy, paralytic ileus.

Psychotic manifestations, including mania and paranoid delusions, may be exacerbated during treatment with tricyclic anti-depressants.

Withdrawal symptoms may occur on abrupt cessation of therapy and include insomnia, irritability and excessive perspiration.

Adverse effects such as withdrawal symptoms, respiratory depression and agitation have been reported in neonates whose mothers had taken amitriptyline during the last trimester of pregnancy.

Precautions: Amitriptyline exerts an anticholinergic effect as well as antihistamine and adrenaline blocking actions. Large doses produce convulsions, coma, apnoea and cardiac irregularities, with intestinal stasis.

Treatment: Gastric lavage and emesis if appropriate. Vital signs should be continuously monitored and patients should be treated in ICUs wherever possible. General supportive measures with careful attention to electrolyte balance. Cardiac irregularities may need controlling with antiarrhythmic drugs and physostigmine salicylate is also indicated. Forced diuresis and haemodialysis have no place in treatment.

Pharmaceutical precautions Store in a dry place at temperature not exceeding 25°C.

Legal category POM.

Package quantities 50 mg: Bottles containing 50 and 250 capsules.

5 mg: Bottles containing 50 and 250 capsules.

Further information Nil.

Product licence numbers

0 mg 0019/5046

5 mg 0019/5045

MUCOLEX

Presentation *Mucorex Syrup*: Clear reddish syrup with a raspberry-menthol flavour containing carbocysteine 250 mg/5ml.

Mucorex Tablets: Round, convex orange tablet, each tablet containing 375 mg carbocysteine.

Uses Mucolytic agent for use in disorders of the respiratory tract in which an increase in the amount or viscosity of mucus is a prominent feature.

Dosage and administration Oral administration.

Mucorex Syrup: **Adults**: Three 5 ml spoonfuls three times a day initially; after a satisfactory response, this may be reduced to two 5 ml spoonfuls three times daily.

Children: (6–12 years): One 5 ml spoonful three times a day.

(2–5 years): 5–10 ml daily in divided doses.

Not recommended for children under 2 years.

Mucorex Tablets: **Adults**: Two tablets three times daily initially, after a satisfactory response, this may be reduced to one tablet four times daily.

Children: Not recommended.

Contra-indications, warnings, etc Carbocysteine is contra-indicated in cases of peptic ulcer, and is not recommended during the first trimester of pregnancy.

Treatment of overdose: Gastric lavage and supportive therapy.

Pharmaceutical precautions Protect from light.

Legal category POM.

Package quantities

Mucorex Syrup is contained in 250 ml glass bottles.

Mucorex Tablets are available in containers of 100.

Further information Nil.

Product licence numbers

Mucorex Syrup 0019/0066

Mucorex Tablets 0019/0069

NARDIL

Presentation Orange, sugar-coated tablets each containing 15 mg phenelzine (as the Sulphate BP).

Uses Phenelzine is a monoamine oxidase inhibitor. Nardil is indicated as follows:

Symptoms of depressive illness, especially where phobic symptoms are present or where treatment with other anti-depressants has failed.

Dosage and administration **Adults**: Oral administration.

One 15 mg tablet three times a day. A response is usually seen within the first week. If no response is evident after two weeks, the dosage may be increased to a maximum of one 15 mg tablet four times a day. Doses of up to two 15 mg tablets three times a day may be used in hospitals. The effectiveness of the drug may not become apparent in less than four weeks' therapy. After a satisfactory response has been achieved, the dosage may be reduced very gradually to a suitable maintenance level. This may be as low as one 15 mg tablet every other day.

Children: Nardil is not indicated for children.

Contra-indications, warnings, etc

Contra-indications: Nardil should not be given where there is any history of hepatic damage or insufficiency. Toxic hepatitis due to Nardil, as well as other monoamine oxidase inhibitors, has been reported. Incidence is low, occurring no more than once in every 37,500 courses of

treatment with Nardil. Contra-indicated in cerebrovascular disease. In general tricyclic anti-depressants, e.g. clomipramine, imipramine, desipramine, butriptyline, nortriptyline, protriptyline, should not be given with, or within 14 days of treatment with MAOI therapy; although it is recognised that there is some division of consultant opinion on this matter.

Nardil tablets contain gluten and are therefore contra-indicated in coeliac disease or gluten enteropathy.

Use in pregnancy: Do not use during pregnancy, especially during the first and last trimesters, unless there are compelling reasons. There is no evidence as to drug safety in human pregnancy nor is there evidence from animal work that it is free from hazard.

Precautions: Nardil may potentiate the action of pethidine, morphine, adrenaline, amphetamines and other sympathomimetic amines such as fenfluramine, ephedrine, phenylpropanolamine, dopamine and levodopa. Many patients on Nardil react quite normally to therapeutic doses of pethidine or morphine. However, if it is necessary to administer either of these drugs to a patient on Nardil, a trial dose of one-tenth to one-fifth of the normal dose should be given initially. If this is without adverse effect the dosage may be built up to the normal over a further period of two to three hours. Nardil may also potentiate the effects of anti-hypertensives, hypoglycaemic agents, sympathomimetics, anti-parkinson drugs, local anaesthetics and CNS depressants including barbiturates.

Nardil should be withdrawn two weeks before elective surgery/dentistry.

Patients under treatment with Nardil should avoid cheese, cooked or plain, and foods containing a high proportion of degraded protein – Oxo, Bovril, Marmite, etc – during treatment, and up to 14 days after ceasing treatment. Flavoured textured vegetable protein, hung game, pickled herrings or broad bean pods may also present a hazard. Patients should severely restrict their alcohol intake and heavy red wines, particularly Chianti, should be avoided completely. Patients should be warned against self-medication, particularly cold cures. Where a reaction between Nardil and certain foodstuffs occurs the intensity of the reaction is usually related to the tyramine content of the food. The reaction is now well recognised and serious hypertensive episodes are extremely rare. Should such a reaction occur, the hypertension should promptly be controlled by slow administration of phentolamine 5–10 mg i.v., repeated if necessary. Care should be taken in administering Nardil with trimipramine or amitriptyline.

Nardil should only be used with great caution in elderly or agitated patients, or those who have cardiovascular disease, epilepsy, blood dyscrasias, phaeochromocytoma or patients with liver toxicity, or diabetes; patients taking diuretics. Nardil may also potentiate the effects of alcohol.

Warnings and adverse effects: Minor side-effects are: dizziness, drowsiness, weakness and fatigue, oedema and gastro-intestinal disturbances (nausea, vomiting, dryness of the mouth, constipation), insomnia, blurred vision, adverse effects on driving ability and postural hypotension. Less common side-effects are: headache, nervousness, euphoria, paraesthesia, sweating, increased appetite and weight, rash, difficulty in micturition, muscle tremor, peripheral neuritis, behavioural changes, arrhythmias, convulsions, impotence and delayed ejaculation, purpura and blood dyscrasias.

Overdosage: Large doses may produce hypomania, followed by coma with hypotension, or acute hypertension with sometimes sub-arachnoid haemorrhage. In a few cases, extra-pyramidal symptoms have been recorded. Treatment – gastric lavage (tablets dissolve slowly in stomach). Absolute bed rest: raise feet in hypotension. Vasopressors are best avoided. Hypertension should be urgently controlled with phentolamine i.v. Avoid hypnotics, such as morphine, pethidine, barbiturates. Use phenothiazine derivatives (chlorpromazine) to control restlessness and intravenous therapy maintain fluid and electrolyte balance. In deep coma a severe hypotension hydrocortisone by injection may be tried. There is no specific antidote for Nardil.

Pharmaceutical precautions Store in a dry place at a temperature not exceeding 25°C.

Legal category POM.

Package quantity Bottles of 100 tablets.

Further information Nil.

Product licence number 0019/5018R.

OPILON* AMPOULES

Presentation Ampoules containing a sterile, colourless aqueous solution, free from turbidity and foreign particles. Each 1 ml Opilon Ampoule contains:

Thymoxamine hydrochloride BP	5.65 mg
(Moxisylyte Hydrochloride INN)	
equivalent to thymoxamine base	5.00 mg

Each 2 ml Opilon Forte Ampoule contains:

Thymoxamine hydrochloride BP	33.92 mg
(Moxisylyte Hydrochloride INN)	
equivalent to thymoxamine base	30.00 mg

Uses All conditions characterised by peripheral ischaemia responsive to alpha adrenergic blockade.

Intra-arterially, to counteract vasospasm in reconstructive surgery and before withdrawal of a needle catheter.

As an intra-arterial perfusion for treatment of rest pain and incipient gangrene.

Dosage and administration *Adults:* Parenteral administration.

1. As a single dose of 0.1 mg/kg body weight i.v. The dose may be given four times a day.

2. As a single dose of 0.1 mg/kg body weight i.v. which may be followed by oral therapy.

3. As an intra-arterial perfusion for treatment of rest pain and incipient gangrene. It is not recommended that this technique be carried out prior to consultation with the Product Licence Holder.

4. As a single dose of 5 mg into the distal end of an artery following arterial surgery or before withdrawal of a cardiac catheter.

Children: No dose recommended.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to any of the ingredients.

Warnings: The alpha adrenergic blocking action of Opilon may potentiate the effect of a number of drugs used in the management of hypertension. In practice with the recommended dosage of Opilon, difficulties have not been reported.

Precautions: Opilon should be used with caution in diabetes, theoretically, insulin requirements may be reduced. Tricyclic antidepressants may increase any potent effect produced by α -blockade. Opilon could also be used with caution in patients with anginal symptoms and in subjects who have had a recent coronary infarction.

The safety of Opilon for use during pregnancy and lactation has not been established.

Side-effects: Occasionally mild nausea, diarrhoea, vertigo, headache, and facial flushing may be encountered. These are, however, rare and transient.

Overdosage: In excessive overdosage, a fall in blood pressure is the main symptom. Nurse in head-down position and give an i.v. infusion of noradrenaline until the blood pressure has been restored to normal.

Pharmaceutical precautions Store at a temperature 2–8°C. Do not freeze. Protect from light.

Legal category POM.

Package quantities Opilon and Opilon Forte Ampoules are supplied in boxes of 10.

Further information Nil.

Product licence numbers

Opilon Ampoules 0019/5019
Opilon Forte Ampoules 0019/5020

PILON* TABLETS

Presentation Pale yellow, bi-convex tablets approximately 11 mm in diameter debossed 'Opilon' on one side and a bisecting score on the other. Each tablet contains:

Thymoxamine hydrochloride BP	45.22 mg
Moxisylyte Hydrochloride INN(M)	
Equivalent to thymoxamine base	40.00 mg

Uses Thymoxamine is an α adrenergic blocking agent. Opilon is indicated in all conditions characterised by peripheral ischaemia responsive to α adrenergic blockade, in particular those due to vasospasm such as Raynaud's phenomenon, chilblains, acrocyanosis, erythrocyanosis, excessively cold hands and feet and labyrinthine ischaemia (Ménière's syndrome).

Dosage and administration *Adults* – Oral administration.

One tablet to be swallowed four times a day. For those conditions affected by climatic environment 1 tablet should be administered every three hours during the 12-hour period when symptoms are most likely to occur.

Children: Opilon is not indicated for use in children.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to any of the ingredients.

Warnings: The α adrenergic blocking action of Opilon may potentiate the effect of a number of drugs used in the management of hypertension. In practice, with the recommended dosage of Opilon, difficulties have not been reported.

Precautions: Opilon should be used with caution in diabetes, theoretically, insulin requirements may be reduced. Tricyclic antidepressants may increase any hypotensive effect produced by α -blockade. Opilon should also be used with caution in patients with anginal

symptoms and in subjects who have had a recent coronary infarction.

The safety of Opilon for use during pregnancy and lactation has not been established.

Side-effects: Occasionally mild nausea, diarrhoea, vertigo, headache and facial flushing may be encountered. These are, however, rare and transient.

Overdosage: In excessive overdosage, a fall in blood pressure is the main symptom. Nurse in head-down position and give an i.v. infusion of noradrenaline until the blood pressure has been restored to normal.

Pharmaceutical precautions Store in a cool dry place, not exceeding 30°C.

Legal category POM.

Package quantities Opilon is supplied in bottles containing 50 and 250 tablets.

Further information Nil.

Product licence number 0019/5021.

ORALDENE*

Presentation A clear, red-coloured solution containing hexetidine 0.10%.

Uses Oraldene is an anti-infective agent indicated for mouth infections such as gingivitis, pyorrhoea, stomatitis. Also of value in aphthous ulcers, dental ulcers, halitosis, pre- and post-dental surgery and oral thrush and in geriatric nursing. It is also of value as an adjuvant to systemic therapy in tonsillitis and pharyngitis.

Dosage and administration *Adults and children:* Rinse the mouth or gargle with at least 15 ml of Oraldene two to three times a day. Oraldene should not be diluted.

Contra-indications, warnings, etc

Contra-indications: None known.

Warning: Oraldene is not to be taken internally.

Precautions: None applicable.

Side-effects: Very rarely, mild local irritation of the buccal tissues.

Overdosage: Hexetidine is a bactericide and fungicide. It is non-toxic in the strength used in this preparation. Acute intoxication with alcohol contained in the vehicle is unlikely even with massive doses.

Treatment: Treatment is rarely necessary.

Pharmaceutical precautions Store away from direct light.

Legal category GSL.

Package quantities Oraldene is supplied in clear glass bottles containing 100 ml, 200 ml and 1 litre (this size for hospital use only).

Further information Nil.

Product licence number 0019/5022.

RINUREL* LINCTUS

Presentation Yellow-coloured linctus. Each 5 ml contains:

Paracetamol Ph Eur	150.00 mg
Phenylpropanolamine Hydrochloride BP	12.50 mg

Phenyltoloxamine citrate	11.00 mg
Pholcodine Ph Eur	5.00 mg

Uses Rinurel Linctus provides analgesic, antipyretic, decongestant, antihistamine and antitussive properties.

Rinurel Linctus is indicated for symptomatic relief of unproductive cough, headache, sinus and facial pain, nasal and sinus congestion often associated with acute and chronic sinusitis, allergic and vasomotor rhinitis and upper and lower respiratory tract infections including influenza and the common cold.

Dosage and administration *Adults:* Two 5 ml spoonfuls to be taken orally four times daily.

Children (6–12 years): One 5 ml spoonful to be taken orally four times daily.

(2–5 years): 2.5 ml to be taken orally four times daily.

Contra-indications, warnings, etc

Contra-indications: Contra-indicated in persons whose sensitivity to small doses of sympathomimetic agents is manifested by sleeplessness, dizziness, light-headedness, weakness, tremors or cardiac arrhythmias.

Warnings: If drowsiness occurs, patients should not drive or operate machinery.

Alcohol or barbiturates should not be taken concomitantly.

Precautions: Caution should be exercised in patients with hyperthyroidism, hypertension, cardiac dysfunction, diabetes mellitus and liver disorders. Rinurel Linctus should not be used during treatment with MAO inhibitors or for two weeks after completion of therapy.

Not recommended during the first trimester of pregnancy.

Side-effects: Drowsiness, dryness of mouth and mild stimulation have been occasionally reported.

Overdosage: Drowsiness, palpitations, weakness and inco-ordination. Later delayed acute liver failure.

Treatment: Gastric lavage. If possible check plasma paracetamol level. Within 10 hours of ingestion give methionine orally or cysteamine i.v. Otherwise take generally supportive measures.

Pharmaceutical precautions No special precautions.

Legal category P.

Package quantities Bottles containing 200 ml.

Further information Rinurel Linctus may be diluted with Syrup BP when prescribing for young children.

Product licence number 0019/5031.

RINUREL* TABLETS

Presentation Pink tablets, scored once. Each tablet contains:

Paracetamol Ph Eur	300.0 mg
Phenylpropanolamine Hydrochloride BP	25.0 mg
Phenyltoloxamine citrate	22.0 mg

Uses Rinurel Tablets provide analgesic, antipyretic, decongestant and antihistamine properties.

Rinurel Tablets are indicated for the symptomatic relief of headache, sinus and facial pain, nasal and sinus congestion often associated with acute and chronic sinusitis, allergic and vasomotor rhinitis, influenza and the common cold.

Dosage and administration *Adults:* 2 tablets to be swallowed initially, followed by 1 tablet every four hours. Do not exceed 6 tablets in 24 hours.

Children (5–12 years): Half adult dose.

Contra-indications, warnings, etc

Contra-indications: Contra-indicated in persons whose sensitivity to small doses of sympathomimetic agents manifested by sleeplessness, dizziness, light-headedness, weakness, tremors or cardiac arrhythmias.

Warnings: If drowsiness occurs, patients should not drive or operate machinery.

Alcohol or barbiturates should not be taken concomitantly.

Precautions: Caution should be exercised in patient with hyperthyroidism, hypertension, cardiac dysfunction, diabetes mellitus and liver disorders. Rinurel should not be used during treatment with MAO inhibitors or for two weeks after completion of therapy.

Not recommended during the first trimester of pregnancy.

Side-effects: Drowsiness, dryness of mouth and mild stimulation have been occasionally reported.

Overdosage: Drowsiness, palpitations, weakness and inco-ordination. Later delayed acute liver failure.

Treatment: Gastric lavage. If possible check plasma paracetamol level. Within 10 hours of ingestion give methionine orally or cysteamine i.v. Otherwise take generally supportive measures.

Pharmaceutical precautions Store in a dry place.

Legal category P.

Package quantity Bottles containing 250 tablets.

Further information Nil.

Product licence number 0019/5029.

RINUREL* SA TABLETS

Presentation Pink, oval-shaped tablets, two layered and scored once. Each tablet contains:

Paracetamol Ph Eur	600.0 mg
Phenylpropanolamine Hydrochloride BP	100.0 mg
Phenyltoloxamine citrate	66.0 mg

Uses Rinurel SA Tablets provide analgesic, antipyretic, decongestant and antihistamine properties.

Indicated for prolonged symptomatic relief of headache, sinus and facial pain, nasal and sinus congestion often associated with acute and chronic sinusitis, allergic and vasomotor rhinitis, influenza and the common cold.

Dosage and administration *Adults:* 1 tablet to be swallowed whole every 12 hours.

Children (5–12 years): Half adult dose.

Contra-indications, warnings, etc

Contra-indications: Contra-indicated in persons whose sensitivity to small doses of sympathomimetic agents is manifested by sleeplessness, dizziness, light-headedness, weakness, tremors or cardiac arrhythmias.

Warnings: If drowsiness occurs, patients should not drive or operate machinery.

Alcohol or barbiturates should not be taken concomitantly.

recautions: Caution should be exercised in patients with hyperthyroidism, hypertension, cardiac dysfunction, diabetes mellitus and liver disorders. Rinurel SA tablets should not be used during treatment with MAO inhibitors or for two weeks after completion of therapy. Not recommended during the first trimester of pregnancy.

ide-effects: Drowsiness, dryness of mouth and mild stimulation have been occasionally reported.

verdosage: Drowsiness, palpitations, weakness and inco-ordination. Later delayed acute liver failure.

reatment: Gastric lavage. If possible check plasma acetamol level. Within 10 hours of ingestion give methionine orally or cysteamine i.v. Otherwise take generally supportive measures.

harmaceutical precautions Store in a dry place.

egal category POM.

ackage quantity Bottles containing 250 tablets.

urther information Nil.

roduct licence number 0019/5030.

TEDRAL* TABLETS

resentation Each white, bi-convex tablet contains:

Theophylline Ph Eur	120 mg
Ephedrine Hydrochloride Ph Eur	24 mg

Uses Tedral is for symptomatic relief of bronchospasm in bronchial asthma, chronic bronchitis and hay fever.

Dosage and administration Oral. *Adults:* 1 tablet every four hours.

Children (6–12 years): $\frac{1}{2}$ tablet every four hours, preferably after meals.

Contra-indications, warnings, etc

Contra-indications: Sensitivity to any of the ingredients.

Precautions and warnings: Tedral should not be administered to patients who are being treated with MAO inhibitors, or have received them within the preceding 14 days. It should not normally be administered during pregnancy and lactation. It should be used with caution in patients who are suffering from cardiovascular disorders, severe hypertension, hyperthyroidism, prostatic hypertrophy or glaucoma.

Side-effects: Difficulty in micturition, mild epigastric distress, palpitations, tremulousness, insomnia and CNS stimulation have been reported.

Overdosage: Irritation of alimentary tract. Nausea, vomiting and giddiness.

Treatment: Gastric lavage. Use general supportive measures.

Pharmaceutical precautions No special precautions.

Legal category POM.

Package quantities Tedral Tablets are packed in brown glass bottles containing 50 and 500 tablets.

Further information Nil.

Product licence number 0019/5036.

TEDRAL* EXPECTORANT

Presentation Tedral Expectorant is a clear viscous liquid with an orange-ginger taste, each 5 ml containing:

Diprophylline Ph Eur	100 mg
Ephedrine Hydrochloride Ph Eur	10 mg
Guaiphenesin BPC 1973	50 mg

Uses Tedral Expectorant is a bronchodilator and expectorant indicated in chronic bronchitis, coughs associated with bronchial congestion, influenza, bronchial asthma associated with retained bronchial secretions, and other conditions where tenacious sputum is a problem.

Dosage and administration *Adults:* Two 5 ml spoonfuls every four hours, preferably after meals.

Children (6–12 years): One 5 ml spoonful every four hours, preferably after meals.

Contra-indications, warnings, etc

Contra-indications: Sensitivity to any of the ingredients.

Precautions and warnings: Tedral Expectorant should not be administered to patients who are receiving MAO inhibitors, or who have received them within the preceding 14 days. It should not normally be administered during pregnancy and lactation. It should be used with caution in patients who are suffering from cardiovascular disorders, severe hypertension, hyperthyroidism, prostatic hypertrophy or glaucoma.

Side-effects: Difficulty in micturition, mild epigastric distress, palpitation, tremulousness, insomnia and CNS stimulation have been reported.

Overdosage: Irritation of alimentary tract. Nausea, vomiting and giddiness.

Treatment: Gastric lavage. Use general supportive measures.

Pharmaceutical precautions Store at a temperature, not exceeding 25°C.

Legal category POM.

Package quantities Tedral Expectorant is available in brown glass bottles containing 200 ml.

Further information Nil.

Product licence number 0019/0039.

TEDRAL* SA

Presentation A double-layered tablet consisting of a mottled coral colour, sustained-release layer and a white with pink mottled, immediate-release layer. Each tablet contains:

Theophylline Ph Eur	180.0 mg
Ephedrine Hydrochloride Ph Eur	48.0 mg

Uses Tedral SA is for symptomatic relief of bronchospasm in bronchial asthma, chronic bronchitis and hay fever.

Dosage and administration Oral. *Adults:* 1 tablet in the morning and 1 tablet 12 hours later.

Children (6–12 years): $\frac{1}{2}$ tablet in the morning and $\frac{1}{2}$ tablet 12 hours later, preferably after meals. The tablet should be cut from the pink layer through to the white layer.

Contra-indications, warnings, etc

Contra-indications: Sensitivity to any of the ingredients.

Precautions and warnings: Tedral SA should not be administered to patients who are receiving MAO inhibitors, or who have received them within the preceding 14 days. It should not normally be administered during pregnancy and lactation. It should be used with caution in patients who are suffering from cardiovascular disorders, severe hypertension, hyperthyroidism, prostatic hypertrophy or glaucoma.

Side-effects: Difficulty in micturition, mild epigastric distress, palpitations, tremulousness, insomnia and CNS stimulation have been reported.

Overdosage: Irritation of alimentary tract. Nausea, vomiting and giddiness.

Treatment: Gastric lavage. Use general supportive measures.

Pharmaceutical precautions No special precautions.

Legal category POM.

Package quantities Tedral SA Tablets are packed in bottles containing 100 and 500 tablets.

Further information Nil.

Product licence number 0019/5037.

VEGANIN*

Presentation White scored tablets containing:

Paracetamol Ph Eur	250.0 mg
Aspirin Ph Eur	250.0 mg
Codeine Phosphate Ph Eur	6.80 mg

Uses Veganin provides analgesic and antipyretic properties. It is indicated in influenza and other conditions which require an antipyretic and for all kinds of mild to moderate pain, especially headache, dysmenorrhoea, rheumatism and toothache.

Dosage and administration Oral. *Adults:* 1 or 2 tablets to be swallowed every three to four hours up to a maximum of 8 tablets in 24 hours.

Children (6–12 years): Half to one tablet to be swallowed every four hours up to a maximum of four tablets in 24 hours.

(under 6 years): Not recommended.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to any of the components. Veganin is contra-indicated in patients suffering from active peptic ulceration and haemophilia.

Precautions and drug interactions: There is clinical and epidemiological evidence of safety of aspirin and paracetamol in human pregnancy, but the safety of codeine in pregnancy has not been established. Aspirin may prolong labour and contribute to maternal and neonatal bleeding and is best avoided at term. Aspirin may increase the anticoagulant effects of coumarin derivatives, and inhibit the action of uricosurics. It may also precipitate bronchospasm and induce attacks of asthma in susceptible subjects. Veganin should be used with caution in patients with impaired renal or hepatic function.

Warnings and adverse effects: Codeine is a narcotic analgesic and tolerance, psychological and physical dependence and constipation may occur. Aspirin may induce gastro-intestinal haemorrhage, which may very occasionally be severe.

Overdosage: Nausea, dizziness, ataxia, tinnitus, deafness, vomiting, electrolyte imbalance, delayed acute liver failure. An overdose can cause hepatic necrosis.

Treatment: Urgently check plasma levels of acetylsalicylic acid and paracetamol. If the a.s.a. level is above 50 mg/100 ml use forced alkaline diuresis. If more than 30–40 tablets taken and within 10 hours of ingestion give methionine immediately by mouth or acetylcysteine i.v.

Pharmaceutical precautions Store in a dry place.

Legal category P.

Package quantities Veganin is supplied in blister packs containing 10, 20 and 50 tablets.

Further information Nil.

Product licence number 0019/5041R.

*Trade Mark

VB Pharmaceuticals Limited

P.O. Box 23

Bracknell

Berkshire RG12 4YS



EROTEC*

Presentation Pressurised metered inhaler: 10 ml vial (200 metered doses) available as complete unit with mouthpiece. Each metered dose contains fenoterol hydrobromide 0.2 mg (0.18 mg available to the patient).

Uses *Action:* Berotec is a highly potent, rapidly acting, selective β_2 - adrenergic stimulant with a duration of action of 6-8 hours. The degree of selectivity coupled with administration by inhalation allows maximal bronchodilator effect with minimal side-effects.

Indications: For the treatment of reversible airways obstruction as in bronchial asthma, bronchitis and emphysema.

Dosage and administration By inhalation.

As Berotec has a longer duration of action than other bronchodilators a dosage of 1 or 2 puffs three times daily is usually sufficient to control bronchospasm in adults. If necessary this may be increased up to 2 puffs every four hours. Children (6-12 years) will normally require 1 puff three times daily but this may be increased up to 1 puff every four hours if necessary. It is recommended that administration of Berotec to children should be supervised by a responsible adult.

Contra-indications, warnings, etc

Contra-indications: There are no absolute contra-indications to the use of Berotec.

Precautions: Caution should be observed should it be necessary to administer Berotec to patients with thyrotoxicosis, myocardial insufficiency, angina, cardiac dysrhythmias, hypertension or hypertrophic subvalvular aortic stenosis.

In view of the possible interaction between sympathomimetic amines and monoamine oxidase inhibitors or cyclic anti-depressants, care should be exercised if it is proposed to administer these compounds concurrently with Berotec.

Berotec should be used with caution in patients already receiving other sympathomimetic agents as cardiovascular effects may be additive.

Patients must be instructed in the correct use of a metered inhaler and warned not to exceed the prescribed dose. If relief is not obtained after correct use of the inhaler, the dose should not be exceeded and the patient should contact the doctor for advice.

Although Berotec has been in wide general use for several years, there is no definite evidence of ill consequence during human pregnancy. Animal studies have shown no hazard.

Berotec treatment may result in the prolongation of pregnancy and inhibition of labour.

Medicines should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

Beta-adrenergic blocking agents may antagonise berotec and reduce its bronchodilator effect if administered concurrently.

A temporary dose-related decrease in serum potassium levels has been observed in some patients.

Side-effects: Transient sympathomimetic side-effects, such as palpitation, tachycardia, headache and tremor may occur, as with other beta-adrenergic agonists, but are uncommon with administration by inhaler.

Overdosage: Accidental overdosage may give rise to tachycardia, palpitation and tremor. It is suggested that the patient should be treated symptomatically.

Should the administration of a beta-adrenergic blocking agent be considered necessary to counteract the effects of overdosage, its use in a patient liable to bronchospasm should be carefully monitored.

Pharmaceutical precautions Protect from heat, including the sun.

The inhaler vial should not be incinerated or opened even when empty.

Legal category POM.

Package quantities 10 ml vial (200 metered doses) complete with mouthpiece.

Further information There is evidence to suggest that Berotec may reduce the allergic response of tissues. Animal studies have shown that Berotec also produces an increase in the frequency of movement of the respiratory epithelial cilia and in the rate of mucus transport.

Long-term use has shown Berotec to be free from significant adverse effects, particularly with respect to the blood gases and general biochemistry. Tolerance is not a feature of long-term use.

Product licence number 0015/0034.

CELEVAC*

Presentation Methylcellulose 450 BP as pink granules containing 64% and pink tablets containing 500 mg.

Uses *Action:* Methylcellulose is a hydrophilic colloid which absorbs water to swell to a soft gel of uniform consistency.

Indications:

1. Colostomy, ileostomy and simple diarrhoea.
2. Diverticular disease and ulcerative colitis.
3. Simple constipation.
4. Obesity.
5. Liquid and tube fed diets.

Dosage and administration

1. *Colostomy and ileostomy control and for simple diarrhoea:* 1-2 level 5 ml spoonfuls of granules (or 3-6 tablets) twice daily with the minimum of liquid. Liquids should be avoided for 30 minutes before and after each dose. Dosage should be adjusted to give stools the required consistency.

2. *Diverticular disease and ulcerative colitis:* 3-6 tablets

or 1–2 level 5 ml spoonfuls of granules twice daily, adjusted according to the degree of constipation, diarrhoea or spastic pain.

3. **Simple constipation:** 1–2 level 5 ml spoonfuls of granules (or 3–6 tablets) twice daily, to be taken with at least 300 ml of liquid. The dose may be reduced as normal bowel function is restored.

4. **Obesity:** 3 tablets, with at least 300 ml of warm liquid, half an hour before each meal, and between meals when hunger pangs are severe.

5. **Liquid diet and intragastric tube feeding:** 1 level 5 ml spoonful of granules, dispersed in hot water, added to each litre of diet mix.

Contra-indications, warnings, etc Imminent or threatened bowel obstruction. Bowel obstruction is a rare complication of treatment with any bulk-forming hydrophilic colloid.

Although Celevac has been in wide general use for many years there is no evidence of ill-consequence during human pregnancy.

Medicines should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

Overdosage: Methylcellulose is not absorbed. The features to be expected would be abdominal distension which may be followed by intestinal obstruction.

Gastric lavage should be employed where appropriate. The patient should be observed and fluids given. If obstruction develops, appropriate measures such as rectal washout must be taken.

Pharmaceutical precautions Protect from heat and moisture.

Legal category GSL.

Package quantities Granules packs of 500 g. Tablets packs of 250.

Further information Methylcellulose is a hydrophilic colloid which bonds loosely with H₂O and with H₂S, thus acting as a bulking agent and a deodorising agent. In diverticular disease its use has been associated with a fall in intracolonic pressures as well as relief of symptoms.

Product licence numbers

Celevac Granules 1416/5000
Celevac Tablets 1416/5003

DIXARIT®

Presentation Blue, bi-convex, sugar-coated tablets with the Company initials on one side. Each tablet contains clonidine hydrochloride 0.025 mg.

Uses **Action:** Treatment with Dixarit diminishes the responsiveness of peripheral vessels to constrictor and dilator stimuli, thereby preventing the vascular changes associated with migraine. The same direct action on peripheral vessels moderates the vascular changes associated with menopausal flushing.

Indications:

1. The prophylactic management of migraine or recurrent vascular headache.

2. The management of vasomotor conditions commonly associated with the menopause and characterised by flushing.

Dosage and administration **Adults:** Initially 2 tablets

twice daily. If after two weeks there has been a remission, increase to 3 tablets twice daily.

Children: Not generally recommended for administration to children under 12 years.

The duration of treatment depends upon the severity of the condition.

Contra-indications, warnings, etc

Contra-indications: There are no known absolute contraindications to the use of Dixarit.

Precautions: Dixarit may be unsuitable for patients who have co-existing or a previous history of depressive illness, since further depressive episodes have occasionally been reported in such patients.

Although clonidine has been in wide general use for many years there is no definite hazard during human pregnancy.

In animal studies involving doses higher than the equivalent maximum therapeutic dose in man, effects on foetal development were only seen in one species. Foetal malformations did not occur.

Medicines should not be used in pregnancy, especially the first trimester unless the expected benefit is thought to outweigh any possible risk to the foetus.

Using higher doses than those recommended above, clonidine is an effective antihypertensive agent. Caution should therefore be observed where antihypertensive agents are being used as potentiation of hypotensive effect may occur. Provided the recommended Dixarit dosage regimen is followed, no difficulty with hypertension should arise during the routine management of patients with either migraine or menopausal flushing.

Clonidine is available for the management of hypertension as Catapres Tablets (0.10 mg and 0.30 mg Perlongets (0.25 mg) and Ampoules (0.15 mg in 1 ml (Boehringer Ingelheim Ltd). Where Catapres is already being used Dixarit therapy is obviously illogical.

Side-effects: Initially there may be sedation or dry mouth in some patients. Dizziness, nausea and nocturnal urination have been reported, and occasionally rashes have been attributed to Dixarit.

In the management of hypertension a single case of toxic hepatitis has been reported with clonidine. However, the role of clonidine in hepatotoxicity in this patient remains questionable. Monitoring of haematological, renal and hepatic status in large numbers of patients has revealed no drug-related adverse effects.

Overdosage: Accidental overdosage may cause hypotension, bradycardia, sedation and coma. Transient hypertension may be seen if the total is over 10 mg.

Gastric lavage should be performed where appropriate. In most cases all that is required are general supportive measures. Forced diuresis has been employed. Where bradycardia is severe atropine will increase the heart rate. If hypotension is giving rise to concern the administration of an alpha-adrenergic blocking drug such as phentolamine may help.

Pharmaceutical precautions Protect from heat and moisture and light.

Legal category POM.

Package quantities Packs of 100.

Further information There is no information which suggests that Dixarit will interact with any other preparation used routinely in the management of either migraine or menopausal flushing.

Product licence number 0015/5014.

ENDOXYANA®

resentation White, compression-coated tablets containing Cyclophosphamide BP 10 mg or 50 mg; marked /BP E1 on one side and either 10 or 50 on the reverse. /hite powder in vials for injection containing Cyclophosphamide BP 107 mg, 214 mg, 535 mg or 1,069 mg (equivalent to 100 mg, 200 mg, 500 mg or 1,000 mg anhydrous cyclophosphamide, respectively) and sodium chloride sufficient to render isotonic when diluted with water for Injections using the volume recommended for each strength.

ses Action: Cyclophosphamide is a potent alkylating agent although the compound itself is inert until activated by microsomal enzymes. The main organ of activation is the liver. Several of the metabolites are cytotoxic.

indications: Endoxana is a cytotoxic drug for the treatment of malignant disease.

Used as a single agent it has successfully produced an objective remission in a wide range of malignant conditions. Endoxana is also frequently used in combination with other cytotoxic drugs.

osage and administration Endoxana should only be used by clinicians experienced in the use of cytotoxic drugs.

osage: The dose, route of administration and frequency of administration should be determined by the tumour type, tumour staging, the general condition of the patient and whether other chemotherapy or radiation is to be administered concurrently.

A guide to the dosage regimes used for most indications is given below:

ow dose – 2–6 mg/kg (80–240 mg/m²) daily as a single i.v. dose or orally.

Medium dose: 10–15 mg/kg (400–600 mg/m²) as a single i.v. dose weekly.

Large dose: 20–40 mg/kg (800–1600 mg/m²) as a single i.v. dose given at 10–20 day intervals.

High dose: 60–80 mg/kg (2.4–3.2 g/m²) as a single i.v. dose at three to four week intervals.

administration: The dry contents of a vial may be mixed with sterile water (5 ml per 100 mg Endoxana) and used within two hours. The pH of an aqueous solution is between 4.5 and 5.5. Endoxana is usually given directly into the vein over one or two minutes or directly into the tubing of an infusion with the patient supine. It is not recommended that Endoxana be given by infusion over longer than 30 minutes. Should the drug accidentally be given paravenously local tissue damage is unlikely and no specific measures need be taken. Endoxana injection may also be given intraperitoneally, intrapleurally, intrathecally or by local perfusion but these routes offer no therapeutic advantages over the i.v. route. The dosage recommendations are as above.

A minimum urine output of 2–3 l/day should be maintained during therapy to avoid cystitis. If larger doses are used a urine output of 4–5 l/day should be maintained for 24 hours following administration, by a forced alkaline diuresis.

Endoxana should be given during the day so that the bladder may be voided frequently. Nausea and vomiting may be reduced by the prior administration of an antiemetic. Treatment with Endoxana should be temporarily withheld if the leucocyte count is below 4,000/mm³ or the platelet count below 100,000/mm³.

An elixir may be prepared by dissolving the contents

of the dry powder vials in Aromatic Elixir USP shortly before use.

Contra-indications, warnings, etc *Contra-indications:* Endoxana should only be administered under the direction of a specialist oncology service having facilities for regular monitoring of clinical, biochemical and haematological effects during and after administration.

Endoxana is contra-indicated in patients with haematuria or cystitis, with known hypersensitivity, with acute infections, or with bone marrow aplasia.

Endoxana should not be used in the management of non-malignant disease, except for immuno-suppression in life-threatening situations.

Endoxana should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh the substantial risk to the foetus.

Contraception is advised during Endoxana therapy and for at least nine months following treatment. Mothers should not breast-feed while being treated with Endoxana.

Precautions: Care should be exercised in patients who are elderly, debilitated, have diabetes mellitus or evidence of myelosuppression or who have recently received radiotherapy or cytotoxic agents.

Endoxana is not recommended in patients with serum creatinine greater than 120 µmol/l, bilirubin greater than 17 µmol/l or with transaminases or alkaline phosphatase more than 2–3 times the normal value.

Increased myelosuppression may be seen following concurrent administration of other marrow depressant drugs.

Endoxana potentiates the hypoglycaemic effects of the sulphonylurea compounds. An alteration in carbohydrate metabolism may be seen in patients on Endoxana.

Side-effects: Nausea and vomiting. This may be reduced by the prior administration of an anti-emetic.

Epilation occurs to some degree in about 20% of patients receiving over 100 mg daily and is inevitable following high doses. Epilation commences usually after the first three weeks of treatment but regrowth is evident after three months in most patients even though they remain on treatment.

The reticulo-endothelial system is depressed, granulopoiesis and lymphopoiesis being more affected than thrombopoiesis and erythropoiesis, but this depression is reversible. Following a single dose the fall in the peripheral white cell count reaches a nadir between 5 to 10 days following administration. Recovery is seen from 10–14 days following administration with full recovery in most cases by 21–28 days. The fall in the peripheral count and the recovery time increase with increasing amounts of Endoxana administered. If the peripheral white cell count is very low, increased risk of infection should be considered but since recovery is usually spontaneous steroids are not recommended.

Cystitis is usually controllable by maintaining an adequate urine output. The daily urine output should never be less than 2–3 litres on low and medium doses and should be increased with larger doses of Endoxana. The administration of a diuretic is sometimes advisable especially with larger doses as Endoxana may cause water retention. Frequent emptying of the bladder is recommended. Endoxana should be withheld from patients with cystitis from any cause, until it has been treated.

Amenorrhoea and azoospermia often occur but can be reversible.

Other side-effects such as pigmentation, macrocytosis, water retention and induction of hyperglycaemia have been reported. Following large doses, ECG changes, elevation of LDH, SGOT and CPK have been reported in some patients.

Endoxana has been shown to be mutagenic, teratogenic and carcinogenic in certain laboratory tests, and, as with other cytotoxic agents, there have been reports of possible drug-induced neoplasia.

Overdosage: The most serious consequences of overdosage are suppression of the reticulo-endothelial system and haemorrhagic cystitis. The former usually recovers spontaneously, but until it does, administration of a broad spectrum antibiotic (or possibly gammaglobulin) may be advisable. Transfusions of whole-blood, platelets or white cells are rarely necessary.

Cystitis should be treated with analgesics and the maintenance of a high urine output by a high IV fluid intake in conjunction with a diuretic if necessary. Haemorrhagic cystitis usually resolves on stopping Endoxana. In severe cases more intensive management may be necessary. Intravesical instillation of 200–300 ml of a 5% formalin solution for 15 minutes followed by a washout with 1 litre distilled water has been successful. Care should be taken to prevent ureteric reflux. If this fails a urological opinion should be sought with a view to bladder tamponade, cautery or surgery. Blood transfusions should also be given if clinically indicated.

No further courses of Endoxana should be given until the patient has fully recovered.

Cardiotoxicity has been observed with high doses of Endoxana. Endoxana should be discontinued and where necessary, treatment with bed-rest, diuretics, oxygen and digitalis should be considered.

Pharmaceutical precautions Store below 30°C; protect from light. The solution for parenteral use should be used within two hours of preparation.

Legal category POM.

Package quantities

10 mg tablets in containers of 100.
50 mg tablets in containers of 300.
100 mg dry vials in boxes of 10.
200 mg dry vials in boxes of 10.
500 mg dry vials, singles.
1,000 mg dry vials, singles.

Further information Nil.

Product licence numbers

Tablets of 10 mg	1416/5011
Tablets of 50 mg	1416/5012
Vials of 100 mg	1416/5013
Vials of 200 mg	1416/5014
Vials of 500 mg	1416/5015
Vials of 1,000 mg	1416/5016

HERPID*

Presentation A clear, colourless solution containing Idoxuridine BP in dimethyl sulphoxide, of spectroscopic quality 5%.

Uses Action: The antiviral agent idoxuridine arrests replication of DNA viruses, e.g. varicella/zoster; herpes-virus hominis; vaccinia. The idoxuridine is dissolved in dimethyl sulphoxide which penetrates the skin and carries the antiviral agent to the deeper levels of the epidermis where the virus is replicating.

Indications: Cutaneous herpes simplex and herpes zoster (shingles).

Dosage and administration Herpid should be painted on the lesions and their erythematous bases times daily for four days. Treatment should start as soon as the condition has been diagnosed, ideally within two to three days after the rash appears. Good results are less likely if treatment is not started within seven days.

Contra-indications, warnings, etc

Contra-indications: Animal studies have shown idoxuridine to be teratogenic. Consequently, Herpid should not be prescribed for women who are pregnant or at risk of becoming pregnant. In a small number of cases, women who used Herpid inadvertently in early pregnancy and who were followed to term, the infant was normal in each case.

Known hypersensitivity to either idoxuridine or dimethyl sulphoxide.

Dermographia.

Side-effects: Patients often experience stinging when applying Herpid and a distinctive taste during a course of treatment; both effects are transient.

Over-usage of the solution may lead to maceration of the skin.

Warning: Herpid in the eye causes stinging; treat by washing out with water.

Overdosage: There is no clinical experience of overdosage. Standard supportive measures should be adopted.

Pharmaceutical precautions Herpid should be stored in its box at room temperature. Do not refrigerate as the contents of the bottle may solidify. If crystals do form, allow to redissolve before use.

Because the solution is hygroscopic, any remaining after completion of treatment should be discarded.

Legal category POM.

Package quantities 5 ml bottle, with brush.

Further information Herpid can damage some synthetic materials (e.g. artificial silk and terylene) and printed cotton fabrics. Contact between Herpid and these materials should therefore be avoided.

The use of Herpid in children with malignant disease might be justified but, although not a contra-indication its use in children under the age of 12 years is not recommended.

Product licence number 1416/0001.

HONVAN*

Presentation White tablets marked $\frac{WBP}{H}$ on one side containing tetrasodium fosfestrol 100 mg and 5 ml ampoules containing tetrasodium fosfestrol 276 mg.

Uses Action: Honvan is a water-soluble synthetic oestrogen which is inert until activated by dephosphorylation at sites of high phosphatase (particularly acid phosphatase) activity, releasing high local concentrations of oestrogen which have been demonstrated to exert a cytotoxic effect in animals. The localisation of activity reduces systemic effects, in particular adrenal hypertrophy, often associated with conventional hormonal treatment. Honvan administered in lower oral doses is comparable with conventional hormonal therapy.

Indications: Honvan is a cytotoxic drug for the treatment of all stages of prostatic carcinoma. Honvan may be used as an adjuvant to surgery, in inoperable cases and for the reduction of pain due to metastases. Patients who are resistant to conventional hormone therapy have responded to Honvan. Where acute retention has occurred the use of Honvan may reduce the need for transurethral resection.

Dosage and administration *Initial therapy: Acute retention of urine and Relapse:* 2–4 ampoules Honvan intravenously as a single injection daily for at least five days or until a response has been obtained (seven to ten days). The patient should preferably be lying down and the injection given slowly, directly into the vein. Slow infusions are not recommended as high local cytotoxic levels may not be achieved.

Maintenance: 1 ampoule intravenously one to four times weekly.

Oral maintenance therapy is usually 1–6 tablets daily in divided doses. The initial dose should be up to 2 tablets three times daily for the first week, reducing over the next two weeks to the lowest dose that will control the disease which is usually from 1 to 3 tablets daily in divided doses.

Contra-indications, warnings, etc There are no absolute contra-indications to the use of Honvan. Honvan should only be administered under the direction of a specialist oncology service having facilities for the regular monitoring of clinical, biochemical and haematological effects during and after administration.

Caution is advised when using Honvan in patients with poor cardiac reserve or fluid retention, and in these cases concomitant diuretic therapy may be indicated. In rare cases hypersensitivity to Honvan has been noted.

Honvan should not be administered to pregnant women as oestrogens have been shown to produce a teratogenic effect in the female foetus.

Side-effects: A burning in the perineum and pain in bony metastases may occur during or immediately after intravenous injection. Perineal discomfort may be reduced by prior administration of a sedative.

Nausea and vomiting may occur, but will be less severe than with hormone therapy; oedema and lung congestion have been reported, but there is no evidence of an increased incidence of cardiovascular disease. After prolonged high dosage, feminising side-effects which may occur, due to leak of oestrogen from sites of ephosphorylation, will be less marked than those occurring during conventional hormonal therapy.

Honvan is non-irritant to the veins and should not be injected accidentally into the paravenous tissue no specific action is necessary.

Overdosage: In the event of overdosage, monitoring for fluid retention should be undertaken and in patients with cardiac disease, the administration of diuretics and digitalis should be considered.

Pharmaceutical precautions Store in a cool place. Incompatible with aqueous solutions of pH less than 7 and solutions containing calcium or magnesium ions.

Legal category POM.

Package quantities Ampoules in boxes of 10 × 5 ml. Tablets in containers of 100.

Further information Response to treatment with

Honvan may be objectively assessed by the degree of reduction in plasma acid phosphatase concentrations and by the reduction in size of: the primary prostatic tumour, cutaneous, subcutaneous or lymph node metastases, bone lesions or visceral metastases. Subjective assessment may be made by the reduction in pain, improvement in urinary function and improvement in patient well-being.

Product licence numbers

Honvan Tablets	1416/5023
Honvan Ampoules	1416/5022

LAXOBERAL®

Presentation A clear, yellowish orange, fruit-flavoured liquid containing sodium picosulphate 5 mg per 5 ml.

Uses Action: Laxoberal contains a synthetic laxative, sodium picosulphate, which is broken down by bacteria in the large intestine to the active substance, bis-(p-hydroxyphenyl)-2-pyridyl methane. A predictable evacuation of soft formed stools occurs usually 10–14 hours after administration.

Indications: Constipation, either recent or chronic, whenever a stimulant laxative is required. Bowel clearance before surgery, labour or radiological investigations.

Laxoberal is suitable for routine use in both adults and children.

Dosage and administration *Adults:* 5–15 ml at night.

Children: 5–10 years: 2.5–5 ml at night.

0–5 years: 2.5 ml at night.

Diluent: Laxoberal may be diluted with purified water.

Contra-indications, warnings, etc

Contra-indications: As with any laxative. Laxoberal should not be given to patients with undiagnosed abdominal pain, or where intestinal obstruction is suspected.

Precautions: It is generally recommended that laxatives should not be given to patients being prepared for barium enema examinations where inflammatory bowel disease, such as ulcerative colitis, is suspected. This recommendation applies also to Laxoberal.

As Laxoberal is broken down by bacteria in the large intestine, it is possible that in patients taking broad-spectrum antibiotics there may be some loss of laxative action.

Although Laxoberal has been in wide general use for many years, there is no evidence of ill-consequence during human pregnancy.

Only in doses much higher than the equivalent maximum therapeutic dose in man were effects on foetal development seen in animals. Drug-induced foetal malformations did not occur.

Medicines should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

Side-effects: As with most laxatives of this group there have been occasional reports of mild abdominal discomfort following Laxoberal administration.

Overdosage: Colicky lower abdominal pain and possible signs of dehydration may be expected particularly in the elderly and the very young.

Gastric lavage should be performed where appropriate. Adequate hydration must be maintained and the serum potassium should be measured. Antispasmodics may be

of value. Particular care about fluid balance should be taken in the elderly and young.

Pharmaceutical precautions Laxoberal should be stored at room temperature and protected from light.

Legal category P.

Package quantities 100 ml and 500 ml.

Further information Nil.

Product licence number 1416/0007.

METHRAZONE*

Presentation Orange opaque hard gelatin capsules imprinted with the company symbol on each half of the capsule. Each capsule contains feprazone 200 mg.

Uses Action: Methrazone is a non-steroidal anti-inflammatory agent of the pyrazole group, with analgesic and antipyretic activity.

Indications: The treatment of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and gout.

Dosage and administration Adults: 200–600 mg daily in divided doses by mouth after food.

Paediatric usage has not been established

Contra-indications, warnings, etc

Contra-indications: Where there is a danger of cardiac decompensation; hepatic disease including recent hepatitis; history of peptic ulceration; blood dyscrasia; drug rash or known sensitivity to pyrazoles; renal disease.

Precautions: Concurrent therapy with plasma protein-bound agents may necessitate modification of dosage.

Methrazone may potentiate the effect of some oral hypoglycaemic and sulphonamide agents and coumarin type anticoagulants. In the case of the latter, the prothrombin level should be checked regularly.

Because of rare reports of blood dyscrasias, blood count should be monitored both before and during treatment.

Patients receiving this drug should also be kept under regular surveillance for sodium and water retention and effects on the upper intestinal tract.

Although Methrazone has been in general use for several years, there is no evidence of ill-consequence during pregnancy. Animal studies have shown no hazard.

Medicines should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

Side-effects: Rashes occur in some patients, usually within 2 weeks of starting treatment; those appearing within one week are mainly urticarial, whilst those appearing in the second week tend to be morbilliform. Purpura and angioedema have occasionally been reported.

Headache, dizziness, jaundice, alimentary tract disorders (including stomatitis, diarrhoea, and bleeding) have been reported as have occasionally thrombocytopenia, granulocytopenia, tinnitus and reversible visual disturbances.

Overdosage: Up to 96 capsules have been ingested without any long-term consequences. Prothrombin time, clotting factors and platelet counts were not affected at these doses.

Symptoms include nausea, vomiting, disorientation and twitching. Treatment should include gastric lavage and general supportive measures.

Pharmaceutical precautions Store in a cool place

Legal category POM.

Package quantities Containers of 100 capsules.

Further information Nil.

Product licence number 0015/0071R

MITOXANA* ▼

Presentation White powder in vials for injectable containing ifosfamide 500 mg, 1 g or 2 g for dissolving in Water for Injections using the volume recommended for each strength.

Uses Action: Mitoxana, a cytotoxic alkylating agent does not show *in vitro* cytotoxic activity until activated by hepatic microsomal enzymes.

Indications: Following the administration of Mitoxana good response has been shown in tumours of lung, ovary, breast and testis and in soft tissue sarcoma. Responses have also been reported in tumours of uterus, kidney, pancreas, GI tract, bone, ENT and in lymphoma.

Mitoxana has been used in combination with radiotherapy, vincristine, doxorubicin, bleomycin, methotrexate, 5FU, BCNU, cytarabine, etoposide and the following regimens: doxorubicin, vincristine and prednisone; methotrexate and prednisone; 5 azacytidine and cisplatin; bleomycin and doxorubicin; bleomycin and vinblastine; vincristine and fluorouracil; doxorubicin and fluorouracil; and a modified DeVita scheme.

Dosage and administration Mitoxana should be used only by clinicians experienced in the use of cytotoxic drugs.

Dosage: The usual total dose for each course is 10 g/m² which is equally fractionated as single daily doses over 5 days. Courses are normally repeated at intervals of 2–4 weeks depending on haematological or biochemical monitoring. The white cell count should not be less than 4,000/mm³ or the platelet count less than 100,000/mm³ before the start of each course. The drug should be used only by clinicians experienced in the use of cytotoxic drugs.

The usual number of courses given is four, but maximum of seven courses has been given. Retreatment is sometimes possible following relapse.

The total course dose, the number of days over which it is fractionated and the number of courses per treatment period should be determined by the tumour type, tumour staging, the general condition of the patient and whether other chemotherapy or radiation is to be administered concurrently.

Administration: The dry contents of a vial should be dissolved in Water for Injections as follows:

500 mg vial: Add 6.5 ml of Water for Injections.

1 g vial: Add 12.5 ml of Water for Injections.

2 g vial: Add 25 ml of Water for Injections.

The resultant solution of 8% ifosfamide should not be injected directly into the vein. With the patient supine the solution may be:

1. diluted to less than a 4% solution and injected directly into the vein, or
2. infused in 5% dextrose-saline over 30–120 min or
3. injected directly into a fast running infusion.

Should the drug accidentally be given intravenously

id no specific measures
nous injections of large
in local irritation.

atients should be fully
asis established before
uld be encouraged to
d an output of not less
ntained. Mitoxana may
re diuretic therapy may
equired urine output.
e useful in preventing

y protein, erythrocytes
urea is recommended.
ould be given before
nausea and vomiting.

s, etc

contra-indicated in pa-
y with serum creatinine
above 17 $\mu\text{mol/l}$, with
inases more than 2-3
cystitis or bone marrow

r pregnancy, especially
ected benefit is thought
o the foetus.

g Mitoxana therapy and
ng treatment. Mothers
being treated with

shown to be mutagenic,
certain laboratory tests
ed neoplasia following
ioea and azoospermia
e warned of a potential

ppressive drug and the
be borne in mind.

atients who are elderly,
s or evidence of mylo-
y received radiotherapy

s the usual dose limiting
emorrhagic cystitis, but
creatinine, glycosuria,
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dministration of a large
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a nadir 7-10 days after
for regimes of 5 days or
ld be expected to have
than 2 g/100 ml and a
mm³ but only about 5%
latelet count less than
only occasional reports

t the hair usually grows

unction have been re-
ent. Other side-effects
ea, pulmonary fibrosis,
itation.

Overdosage: The most serious consequences of over-
dosage are due to haemorrhagic cystitis and suppression
of the reticulo-endothelial system. The latter usually
recovers spontaneously, but until it does, administration
of a broad spectrum antibiotic (or possibly gammaglob-
ulin) may be advisable. Transfusions of whole-blood,
platelets or white cells are rarely necessary.

Cystitis should be treated with analgesics and the
maintenance of a high urine output by a high IV fluid
intake in conjunction with a diuretic if necessary. Haem-
orrhagic cystitis usually resolves on stopping Mitoxana.
In severe cases more intensive management may be
necessary. Intravesical instillation of 200-300 ml of a
5% formalin solution for 15 minutes followed by a
washout with 1 litre distilled water has been successful.
Care should be taken to prevent ureteric reflux. If this
fails a urological opinion should be sought with a view
to bladder tamponade, cautery or surgery. Blood trans-
fusions should also be given if clinically indicated.

No further courses of Mitoxana should be given until
the patient has fully recovered.

Cardiotoxicity has been observed with high doses of
Endoxana but as yet there have been no reports with
Mitoxana. Mitoxana should be discontinued and where
necessary, treatment with bed-rest, diuretics, oxygen
and digitalis should be considered.

Pharmaceutical precautions Store below 30°C;
protect from light. The solution should be used within
two hours of preparation.

Legal category POM.

Package quantities

500 mg dry vials, singles.

1 g dry vials, singles.

2 g dry vials, singles.

Further information Mitoxana is not recommended
for use in non-malignant conditions.

Product licence numbers

Vials of 500 mg 1416/0015

Vials of 1 g 1416/0016

Vials of 2 g 1416/0017

MYDRILATE*

Presentation Isotonic, sterile, aqueous solutions of
Cyclopentolate Hydrochloride BP 0.5% and 1.0% w/v
buffered to pH5 and containing 0.01% w/v benzalko-
nium chloride.

Uses Action: A cycloplegic and mydriatic agent: it
produces paralysis of the iris sphincter and ciliary muscle
by local anticholinergic action.

Indications: The primary indication is refraction, but
Mydrilate may be used whenever mydriasis is required
for diagnosis or treatment, e.g. in corneal ulceration,
keratitis, iritis, iridocyclitis, choroiditis, especially where
atropine or homatropine cannot be used.

**Dosage and administration Refraction: Adults (16
and over):** 1 drop of 0.5% solution. Repeat in 15-20
minutes only if no apparent effect is produced.

Children (6 to 16 years): 1 drop of 1% solution. Repeat
in five minutes. Refraction can be carried out in 40-50
minutes after instillation.

Under 6 years: 1 or 2 drops of 1% solution 40-50 minutes
before refraction. It may sometimes be necessary to instil
1 drop in the evening before examination.

Mydriasis: 1 drop of 0.5% or 1% solution as required.

Treatment: 1–2 drops of 0.5% or 1% solution as required.

Cycloplegia following administration is quick in onset and short-lived. Maximal cycloplegia is achieved within 15–45 minutes of instillation, and lasts on average about 20 minutes. Recovery normally takes place in about four hours, but very occasionally some effect persists for up to 24 hours.

Mydriasis is produced very rapidly and an average pupil diameter of 7 mm is usually reached 15–30 minutes after instillation of 1 drop of 0.5% solution. Complete recovery from the mydriatic effect generally occurs spontaneously in not more than 20 hours.

Contra-indications, warnings, etc Where intra-ocular pressure is high, caution should be observed, but the effect on tension is less and does not last as long as that produced by conventional cycloplegic mydriatic drugs.

Caution should be observed when drugs of this group are administered to patients with prostatic enlargement, coronary insufficiency or cardiac failure. They are contra-indicated in patients with paralytic ileus. Systemic side-effects have rarely been reported, but have included ataxia and other atropine-like effects. Physostigmine Eye Drops BNF or any miotic agent will reverse the effect of Mydrilate.

Although Mydrilate has been in wide general use for many years, there is no evidence of ill-consequence during human pregnancy.

Medicines should not be used in pregnancy especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

Overdosage: Symptoms of overdose include dry mouth, tachycardia, dilated pupils, ataxia, nightmares and other atropine-like effects. Treat with gastric lavage where appropriate. Neostigmine by injection may be necessary.

Pharmaceutical precautions Store in a cool place. The BPC recommends that when eye drops are dispensed for domiciliary use a caution should be given to the user to avoid contamination during use and not to use the eye drops later than one month after first opening the container. When eye drops are used in hospital wards, a separate container should be provided for each patient, and, when both eyes are being treated, a separate container for each eye. They should be discarded not later than one week after first opening the container. In out-patient and casualty departments, opened containers should be discarded at the end of each day, but each patient who has undergone out-patient surgery should be treated with a separate supply of the drops. In operating theatres, a previously unopened container should be used for each patient.

Legal category POM.

Package quantities 5 ml dropper bottles of 0.5% and 1.0% solutions.

Further information Mydrilate is non-irritant and sensitivity reactions are uncommon. The onset of cycloplegia is at least as fast as that obtained by any other preparation used for the purpose. In the normal eye it has little or no effect on intra-ocular tension.

Product licence numbers

Mydrilate 0.5% 1416/5030

Mydrilate 1.0% 1416/5031

ORGANIDIN*

Presentation Light yellow elixir containing iodinated glycerol 60 mg and alcohol (96%) 1.25 ml per 5 ml.

Uses Action: Mucosecretory stimulating agent.

Indications: For the treatment of diseases of the respiratory tract in which thick, tenacious mucus, or lack of mucous secretion, is an undesirable feature, e.g. bronchitis, asthma, laryngitis.

Dosage and administration *Adults and children over 12 years:* One 5 ml spoonful four times daily.

Children: Up to half the adult dosage.

Diluent: Organidin may be diluted with a 1:1 mixture of glycerol and water.

Contra-indications, warnings, etc In view of the association of neonatal goitre and/or hypothyroidism with maternal ingestion of iodides. Organidin therapy is not advocated during pregnancy, particularly during the last two trimesters. Long-term administration of iodide to children is also best avoided because of this goitrogenic hazard. Caution is recommended in cases of known hypersensitivity to iodides. Most patients, however, tolerate Organidin, and any adverse reactions which may occur are likely to be less severe than those resulting from inorganic iodide therapy.

Overdosage: Symptoms may be those of alcohol intoxication or excessive salivation. Elimination of the drug may be hastened by increasing the water and sodium chloride intake or by forced diuresis with mannitol.

Pharmaceutical precautions Store in a cool place, protect from light.

Legal category P.

Package quantities Bottles of 250 ml.

Further information Nil.

Product licence number 1416/5034.

PAVACOL*-D

Presentation Dark-brown cough mixture. Each 5 ml contains Papaverine Hydrochloride BP 1 mg and Pholcodine BP 5 mg, together with balsam of tolu, oil of clove, tincture of ginger, oil of aniseed, tincture of capsicum, oil of peppermint, alcohol and chloroform.

Uses Action: Papaverine is a myotropic spasmolytic which relaxes the bronchi by direct action on the smooth muscle of their walls.

Pholcodine exerts an inhibitory action on the cough centre, and has been found to be as effective as heroin as a cough suppressant. It is not a drug of addiction, and does not cause constipation.

Indications: For the symptomatic treatment of cough due to upper respiratory tract infection, influenza, bronchitis, pulmonary tuberculosis, carcinoma of the bronchus, etc, particularly in diabetic patients who require strict control of carbohydrate intake. It is a suitable for obese patients who are on a weight-reducing diet.

Dosage and administration *Adults:* One or two 5 ml spoonfuls as required.

The above dosage is adequate for most patients, but higher doses can safely be prescribed if necessary.

Children: from 6 to 12 years: One 5 ml spoonful four or five times daily.

From 3 to 5 years: One 5 ml spoonful three times daily.

From 1 to 2 years: Half a 5 ml spoonful three or four times daily.

Pavacol-D may be diluted with Sorbitol Solution BPC.

Contra-indications, warnings, etc Hypersensitivity to papaverine has been recorded. Nausea and drowsiness occur occasionally after pholcodine.

Although Pavacol-D has been in general use for many years, there is no evidence of ill-consequence during human pregnancy.

Medicines should not be used in pregnancy, especially in the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

Overdosage: Overdosage may be manifest by drowsiness, nausea and should be treated by emesis or gastric lavage followed by oral hydration.

Pharmaceutical precautions Store in a cool place and protect from light.

Legal category P.

Package quantities Bottles of 100 ml and 250 ml.

Further information Previously known as Pavacol ibetic. Suitable for both diabetic and non-diabetic patients.

Product licence number 1416/5039.

NOTRANE* PESSARIES

Presentation White, bluntly conical pessaries containing hydragraphen 1.5 mg or 5 mg.

Uses Action: Anticandidal, antitrichomonal, antibacterial antiseptic.

Indications: For the treatment of vaginitis and for routine prophylaxis in gynaecological surgery.

Dosage and administration 1. Infective vaginitis. Two 1.5 mg pessaries to be inserted into the posterior fornix of the vagina each night for 15 nights, treatment being continued throughout menstruation, if appropriate. Further 15 day course should be initiated at the start of the next menstrual cycle. For severe or resistant infection or for relapse or reinfection, two 5 mg pessaries each night for 15 nights repeated at the commencement of the next menstrual cycle.

2. Prophylaxis (before vaginal surgery or cervical uterine). Two 5 mg pessaries at night for 10 nights pre-operatively and continued for 10 nights after operation.

Contra-indications, warnings, etc Known hypersensitivity to organic mercurials. Should not be used with copper IUDs, PVC ring pessaries or in the absence of vaginal secretions, e.g. in atrophic vaginitis. Penotrane pessaries should only be used during pregnancy if considered essential by the physician.

This product possesses spermicidal properties and should not be used when conception is desired.

Overdosage: There is no clinical experience of overdosage. Standard supportive measures should be adopted.

Pharmaceutical precautions Store in a cool place. Penotrane is incompatible with metals, halides and phosphides.

Legal category POM.

Package quantities Packs of 15 and 60 pessaries.

Further information In trichomoniasis concurrent treatment with a systemic trichomonocide is recommended.

Product licence numbers

Pessaries 1.5 mg 1416/5044

Pessaries 5 mg 1416/5045

UVISTAT* CREAM

Presentation Off-white cream containing Mexenone BPC 4% w/w in an oil-in-water emulsion base.

Uses Action: Ultraviolet screen.

Indications: For the prevention of photodermatoses, acute solar dermatitis, solar urticaria and lesions or eruptions resulting from drug-induced photosensitivity and the precipitation or aggravation of ultraviolet-sensitive conditions such as lupus erythematosus, herpes labialis (simplex), rosacea, erythema multiforme and other dermatoses.

Dosage and administration The cream should be applied liberally and rubbed into all areas of the skin likely to be exposed to ultraviolet radiation, including the scalp if hair is sparse. Application twice a day may be sufficient but more frequent application is often necessary, depending on the sensitivity of the skin, the extent of exposure to ultraviolet radiation and whether sweating is profuse or the skin becomes wet.

Contra-indications, warnings, etc Although Uvistat has been in wide general use for many years, there is no evidence of ill-consequence of use during human pregnancy.

Overdosage: There is no clinical experience of overdosage. Standard supportive measures should be adopted.

Pharmaceutical precautions Nil.

Legal category GSL.

Package quantities Tubes of 50 and 100 g.

Further information Nil.

Product licence number 1416/5054.

UVISTAT-L*

Presentation Mexenone BPC 4% w/w in a base suitable for application to the lips.

Uses Action: Ultraviolet screen.

Indications: For the prevention of photodermatitis of the lips (including actinic cheilosis) and herpes labialis.

Dosage and administration Uvistat-L should be applied to the lips before they are exposed to sunlight. Maximal protection is afforded if Uvistat-L is applied frequently in a thin layer.

Further application is necessary immediately after meals, swimming or washing.

Contra-indications, warnings, etc Although Uvistat-L has been in wide general use for many years, there is no evidence of ill-consequence of use during human pregnancy.

Overdosage: There is no clinical experience of overdosage. Standard supportive measures should be adopted.

Pharmaceutical precautions Nil.

Legal category GSL.

Package quantities Single lipsticks of 5 g.

Further information Cosmetic coloured lipstick can be worn over Uvistat-L.

Product licence number 1416/5055.

WARFARIN WBP

Presentation Compressed tablets containing Warfarin Sodium BP, impressed with the letters **WBP** on one side and coloured according to strength; 1 mg—brown; 3 mg—blue, 5 mg—pink.

Uses *Action:* Oral anticoagulant.

Indications: For prophylaxis against venous thrombosis and pulmonary embolism, and for use in the treatment of these conditions to prevent their extension.

Dosage and administration Effective blood levels are rapidly reached by administering an *initial loading dose* usually of the order of 0.45–0.50 mg/kg for adults.

Maintenance dosage is started when the peak effect of the initial dosage is passed, usually after 48 hours. Its size depends on the prothrombin time or other appropriate coagulation tests. The single daily maintenance requirement is usually between 5 mg and 12 mg, but can vary between 2 mg and 30 mg.

The maintenance dose is omitted if the prothrombin time is excessively prolonged. Once the maintenance dose is stabilised in the therapeutic range it is rarely necessary to alter it.

Contra-indications, warnings, etc Animal studies have shown warfarin to be teratogenic and there have been reports of foetal death associated with its administration during human pregnancy. Warfarin should not be prescribed for pregnant women.

Warfarin should not be given to patients within three days of surgery.

The use in patients known to be hypersensitive to warfarin is contra-indicated.

When warfarin therapy is first introduced, patients should be told what to do if bleeding occurs.

Warfarin should be given with caution to patients with impaired liver or kidney function or in severe hypertension.

Warfarin should be given with caution to patients where there is a risk of serious haemorrhage such as haemorrhagic blood dyscrasias, haemophilia, ulcerative disorders, threatened abortion, subacute bacterial endocarditis, in the presence of extensive surgical wounds and after recent surgery to the eye and central nervous system.

Prothrombin times should be determined at least twice weekly for the first two weeks and subsequently longer intervals (every two to three weeks).

Overdosage may be manifest by haematuria or spontaneous bruising. This should be treated with vitamin (5–10 mg) intravenously. Significant correction occurs within four hours.

There is some evidence that abrupt conclusion or interruption of anticoagulant therapy leads to complications in the form of relapses or exacerbations of the underlying disease and it is probably wiser to 'taper' oral anticoagulants when therapy has to be concluded. Many factors *potentiate* the effect of warfarin:

1. Warfarin in the circulation is firmly bound to plasma protein and will have an increased effect if displaced by other drugs such as diuretics, oral anti-diabetic agents and anti-inflammatory agents.

2. Certain drugs, for example D-thyroxine, potentiate the effects of warfarin by increasing its affinity for the hepatic receptor site.

3. Alcohol may inhibit liver enzymes, leading to reduced dosage requirement of warfarin.

4. Other drugs which may potentiate the effect of warfarin include anabolic steroids, cimetidine, aspirin, clofibrate, sulphapyrazole, chloral hydrate, some arylglycoside antibiotics, chloramphenicol, disulfiram and paracetamol.

5. Renal damage may reduce the rate of excretion of warfarin and thus decrease the dose requirement.

6. Acute illness, weight loss and a decreased intake of vitamin K will exaggerate the response.

Other factors may *decrease* the effect of warfarin:

1. Warfarin is metabolised in the liver by microsomal enzymes. These enzymes are induced by drugs such as barbiturates and phenytoin leading to rapid metabolism of warfarin and necessitating an increased dose.

2. Oestrogens and oral contraceptives increase the concentration of vitamin K-dependent factors. Increased doses of warfarin may therefore be required.

3. Cholestyramine may absorb warfarin and thus reduce its effect.

4. Weight gain, gastro-intestinal upset and increased intake of vitamin K will necessitate an increase in maintenance dosage of warfarin.

5. Carbamazepine, glutethimide, phenazone, griseofulvin and rifampicin also diminish the effect of warfarin.

Pharmaceutical precautions Protect from heat, light and moisture.

Legal category POM.

Package quantities 1 mg, 3 mg and 5 mg tablets in containers of 100 and 500.

Further information Nil.

Product licence numbers

Tablets 1 mg 1416/5060

Tablets 3 mg 1416/5061

Tablets 5 mg 1416/5062

*Trade Mark

/eddel Pharmaceuticals Limited
/eddel House
4 West Smithfield
London EC1A 9HY



TABUSE* 200

Presentation Plain white tablets with single break. Each tablet contains 200 mg Disulfiram BP.

Uses Anti-alcoholic agent. Antabuse 200 is indicated in adjuvant in the treatment of cooperative chronic alcoholics, but its use should be supported by appropriate psychiatric treatment.

Dosage and administration On the first day of treatment, the patient should be given 4 tablets of antabuse 200 in one dose and told on no account to take any alcohol. The next day, the patient is to take 3 tablets and on the third day 2 tablets.

On the fourth and fifth days the patient should take 1 tablet and subsequently 1 tablet or possibly $\frac{1}{2}$ tablet daily, dosage continuing until, in the opinion of the physician, the patient is restored to the social order.

Dosage may be continued for up to 12 months.

On the fifth day of dosage the physician may give the patient a challenge dose of 10–15 ml of 95% alcohol to test the patient's reaction especially in terms of blood pressure and pulse rate. If the reaction is not marked a further dose of alcohol may be given, which will produce increasingly severe symptoms to make a deep impression on the patient's mind.

Do not give Antabuse 200 until at least 12 hours after last ingestion of alcohol. On no account must the patient take alcohol during treatment with Antabuse 200 as it is given as a challenge dose by the physician. The patient should be warned that many liquid medicines and wines contain sufficient alcohol to cause a reaction.

Antabuse 200 interferes with the metabolism of alcohol and causes a build-up of acetaldehyde in the blood stream. The effect of Antabuse 200 with alcohol is therefore similar to paraldehyde poisoning. Antabuse is rapidly absorbed from the gastro-intestinal tract and is very slowly eliminated.

Contra-indications, warnings, etc Antabuse 200 is contra-indicated in the presence of cardiac failure, coronary artery disease, pregnancy, psychosis and drug addiction. It should be used with caution in the presence of renal, hepatic or respiratory disease, diabetes mellitus or epilepsy.

Great care should be taken when the challenge dose of alcohol is given to patients taking Antabuse 200. The extent of the reaction is very variable. It may not appear at all on the first alcohol challenge, but it may be very severe.

Several deaths have been reported following the drinking of large volumes of alcohol by patients receiving antabuse 200.

The Antabuse/alcohol reaction is characterised by intense flushing, dyspnoea, throbbing headache, palpitations, tachycardia, nausea and vomiting. The reaction to alcohol can occur within ten minutes of taking an alcoholic drink and may persist for several hours.

Drug interactions: Antabuse 200 may potentiate the action of paraldehyde, barbiturates and other centrally acting drugs. Diazepam and chlorpromazine can reduce, and amitriptyline increase, the severity of the Antabuse/alcohol reaction.

Side effects: During initial treatment with Antabuse 200, drowsiness and fatigue are common. Nausea, vomiting, halitosis and reduction in libido can also occur. If side effects are marked the dosage should be reduced.

Rarely, psychotic reactions, including depression, paranoia, schizophrenia and mania, occur in patients on Antabuse therapy. Allergic dermatitis, peripheral neuritis and liver cell damage have been reported.

Treatment of overdose: With alcohol; Intensive supportive therapy; the main aim is to counteract hypotension and to prepare for the possibility of severe vomiting. Intravenous fluids should be administered and oxygen should be available. A pressor agent such as noradrenaline may be needed.

Without alcohol; Gastric lavage. Observation; Antabuse by itself has low toxicity.

Pharmaceutical precautions No special precautions.

Legal category POM.

Package quantities Containers of 50 tablets.

Further information Antabuse is very slowly excreted and may be detected in body fluids up to seven days after cessation of administration.

Product licence number 0495/5900.

CHENDOL*

Presentation Each orange and pearl capsule contains 125 mg of chenodeoxycholic acid.

Uses

1. **Indications:** For dissolution of radiolucent cholesterol-rich gallstones in functioning gallbladders. Cholesterol stones coated with calcium, or stones composed of bile pigments are not dissolved by chenodeoxycholic acid. It has a particular place in the treatment of patients in whom surgery is contra-indicated or who are anxious to avoid surgery.

2. **Pharmacology:** Chenodeoxycholic acid is a normal constituent of human bile. It is known as a primary bile acid since it is one of the two main bile acids synthesised by the liver. Its possible main mechanism of action is that it reduces the output of cholesterol secreted into the bile by inhibiting the enzyme HMG CoA reductase. A secondary mechanism of action is the expansion of the bile acid pool which accompanies taking exogenous chenodeoxycholic acid.

Dosage and administration The present clinical

evidence suggests that optimum results will be obtained on a dose level of 10–15 mg per kg body weight daily either as a single night time dose or in divided doses.

Duration of treatment appears to be correlated with size of stone. Generally speaking the smaller the stones, the shorter the treatment – dissolution may occur after only three months. On the other hand, larger stones may require up to two years' treatment. It is recommended that treatment continues for three months after dissolution.

Contra-indications, warnings, etc Chendol should not be administered to patients with radio-opaque calcified gallstones nor to patients with non-functioning gallbladders. In addition, Chendol should not be administered to women who may become pregnant, nor to patients with chronic liver disease, nor with inflammatory diseases of the small intestine and colon.

Chendol is generally well tolerated; the only side-effects reported to date are diarrhoea and pruritus.

It has been found that after a slight reduction in dose for a few days, diarrhoea ceases and the dose can then gradually be increased to the former level. The clinician's discretion should be applied to the necessity, in individual cases, for laboratory monitoring.

Pharmaceutical precautions Store in a well closed container.

Legal category POM.

Package quantities 100 and 500.

Further information Nil.

Product licence number 0495/0003.

HEPARIN INJECTION BP

Presentation A clear, colourless or straw-coloured pyrogen-free solution of Heparin Sodium (Mucous) in Water for Injections BP adjusted to a pH of 5 to 8. It is supplied in 5 ml multidose vials containing 1,000, 5,000 and 25,000 units heparin per ml, with 0.15% chlorocresol. In addition, single-dose ampoules containing 1,000 units per ml (5 ml) and 5,000 units in 0.2 ml are available.

Uses Heparin is an anticoagulant. It is believed to act by enhancing the effects of antithrombin III, thereby inactivating several activated clotting factors including activated factor X (Xa).

The chief use of heparin is in the treatment of arterial and venous thrombosis. It may also be used as a prophylaxis against postoperative venous thrombosis; in extra-corporeal circulation (heart-lung and dialysis machines); in blood transfusions; and in coronary thrombosis as a cover for the first 36–48 hours of oral anticoagulant therapy.

Dosage and administration *Adults:* An initial intravenous injection of 12,500 units may be given, followed by maintenance doses of about 6,000 to 12,000 units every 4 hours. The dose should, however, be adjusted to individual response, monitored by anticoagulation tests. For continuous infusion, 10,000 to 20,000 units are given in Dextrose Injection or Sodium Chloride Injection over 12 hours. In an emergency, heparin may be given subcutaneously, in doses of 10,000 to 12,500 units at 6 to 12 hour intervals. The intramuscular route of administration is not recommended.

In prophylaxis of postoperative venous thrombosis,

the usual dose is 5,000 units subcutaneously 2 hr before surgery, followed by 5,000 units every 12 hr for about 10 days after surgery.

Children: The initial dose is 50 units per kg body weight by intravenous infusion, increased to about 100 u per kg every 4 hours.

Contra-indications, warnings, etc Heparin is contra-indicated in surgery of the brain, spinal cord and because of the special hazard of post-operative haemorrhage in these patients which could cause significant disability.

The relative risks and benefits of heparin therapy should be carefully assessed in patients with a bleeding tendency (e.g. haemophilia, purpura, severe hypersensitivity or scurvy), or those patients with an actual potential bleeding site (e.g. peptic ulcer, visceral carcinoma, postoperative oozing of blood, subacute bacterial endocarditis, suspected intracranial haemorrhage, cerebral thrombosis or threatened abortion). Neither mstruation nor pregnancy is a contra-indication.

Heparin does not cross the placenta or appear in milk.

In patients with advanced renal or hepatic disease reduction in dosage may be necessary. Although hypersensitivity is rare, it is advisable to give a trial dose of 1,000 units in patients with a history of allergy.

Drugs that interfere with platelet aggregation, such as aspirin, may prolong the anticoagulant action of heparin.

The chief danger of heparin therapy is haemorrhage; but this is usually due to overdosage and is minimised by strict laboratory control. Slight haemorrhage can usually be treated by withdrawing the drug. Overdosage treated by intravenous injection of Protamine Sulphate 1 mg for every 100 units of heparin to be neutralised.

Rare side effects include acute, reversible thrombocytopenia, alopecia and osteoporosis with spontaneous fractures (after prolonged therapy).

Pharmaceutical precautions Heparin should be stored at a temperature not exceeding 25°C, when it is expected to retain its potency for at least 3 years at the date of manufacture. Heparin is incompatible aqueous solution with certain substances e.g. antibiotic hydrocortisone, phenothiazines and antihistamines.

Legal category POM.

Package quantities Vials: Packs of ten. Ampoules: Packs of fifty/ten.

Further information Nil.

Product licence numbers	1,000 units/ml w	
preservative		0495/50
5,000 units/ml with preservative		0495/50
25,000 units/ml with preservative		0495/50
1,000 units/ml without preservative		0495/50
25,000 units/ml without preservative		0495/50

HEPSAL*

Presentation A sterile, pyrogen-free, clear, colourless solution, of Heparin Sodium (Mucous) BP in Sodium Chloride Injection BP adjusted to pH 5 to 8. The solution is preservative free. Each 5 ml ampoule contains 50 u Heparin Sodium (10 units per ml).

Uses Heparin is an anticoagulant. It is believed to act by enhancing the effects of antithrombin III, thereby inactivating several activated clotting factors, including activated Factor X (Xa).

heparin is indicated in any clinical circumstances in which it is desired to maintain the patency of indwelling, intravascular catheters/cannulae, attendant lines or arterial locks.

Hypurin is not recommended for systemic use.

Dose and administration Flush with 5 mls (50 s) every 4 hours or as required.

Contra-indications, warnings, etc The very rare occurrence of established hypersensitivity to heparin is only a contra-indication to Hepsal.

As directed, it is extremely unlikely that the low levels of heparin reaching the blood will have any systemic effect.

Rigorous aseptic technique should be observed at all times in its use.

Pharmaceutical precautions Heparin may be incompatible with solutions of certain other drugs. Hepsal should be stored at a temperature not exceeding 25°C in which it can be expected to retain its potency for at least 5 years after the date of manufacture.

Legal category POM.

Package quantities Packs of 10 x 5 ml Ampoules.

Further information Nil.

Product licence number 0495/0014.

HYPURIN* ISOPHANE

Presentation A sterile suspension of a white crystalline precipitate of isophane insulin (bovine) in an isotonic aqueous medium buffered to a pH of 6.9 to 7.5. It is prepared by adding highly purified crystalline insulin of bovine origin to protamine sulphate in such an amount that the excess of insulin or of protamine in the emulsion is at a minimum. The preparation complies with the requirements of the European Pharmacopoeia for Isophane Protamine Insulin Injection. Two strengths, 40 and 80 international units per ml, are available.

Hypurin Isophane is supplied in 10 ml multidose glass ampoules. The packaging and labels are colour coded. Red and white signify Hypurin Isophane 40 international units per ml and green and white, Hypurin Isophane 80 international units per ml.

Uses Insulin is used in growth onset diabetes mellitus in maturity onset diabetes mellitus, not responding to diet or oral drugs. Its principal action is probably to accelerate the passage of glucose into the cells of certain tissues, notably skeletal muscle and adipose tissue. Hypurin Isophane may be particularly advantageous in the treatment of diabetics with insulin lipodystrophy, insulin allergy, and also in labile diabetes and when intermittent short-term therapy is required.

Dose and administration The practical aims of therapy are to reduce the blood glucose concentration to physiological levels and eliminate glycosuria and ketonuria. The dose required depends on the severity of diabetes and has to be determined empirically. Most adult patients are controlled by 20 to 120 international units per day. Children may require much less.

Isophane insulin is poorly soluble in body fluids and forms a depot from which insulin is slowly released. Its action begins after about two hours and lasts for about 24 hours. A single injection before breakfast is suitable for many patients (usually those requiring less than 40 international units per day), but others require two

injections per day or a combination of Hypurin Isophane and Hypurin Neutral.

Insulin is normally administered subcutaneously in the upper arms, thighs, buttocks or abdomen. Wherever possible, the patient should be taught to give the injection. The injection area should be varied so that the same site is never used more than about once a month. Care should be taken to see that a blood vessel has not been entered. The injection site should not be massaged.

Contra-indications, warnings, etc The vial should be shaken gently before use.

Where Hypurin Isophane is mixed with Hypurin Neutral in the same syringe, care should be taken to draw up the Hypurin Neutral into the syringe first, so as to avoid contaminating it with the longer-acting insulin.

Mixing of Hypurin Isophane with a conventional insulin should be avoided.

In no circumstances should Hypurin Isophane be given intravenously.

Insulin requirements may increase during illness, puberty, pregnancy, emotional upsets or if drugs with hyperglycaemic activity are being taken. Insulin requirements may decrease during periods of increased activity, in liver or kidney diseases or when drugs with hypoglycaemic activity are being taken.

Overdosage causes hypoglycaemia. The warning signs are vomiting (in children), palpitations, trembling, sweating, a tingling in the hands or lips, pallor, impaired vision, listlessness, confusion and dizziness. The patient should take sugar, and rest. If the patient is comatose, Strong Dextrose Injection BPC should be given intravenously.

Patients transferred to Weddel Hypurin Insulins from other commercially available preparations may require dosage adjustment.

Pharmaceutical precautions Hypurin Isophane should be stored in a refrigerator (between 2°C and 8°C) when it may be expected to retain its potency for at least two years after the date of manufacture. It should not be frozen.

Care should be taken to ensure that the syringe and needle are scrupulously cleaned before use.

Legal category P.

Package quantities Packs of 10 vials.

Further information Nil.

Product licence numbers

40 i.u./ml 0495/0017

80 i.u./ml 0495/0018

HYPURIN* LENTE

Presentation A sterile buffered suspension of highly purified bovine insulin with zinc chloride consisting of a mixture of 3 volumes of insulin zinc suspension (amorphous) and 7 volumes of insulin zinc suspension (crystalline). The insulin is in a form insoluble in water and appears as a white suspension which on standing deposits a white sediment and leaves a colourless or almost colourless supernatant liquid. The sediment is readily re-suspended on gentle shaking. The majority of particles are crystals with a maximum dimension greater than 10 µm but rarely exceeding 40 µm; a considerable proportion have no uniform shape and do not exceed 2 µm in maximum dimension. It has a pH of 7.0 to 7.5. Two strengths are available: 40 and 80 international

units per ml. Hypurin Lente is supplied in 10 ml multi-dose glass containers. The packaging and labels are colour coded. Blue and magenta signify Hypurin Lente 40 international units per ml and green and magenta signify Hypurin Lente 80 international units per ml.

Uses Insulin is used in growth onset diabetes mellitus, and in maturity onset diabetes mellitus not responding to diet or oral drugs. Its principal action is probably to accelerate the passage of glucose into the cells of certain tissues, notably skeletal muscle and adipose tissue.

The onset of action of Hypurin Lente is gradual with a maximum lowering of blood sugar concentration 8 to 12 hours after subcutaneous injection and a total duration of action of about 30 hours.

The onset of action after the usual morning dose may be sufficiently rapid to control the rise of blood sugar concentration after breakfast, so that some diabetics needing insulin may be satisfactorily controlled by a single daily injection of the preparation.

Hypurin Lente may be particularly advantageous in the treatment of insulin-related fat atrophy, allergy, and resistance.

Dosage and administration The practical aims of insulin therapy are to reduce the blood glucose concentration to physiological levels and eliminate glucosuria and ketonuria. The dose required has to be determined empirically for each patient. The total daily insulin requirement for most adult patients lies between 20–120 international units per day.

Insulin dependent diabetes is first brought under control with Hypurin Neutral. Hypurin Lente may then be introduced as a supplement in those cases where control with a single daily injection of neutral and depot insulin seems desirable and feasible.

Some diabetics may be controlled with Hypurin Lente alone. An initial dose of 10 to 16 international units is given, and the dose gradually increased in increments of 4 units until the blood sugar concentration and glucosuria are satisfactorily controlled.

Hypurin Lente is administered by subcutaneous injection in the upper arms, thighs, buttocks or abdomen. Wherever possible, the patient should be taught to give the injection. The injection area should be varied so that the same site is never used more than about once a month. Care should be taken to see that a blood vessel has not been entered. The injection site should not be massaged.

Contra-indications, warnings, etc The vial should be shaken gently before use.

Hypurin Lente should never be given intravenously and is not suitable for the emergency treatment of diabetic coma. When, on medical advice, Hypurin Lente is administered with Hypurin Neutral, using the same syringe, care should be taken to draw up the Hypurin Neutral first into the syringe to avoid contamination of the short-acting preparation. Mixtures of Hypurin Lente with Hypurin Neutral should be used immediately after preparation and should not be stored, as there may be pharmaceutical interactions.

Various well-recognised causes of altered insulin requirement exist.

Increased insulin requirement is commonly associated with trauma, intercurrent infection, cardiac infarction and, physiologically, with puberty and the adolescent growth spurt. Early pregnancy and certain types of medication, including steroids, thyroxine and sympathomimetic agents may also increase insulin requirements.

Decreased insulin requirement is associated with increased physical activity and may occur in the later stages of pregnancy. Hypoglycaemic drugs (e.g. salicylates and sulphonamides) may lessen insulin requirements.

Overdosage causes hypoglycaemia. The warnings signs are vomiting (in children), palpitations, trembling, sweating, a tingling in the hands or lips, pallor, impaired vision, listlessness, confusion and dizziness. The patient should take sugar and rest. If the patient is comatose, Strc Dextrose Injection BPC should be given intravenously.

Patients transferred to Weddel Hypurin Insulins from other commercially available preparations may require dosage adjustment.

Pharmaceutical precautions Insulin should be stored in a refrigerator (between 2°C and 8°C) where it may be expected to retain its potency for at least 5 years after the date of manufacture. It should not be frozen.

Legal category P.

Package quantities Packs of 10 vials.

Further information Nil.

Product licence numbers

40 i.u./ml 0495/0020

80 i.u./ml 0495/0021

HYPURIN* NEUTRAL

Presentation A sterile, clear, colourless aqueous solution of highly purified crystalline insulin (bovine) in an isotonic medium buffered to a pH of 6.6 to 7.7. The preparation complies with the requirements of the British Pharmacopoeia for Neutral Insulin Injection. Three strengths, 40 and 80 international units per ml, are available. Hypurin Neutral is supplied in 10 ml multidose glass containers. The packages and labels are colour coded. Blue and brown signify Hypurin Neutral 40 international units per ml and green and brown signify Hypurin Neutral 80 international units per ml.

Uses Insulin is used in growth onset diabetes mellitus and in maturity onset diabetes mellitus, not responding to diet or oral drugs. Its principal action is probably to accelerate the passage of glucose into cells of certain tissues, notably skeletal muscle and adipose tissue.

Hypurin Neutral may be particularly advantageous in the treatment of diabetics with insulin lipodystrophy, insulin allergy, and also in labile diabetes and with intermittent short-term therapy is required.

Dosage and administration The practical aims of insulin therapy are to reduce the blood glucose concentration to physiological levels and eliminate glucosuria and ketonuria. The dose required depends on the severity of the diabetes and has to be determined empirically. Most adult patients are controlled by 20 to 120 international units per day. Children may require much less.

Hypurin Neutral has a rapid onset of action and may be used in the emergency treatment of diabetic coma and pre-coma. It may be used in conjunction with longer acting Hypurin insulin.

Insulin is usually administered subcutaneously in the upper arms, thighs, buttocks or abdomen. Wherever possible, the patient should be taught to give the injection. The injection area should be varied so that the same site is never used more than about once a month.

It should be taken to see that a blood vessel has not been entered. The injection site should not be massaged. Where necessary, Hypurin Neutral may be given amulsarily or, for very rapid effect, intravenously.

Contra-indications, warnings, etc Mixing of Hypurin Neutral and Hypurin Protamine Zinc Insulins in the same syringe is inadvisable because Protamine Zinc insulin contains excess protamine. This will convert a portion of the soluble insulin into long-acting insulin and in some cases, may lead to hyperglycaemia in the early stages and prolonged hypoglycaemia during the night.

Insulin requirements may increase during illness, puberty, pregnancy, emotional upsets or if drugs with hyperglycaemic activity are being taken. Insulin requirements may decrease during periods of increased activity, in liver or kidney diseases or when drugs with hypoglycaemic activity are being taken.

Overdosage causes hypoglycaemia. The warning signs are vomiting (in children), palpitations, trembling, sweating, a tingling in the hands or lips, pallor, impaired vision, weakness, confusion or dizziness. The patient should take sugar, and rest. If the patient is comatose, then Strong Dextrose Injection BPC should be given intravenously.

Patients transferred to Weddel Hypurin Insulins from other commercially available preparations may require dosage adjustment.

Pharmaceutical precautions Insulin should be stored in a refrigerator (between 2°C and 8°C) when it may be expected to retain its potency for at least two years after the date of manufacture. It should not be frozen. Care should be taken to ensure that the syringe and needle are scrupulously cleaned before use.

Legal category P.

Package quantities Packs of 10 vials.

Further information Nil.

Product licence numbers

40 i.u./ml 0495/0015

80 i.u./ml 0495/0016

'PURIN' PROTAMINE ZINC

Presentation A sterile suspension of protamine zinc insulin (bovine) in an isotonic aqueous medium buffered to a pH of 6.9 to 7.5. It is prepared by the addition of protamine sulphate and zinc chloride to a solution of highly purified crystalline insulin of bovine origin. The preparation complies with the requirements of the European Pharmacopoeia for Protamine Zinc Insulin Injection. Two strengths, 40 and 80 international units per ml, are available. Hypurin Protamine Zinc is supplied in 10 ml multidose glass containers. The packaging and labels are colour coded. Blue and pink signify Hypurin Protamine Zinc 40 international units per ml, and green and pink, Hypurin Protamine Zinc 80 international units per ml.

Uses Insulin is used in growth onset diabetes mellitus and in maturity onset diabetes mellitus, not responding to diet or oral drugs. Its principal action is probably to accelerate the passage of glucose into the cells of certain tissues, notably skeletal muscle and adipose tissue.

Hypurin Protamine Zinc may be particularly advantageous in the treatment of diabetics with insulin lipodys-

trophy or insulin allergy, and also in labile diabetes and when intermittent short-term therapy is required.

Dosage and administration The practical aims of therapy are to reduce the blood glucose concentration to physiological levels and eliminate glycosuria and ketonuria. The dose required depends on the severity of the diabetes and has to be determined empirically. Most adult patients are controlled by 20 to 120 international units per day. Children may require much less.

Hypurin Protamine Zinc is poorly soluble in body fluids and forms a depot from which insulin is slowly released. Its action begins after 4 to 6 hours but lasts for 24 to 36 hours. Because its action is slow in onset, it is commonly used in conjunction with Hypurin Neutral.

Insulin is normally administered subcutaneously in the upper arm, thighs, buttocks or abdomen. Wherever possible, the patient should be taught to give the injection. The injection area should be varied so that the same site is never used more than about once a month. Care should be taken to see that a blood vessel has not been entered. The injection site should not be massaged.

Contra-indications, warnings, etc The vial should be shaken gently before use.

Mixing of Hypurin Neutral and Hypurin Protamine Zinc Insulins in the same syringe is inadvisable, since protamine zinc insulin contains excess protamine. This will convert a proportion of the soluble insulin into long-acting insulin, and in some cases may lead to hyperglycaemia in the early stages, and prolonged hypoglycaemia during the night.

In no circumstances should Hypurin Protamine Zinc be given intravenously.

Insulin requirements may increase during illness, puberty, pregnancy, emotional upsets or if drugs with hyperglycaemic activity are being taken. Insulin requirements may decrease during periods of increased activity, in liver or kidney diseases or when drugs with hypoglycaemic activity are being taken.

Overdosage causes hypoglycaemia. The warning signs are vomiting (in children), palpitations, trembling, sweating, a tingling in the hands or lips, pallor, impaired vision, listlessness, confusion and dizziness. The patient should take sugar, and rest. If the patient is comatose, Strong Dextrose Injection BPC should be given intravenously.

Patients transferred to Weddel Hypurin Insulins from other commercially available preparations may require dosage adjustment.

Pharmaceutical precautions Insulin should be stored in a refrigerator (between 2°C and 8°C) when it may be expected to retain its potency for at least two years after the date of manufacture. It should not be frozen.

Care should be taken to ensure that the syringe and needle are scrupulously cleaned before use.

Legal category P.

Package quantities Packs of 10 vials.

Further information Nil.

Product licence numbers

40 i.u./ml 0495/0012

80 i.u./ml 0495/0013

INSULIN INJECTION PhEur, BP (SOLUBLE INSULIN BP)

Presentation A sterile, clear, colourless, isotonic,

aqueous solution of crystalline insulin (bovine), adjusted to a pH of 3.0 to 3.5. Insulin Injection is supplied in 10 ml multidose glass vials. Three strengths, 20, 40 and 80 units per ml, are available.

The packages and labels are colour coded. Yellow alone signifies Insulin Injection BP 20 units/ml, blue alone, Insulin Injection BP 40 units/ml and green alone, Insulin Injection BP 80 units/ml.

Uses Insulin is used in juvenile-onset diabetes mellitus, and in maturity-onset diabetes mellitus unresponsive to diet or oral hypoglycaemic agents.

Insulin Injection is particularly useful in diabetic coma and ketoacidosis, pregnancy, trauma and infection.

Dosage and administration The dose depends on the individual requirements of the patient and should be determined empirically.

Insulin Injection has a rapid onset of action (about 30 minutes); its effects last for 6 to 8 hours. It may be used in conjunction with a longer-acting insulin.

Insulin Injection is normally administered subcutaneously. Suitable sites are the upper arm, upper thigh, buttocks and lower abdomen. Whenever possible, the patient should be taught to give the injection. The same injection site should not be used more than about once a month. Care should be taken to ensure that a blood vessel has not been entered. The Injection site should not be massaged.

Insulin Injection may be given intramuscularly or, for very rapid effect, intravenously.

Contra-indications, warnings, etc When Insulin Injection is mixed with Isophane Insulin in the same syringe, Insulin Injection should be drawn into the syringe first, to prevent contamination with the longer-acting preparation. The mixing of Insulin Injection and Protamine Zinc Insulin Injection in the same syringe is not recommended, as the excess protamine in the latter preparation reacts with the Insulin Injection, reducing its immediate effect. Because of pharmaceutical incompatibility, Insulin Injection should not be mixed with Insulin Zinc Suspension.

Care should be taken if patients are changed from one insulin to another of a different animal source as the dosage required may differ.

Development of insulin antibodies may occasionally lead to a gradual increase in dosage requirement. Insulin requirements may also increase during illness (especially infection), pregnancy, puberty, emotional upsets, and concomitant administration of oral contraceptives, adrenaline, thiazide diuretics and other hyperglycaemic agents. Insulin requirements may decrease during periods of increased activity, liver or kidney disease, and concomitant administration of alcohol, monoamine oxidase inhibitors, propranolol, aspirin and other hypoglycaemic agents.

New patients often experience minor skin reactions, which generally cease spontaneously. Insulin may sometimes cause local lipo-atrophy.

Insulin overdosage causes hypoglycaemia. The early warning signs are weakness, giddiness, pallor, sweating, palpitations, trembling etc. Later symptoms are depression or euphoria, inability to concentrate, drowsiness, amnesia etc. In children, headache, nausea and vomiting are common. Treatment of hypoglycaemia is sugar ingestion, and rest. If untreated, hypoglycaemia leads to convulsions and coma. A comatose patient should be treated intravenously with up to 50 ml of a 50% solution of dextrose.

Pharmaceutical precautions Insulin Injecti should be stored in a refrigerator (between 2°C and 8°C) when it may be expected to retain its potency for at least two years after the date of manufacture. It should not be frozen.

Legal category P.

Package quantities Packs of 10 vials.

Further information Nil.

Product licence numbers

20 units/ml 0495/5004

40 units/ml 0495/5005

80 units/ml 0495/5006

INSULIN ZINC SUSPENSION (MIXED) BP

Presentation A sterile buffered suspension of bovine insulin with zinc chloride consisting of a mixture of three volumes of Insulin Zinc Suspension (Amorphous) and seven volumes of Insulin Zinc Suspension (Crystalline) the insulin is in a form insoluble in water. It is an almost colourless turbid liquid in which the majority of particles are crystals with a maximum dimension greater than 10 µm but rarely exceeding 40 µm; a considerable proportion have no uniform shape and do not exceed 2 µm in maximum dimension. It has a pH of 7 to 7.5. Two strengths are available: 40 and 80 international units per ml. Insulin Zinc Suspension (Mixed) is supplied in 10 ml multidose glass containers. The packaging and labels are colour coded. Blue and purple signify Insulin Zinc Suspension, 40 i.u./ml and green and purple signify Insulin Zinc Suspension, 80 i.u./ml.

Uses Insulin is used in the treatment of diabetes mellitus not responding to diet or oral drugs. Its principal action is probably to accelerate the passage of glucose into the cells of certain tissues, notably skeletal muscle and adipose tissue.

Insulin Zinc Suspension (Mixed) gives suitable control for the average diabetic. Its onset of action is gradual with a maximum lowering of blood sugar concentration 8 to 12 hours after subcutaneous injection and a total duration of action of about 30 hours. The onset of action after the usual morning dose is sufficiently rapid to control the rise of blood sugar concentration after breakfast. Diabetics needing insulin may be satisfactorily controlled by a single daily injection of this preparation. A small proportion may need the addition of Insulin Zinc Suspension (Amorphous) or Insulin Zinc Suspension (Crystalline) for optimum control.

Dosage and administration The practical aims of therapy are to reduce the blood glucose concentration to physiological levels and eliminate glucosuria and ketonuria. The dose required depends on the severity of the diabetes and has to be determined empirically.

Severe diabetes is first brought under control with Insulin Injection and an insulin zinc suspension is then substituted in the same or slightly larger daily dose.

With uncomplicated diabetes of moderate severity, an initial dose of 10 to 16 units is given and the dose gradually increased by four units until the blood sugar concentration and glucosuria are satisfactorily controlled.

When a patient who has been receiving Protamine Zinc Insulin is changed to an insulin zinc suspension, an increase in dose of about 20% will probably be required.

When transferring from other insulin preparations to Insulin Zinc Suspension, the carbohydrate intake may have to be readjusted.

Insulin Zinc Suspension (Mixed) is administered by subcutaneous injection usually 30 to 45 minutes before breakfast in the upper arms, thighs, buttocks or abdomen. Wherever possible, the patient should be taught to give an injection. The injection area should be varied so that the same site is never used more than about once a month. Care should be taken to see that a blood vessel has not been entered. The injection site should not be massaged. Before a dose is withdrawn, the vial should be shaken gently; vigorous shaking may cause excessive foaming.

The insulin zinc suspensions are freely miscible with each other, without affecting the absorbability of the different particles. Mixtures may therefore be prepared which will control the blood sugar concentration by means of a single daily injection. They should not, however, be mixed with other insulins.

Contra-indications, warnings, etc Insulin zinc suspensions should never be given intravenously and are not suitable for the emergency treatment of diabetic coma or for insulin shock therapy.

Insulin requirements may increase during illness, puberty, pregnancy, emotional upsets or if drugs with hyperglycaemic activity are being taken. Insulin requirements may decrease during periods of increased activity, liver or kidney disease, or when drugs with hypoglycaemic activity are being taken.

Because bovine insulin is antigenic in man, insulin requirements may gradually increase over the years. Care should be taken if the patient is switched to a non-bovine insulin as the requirements may be different.

Overdose causes hypoglycaemia. The warning signs are vomiting (in children), palpitations, trembling, sweating, a tingling in the hands or lips, pallor, impaired vision, listlessness, confusion, and dizziness. Patients should be kept warm and sugar and rest.

If the patient is comatose, strong Dextrose Injection PC should be given intravenously.

Minor skin reactions are often seen in new patients. They generally cease spontaneously and do not interrupt therapy. Insulin may sometimes cause local lipoatrophy or, less commonly, fatty swellings.

Pharmaceutical precautions Insulin should be stored at a temperature between 2° and 8°C, when it can be expected to retain its potency for at least two years after the date of manufacture. It should not be frozen.

Legal category P.

Package quantities Packs of 10 vials, each containing 10 ml.

Further information Nil.

Product licence numbers

0 i.u./ml 0495/0010

0 i.u./ml 0495/0011

SOPHANE INSULIN INJECTION BP

Presentation A sterile suspension of a white crystalline precipitate of isophane insulin (bovine) in an isotonic aqueous medium buffered to a pH of 7.1 to 7.4. Two strengths, 40 and 80 international units/ml, are available.

Isophane Insulin Injection BP is supplied in 10 ml multidose glass containers.

The packaging and labels are colour coded. Blue and white signify Isophane Insulin Injection BP, 40 i.u./ml, and green and white, Isophane Insulin Injection BP, 80 i.u./ml.

Uses Insulin is used in growth-onset diabetes mellitus and maturity-onset diabetes mellitus not responding to diet or oral drugs. Its principal action is probably to accelerate the passage of glucose into the cells of certain tissues, notably skeletal muscle and adipose tissue.

Dosage and administration The practical aims of therapy are to reduce the blood glucose concentration to physiological levels and eliminate glycosuria and ketonuria. The dose required depends on the severity of the diabetes and has to be determined empirically. Most adult patients are controlled by 20–120 i.u./day. Children may require much less.

Isophane insulin is poorly soluble in body fluids and forms a depot from which insulin is slowly released. Its action begins after about two hours and lasts for about 18 hours. A single injection before breakfast is suitable for many patients (usually those requiring less than 40 i.u./day), but others require two injections/day or a combination of Isophane Insulin Injection BP and Insulin Injection BP.

Insulin is normally administered subcutaneously in the upper arms, thighs, buttocks or abdomen. Wherever possible, the patient should be taught to give the injection. The injection area should be varied so that the same site is never used more than about once a month. Care should be taken to see that a blood vessel has not been entered. The injection site should not be massaged.

Contra-indications, warnings, etc The vial should be shaken gently before use.

Where Isophane Insulin Injection BP is mixed with Insulin Injection BP in the same syringe, care should be taken to draw up the Insulin Injection BP into the syringe first, so avoiding contaminating it with the longer-acting insulin.

In no circumstances should Isophane Insulin Injection BP be given intravenously.

Insulin requirements may increase during illness, puberty, pregnancy, emotional upsets, or if drugs with hyperglycaemic activity are being taken. Insulin requirements may decrease during periods of increased activity, liver or kidney disease, or when drugs with hypoglycaemic activity are being taken.

Because bovine insulin is antigenic in man, insulin requirements may gradually increase over the years. Care should be taken if the patient is switched to a non-bovine insulin as the requirements may be different.

Minor skin reactions are often seen in new patients. They generally cease spontaneously and do not interrupt therapy. Insulin may sometimes cause local lipo-atrophy or, less commonly, fatty swellings.

Overdosage causes hypoglycaemia. The warning signs are vomiting (in children), palpitations, trembling, sweating, a tingling in the hands or lips, pallor, impaired vision, listlessness, confusion and dizziness. The patient should take sugar, and rest. If the patient is comatose, Strong Dextrose Injection BPC should be given intravenously.

Pharmaceutical precautions Insulin should be stored in a refrigerator (between 2° and 8°C) when it may be expected to retain its potency for at least two years after the date of manufacture. It should not be frozen.

Legal category P.**Package quantities** Packs of 10 vials.**Further information** Nil.**Product licence numbers**

40 i.u./ml 0495/5011

80 i.u./ml 0495/5012

PROTAMINE ZINC INSULIN INJECTION PhEur, BP

Presentation A sterile, white, suspension of a complex of protamine sulphate, zinc chloride and insulin (bovine), in an isotonic aqueous medium, buffered to a pH of 6.9 to 7.5. On standing, a white sediment is deposited, leaving a colourless or almost colourless supernatant. Protamine Zinc Insulin Injection is supplied in 10 ml multidose glass vials.

Two strengths, 40 and 80 units per ml, are available.

The packages and labels are colour coded. Blue and pink signifies Protamine Zinc Insulin Injection BP 40 units/ml and green and pink, Protamine Zinc Insulin Injection BP 80 units/ml.

Uses Insulin is used in juvenile-onset diabetes mellitus, and in maturity-onset diabetes mellitus unresponsive to diet or oral hypoglycaemic agents.

Dosage and administration The dose depends on the individual requirements of the patient and should be determined empirically.

Protamine Zinc Insulin Injection is poorly soluble in body fluids and forms a depot from which insulin is slowly released. Its action begins after 4 to 6 hours, and lasts for 24 to 36 hours. It may be used in conjunction with Insulin Injection BP.

Protamine Zinc Insulin Injection should only be given subcutaneously. Suitable sites are the upper arm, upper thigh, buttocks and lower abdomen. Whenever possible, the patient should be taught to give the injection. The same injection site should not be used more than about once a month. Care should be taken to ensure that a blood vessel has not been entered. The injection site should not be massaged.

Contra-indications, warnings, etc The vial should be shaken gently before use.

The mixing of Insulin Injection and Protamine Zinc Injection in the same syringe is not recommended, as the excess protamine sulphate in the latter preparation reacts with the Insulin Injection, reducing its immediate effect.

Under no circumstances should Protamine Zinc Insulin Injection be given intravenously.

Care should be taken if patients are changed from one insulin to another of a different animal source as the dosage required may differ.

Development of insulin antibodies may occasionally lead to a gradual increase in dosage requirement. Insulin requirements may also increase during illness (especially infection), pregnancy, puberty, emotional upsets, and concomitant administration of oral contraceptives, adrenaline, thiazide diuretics and other hyperglycaemic agents. Insulin requirements may decrease during periods of increased activity, liver or kidney disease, and concomitant administration of alcohol, monoamine oxidase inhibitors, propranolol, aspirin and other hypoglycaemic agents.

New patients often experience minor skin reactions, which generally cease spontaneously. Insulin may some-

times cause local lipo-atrophy. Allergic reactions to protamine sulphate content may occur infrequently.

Insulin overdosage causes hypoglycaemia. The early warning signs are weakness, giddiness, pallor, sweated palpitations, trembling etc. Later symptoms are depression or euphoria, inability to concentrate, drowsiness, amnesia etc. In children, headache, nausea and vomiting are common. Treatment of hypoglycaemia is sug ingestion, and rest. If untreated, hypoglycaemia leads to convulsions and coma. A comatose patient should be treated intravenously with up to 50 ml of a 50% solution of dextrose.

Pharmaceutical precautions Protamine Zinc Insulin Injection should be stored in a refrigerator (between 2°C and 8°C), when it may be expected to retain its potency for at least two years after the date of manufacture. It should not be frozen. It should not be used after the expiry date on the label or at any time if the precipitate appears clumped or granular after gentle shaking.

Legal category P.**Package quantities** Packs of 10 vials.**Further information** Nil.**Product licence numbers**

40 units/ml 0495/5007

80 units/ml 0495/5008

LITAREX*

Presentation Oval, white, biconvex, controlled-release tablets of diameter 16 mm and 8 mm. Each tablet contains lithium citrate 564 mg equivalent to 6 mmol lithium.

Uses Litarex is a source of lithium ions in a controlled release dosage form. Lithium may act by competing with sodium ions at various sites in the body. It changes the electrolyte composition of body fluids and increases the intracellular and total body water volume. The mechanism of action in affective disorders is not known. It is used for the treatment of acute mania and for the prophylaxis of recurrent affective disorders.

Dosage and administration Prophylactic long term treatment with Litarex should be started with a low dosage and then increased step-wise over a period of several weeks. Treatment is managed by measuring serum lithium concentration and monitoring clinical symptoms.

The initial dose is one tablet (6 mmol Li⁺) each morning and evening. Estimation of plasma-lithium concentration should be carried out after 48 hours and then at weekly intervals, and the dosage adjusted to produce a concentration of 0.80 to 1.00 mmol/litre. In some patients effective serum lithium levels may lie within the wider range 0.5 to 1.3 mmol/litre. Toxic symptoms are usually associated with serum lithium levels exceeding 1.5 mmol/litre. When the dosage is stabilised plasma-lithium estimations should be carried out weekly for one month and thereafter at monthly intervals.

Blood samples for estimation of lithium should be taken exactly 12 hours after the evening dose.

There is considerable biological variation in renal lithium clearance and thus the number of Litarex tablets required by individual patients to reach their particu-

ffective plasma concentration is variable. Tablets should be taken in two or three divided doses. Treatment of acute mania should be initiated in hospital. The required initial dose may be high, for example, 48 mmol lithium daily in four divided doses and access to immediate examination of plasma-lithium level is necessary. Lithium concentrations should not exceed 1.5 mmol/litre.

Use in elderly: Elderly patients may require smaller doses. Toxic symptoms are likely with serum concentrations above 1.0 mmol/litre.

Use in children: Not recommended.

Contra-indications, warnings, etc *Contra-indications:* Lithium is contra-indicated in patients with renal disease, cardiovascular disease or Addison's disease, and in women who are breast feeding.

Precautions: Lithium therapy should not be initiated unless adequate facilities for monitoring serum concentrations are available.

The use of lithium for long-term prophylactic treatment requires careful supervision. Serum lithium concentration should be monitored regularly and determined from a blood sample drawn 12 hours after the last dose; frequent monitoring is advisable after a change in dose; during an intercurrent illness provoking fluid loss; after starting a slimming diet; in the treatment of elderly patients; if signs of lithium toxicity or of mania or depressive relapse occur.

As bioavailability varies from product to product, a change of product should be regarded as initiation of new treatment. Blood levels should therefore be monitored weekly until reestablishment is achieved.

ECG, renal function and thyroid function should be determined prior to treatment. Patients should be euthyroid before starting treatment.

Use in pregnancy: The lithium ion crosses the placenta. It is, therefore, advisable that a pregnancy test should be carried out prior to treatment; and that women treated with lithium should adopt adequate contraceptive methods; and that treatment should be withdrawn for the first trimester of pregnancy. Treatment with lithium throughout pregnancy is associated with an incidence of congenital abnormality greater than that for the general population. Lithium dosage requirements may vary during pregnancy and after delivery; serum lithium concentrations should be monitored closely.

Lithium is excreted in breast milk, and therefore lithium treated patients should not breast feed.

Drug interactions: Lithium should be given with great care to patients taking diuretics as lithium clearance is reduced. A low sodium intake facilitates lithium reabsorption in the renal tubules and may lead to lithium accumulation.

Raised plasma levels of ADH may occur during treatment.

Symptoms of nephrogenic diabetes are particularly prevalent in patients receiving concurrent treatment with tri/tetracyclic antidepressants.

Serum lithium concentrations may increase during concomitant therapy with indomethacin or tetracycline.

Long-term treatment with lithium may result in permanent changes in the kidney and impairment of renal function. High serum concentrations of lithium, including episodes of acute lithium toxicity may enhance these changes. The minimum clinically effective dose of lithium should always be used. Patients should be maintained on lithium after 3–5 years only if, on assessment, benefit persists.

Renal function should be routinely monitored in patients with polyuria and polydipsia. Clear instructions regarding the symptoms of impending toxicity should be given by the doctor to all patients receiving long-term lithium therapy. Patients should also be warned to report if polyuria or polydipsia develop. Episodes of nausea and vomiting or other conditions leading to salt/water depletion should also be reported. Patients should be advised to maintain their usual salt and fluid intake.

Overdosage: Symptoms of severe lithium poisoning include hyper-reflexia, attacks of hyper-extension of the limbs, epileptic seizures, toxic psychosis, syncope, oliguria, circulatory failure and coma. Deaths have been reported. Gross overdosage with serum concentration of 3 mmol per litre is managed by haemodialysis or peritoneal dialysis.

Side-effects: Thirst and polyuria, fine tremor of the hands, muscular weakness, nausea and loose stools are the commonest side-effects during the first days or weeks of treatment. These often subside as treatment progresses.

During maintenance therapy fine hand tremor, weight gain, oedema, polyuria, hypothyroidism and goitre may occur.

More serious side-effects which may signal imminent lithium toxicity include loss of appetite, slurred speech, drowsiness, coarse hand tremor, vomiting, diarrhoea, fasciculation, vertigo and confusion.

Mild cognitive impairment may occur during long-term use.

Hypercalcaemia, hypermagnesaemia, hyperparathyroidism and an increase in antinuclear antibodies have also been reported.

Exacerbation of psoriasis may occur.

Pharmaceutical precautions: Tablets should be swallowed whole.

Legal category POM.

Package quantities Containers of 100.

Further information The lithium citrate in Litarex tablets is distributed in a plastic/lipid matrix from which the lithium salt is released over a period of four to five hours during passage through the gastro-intestinal tract. The tablets are formulated in such a way as to give absorption which is slow and even, so that rapid increases and high peak levels in serum lithium concentrations are avoided.

Product licence number 0495/0024.

PROTAMINE SULPHATE INJECTION BP

Presentation A sterile, pyrogen-free, clear, colourless 1% solution of Protamine Sulphate (Salmine) in Sodium Chloride Intravenous Infusion BP (0.9% w/v) adjusted to a pH of 2.5 to 3.5 and supplied in 5 ml glass ampoules.

Uses Protamine is a basic protein which combines with heparin to form a stable, inactive complex. It is used to counteract the anticoagulant effect of heparin; before surgery; after renal dialysis; after open-heart surgery; if excessive bleeding occurs and when an overdose has inadvertently been given.

Dosage and administration Protamine Sulphate Injection should be administered by slow intravenous injection over a period of about 10 minutes. The dose is dependent on the amount of heparin to be neutralised.

1 mg of Protamine Sulphate will usually neutralise at least 100 international units of mucous heparin or 80 units of lung heparin. Since heparin is being continuously excreted the dose of Protamine Sulphate should be reduced if more than 15 minutes have elapsed since the heparin injection. Ideally, the dose required to neutralise the action of heparin should be calculated from the results of determinations of the amount required to produce an acceptable blood clotting time in the patient. In gross excess, protamine itself acts as an anticoagulant.

Contra-indications, warnings, etc Not more than 50 mg Protamine Sulphate (5 ml) should be given at any one time. Protamine is not suitable for reversing the effect of oral anticoagulants.

A sudden fall in blood pressure, bradycardia, dyspnoea, transitory flushing and a feeling of warmth have been observed following injection of Protamine Sulphate.

Pharmaceutical precautions Store between 15°C and 25°C.

Legal category POM.

Package quantities 5 × 10 × 5 ml ampoules.

Further information Nil.

Product licence number 0495/5000.

UNIPARIN*

Presentation A sterile pyrogen-free, clear, colourless or slightly straw coloured solution of Heparin Sodium in Water for Injections BP adjusted to a pH of 5 to 8.

It is available in pre-filled sterile unit-dose syringes containing 5,000 i.u. in 0.2 ml.

Uses Heparin is an anticoagulant and acts by inhibiting thrombin and by potentiating the naturally occurring inhibitors of activated factor X (Xa). It is used in large doses (e.g. 10,000 i.u. six-hourly intravenously) in the treatment of arterial and venous thrombosis. Low blood levels of heparin produced by subcutaneous injections (5,000 i.u. twelve-hourly) exert an anti-thrombotic effect by inactivating factor Xa.

Uniparin is used in the prophylaxis of venous thrombosis and thromboembolism in surgical patients. Uniparin may also be considered in prophylaxis of thromboembolism in other situations, medical or obstetrical, in which there is considered to be increased risk of thromboembolism.

Dosage and administration Prophylactic administration of Uniparin consists of the subcutaneous injection of 5,000 i.u. every 12 hours. In the case of prophylactic administration to surgical patients, the first dose should

be given 2 hours before operation and continued for at least 10 days post-operatively.

Uniparin should be injected into the subcutaneous tissue of the lateral abdominal wall inserting the needle vertically into a pinched-up fold of skin.

Contra-indications, warnings, etc Heparin is contra-indicated in surgery of the brain, spinal cord and eye because of the special hazard of post-operative haemorrhage in these patients which could cause significant disability.

The relative risks and benefits of heparin should be carefully assessed in patients with a bleeding tendency or those patients with an actual or potential bleeding site, e.g. hiatus hernia, peptic ulcer, neoplasm, bacterial endocarditis, retinopathy, bleeding haemorrhoids. Neither menstruation nor pregnancy is a contra-indication. Heparin does not cross the placenta or appear in the milk.

In most patients the recommended low-dose regime produces no alteration in clotting time. However, patients show an individual response to heparin and it is therefore essential that the effect of therapy on coagulation time should be monitored in patients undergoing major surgery. Drugs that interfere with platelet aggregation e.g. aspirin, dextran solutions, should be used with care.

Although the Uniparin syringe is specifically designed to minimise the risk of overdosage, bleeding can occur and, under these circumstances, clotting time and platelet count should be determined. Prolonged clotting time will indicate the presence of an anticoagulant effect requiring neutralisation by protamine sulphate, and the dose should be calculated by titration of the individual patient's requirements.

Thrombocytopenia has been observed occasionally. There is some evidence that prolonged dosing with heparin (i.e. for many months) may cause alopecia or osteoporosis. Hyper-sensitivity reactions occur but are extremely rare.

Pharmaceutical precautions Uniparin should be stored at a temperature not exceeding 25°C when it can be expected to maintain its potency for at least three years after date of manufacture. Store protected from light.

Legal category POM.

Package quantities Packs of 50 pre-filled sterile disposable syringes.

Further information Nil.

Product licence number 0495/0009.

Wellcome Medical Division
The Wellcome Foundation Limited
Crewe Hall
Crewe, Cheshire CW1 1UB



Wellcome

ACTIDIL* TABLETS AND ELIXIR

Presentation Each tablet contains 2.5 mg Triprolidine Hydrochloride BP. Scored and coded Wellcome L2A. White in colour.

Each 5 ml of orange-coloured elixir contains 2 mg Triprolidine Hydrochloride BP and has a flavour of mandarin orange.

Uses Antihistamine.

Symptomatic relief of allergic conditions.

Actidil elixir is particularly suitable for use in children.

Dosage and administration *Adults:* 1–2 tablets or 5–10 ml elixir three times a day. In severe cases of allergy it may be advisable to give 2 or 3 tablets initially followed by 1 or 2 tablets every four hours.

Children: Over 12 years: As for adults.

6–12 years: 7.5 ml three times a day.

1–6 years: 5 ml three times a day.

Under 1 year: 2.5 ml three times a day.

Actidil Elixir may be diluted with Syrup BP.

Contra-indications, warnings, etc

Contra-indications: Contra-indicated in patients with known hypersensitivity to triprolidine.

Precautions: May cause drowsiness. Patients should not drive a vehicle or operate machinery until they have determined their own response. In some patients the drowsiness induced by antihistamines may be potentiated by alcohol or other central sedatives.

In severe hepatic or renal dysfunction a single dose of Actidil should be given initially and the response to it used as a guide to the patient's requirement for further administration of the product.

Side- and adverse effects: Triprolidine may cause drowsiness. Lichenoid skin eruptions due to triprolidine have rarely been reported

Use in pregnancy and lactation: No data are available on the use of Actidil in human pregnancy nor on the excretion of it or its metabolites in human milk.

Toxicity and treatment of overdosage: Drowsiness, dizziness, inco-ordination, weakness, convulsions and respiratory depression may occur.

Necessary measures should be taken to maintain and support respiration. Gastric lavage should be performed if indicated and convulsions controlled with diazepam. There are theoretical grounds for believing that the elimination of triprolidine and its metabolites could be accelerated by dialysis.

Pharmaceutical precautions *Tablets and elixir:* Store below 25°C. Protect from light.

Legal category P.

Package quantities Bottle of 100 tablets. Bottle of 500 ml elixir.

Further information Nil.

Product licence numbers

Tablets 0003/5001

Elixir 0003/5002

ACTIFED* COMPOUND LINCTUS

Presentation Each 5 ml of bright red-coloured syrup contains 1.25 mg Triprolidine Hydrochloride BP, 30 mg Pseudoephedrine Hydrochloride BP and 10 mg Codeine Phosphate BP, and has a mixed fruit flavour.

Uses Relief of cough and cough accompanied by nasal congestion and congestion of mucous membranes of the upper respiratory tract.

Dosage and administration

Adults: 10 ml three times a day.

Children: Over 12 years: 10 ml three times a day.

6–12 years: 7.5 ml three times a day.

1–6 years: 5 ml three times a day.

May be diluted with Syrup BP.

Pharmacology: Pseudoephedrine has direct and indirect sympathomimetic activity and is an orally effective upper respiratory tract decongestant. Pseudoephedrine is substantially less potent than ephedrine in producing both tachycardia and elevation in systolic blood pressure and considerably less potent in causing stimulation of the central nervous system. Codeine provides analgesic and antitussive activity whilst triprolidine provides antihistamine activity by antagonising H₁ receptors.

Contra-indications, warnings, etc

Contra-indications: Contra-indicated in patients with known hypersensitivity to any of the constituents.

Contra-indicated in persons under treatment with monoamine oxidase inhibitors and within two weeks of stopping such treatment.

Precautions: Although pseudoephedrine causes virtually no pressor effect in patients with normal blood pressure, Actifed Compound Linctus should be used with caution in patients with cardiovascular disorders, including hypertension. The effect of antihypertensive agents which modify sympathetic activity may be partially reversed by Actifed Compound Linctus.

Caution should also be exercised in patients taking other sympathomimetic agents, such as decongestants, appetite suppressants and amphetamine-like psychostimulants. The effects of a single dose on the blood pressure of these patients should be observed before recommending repeated or unsupervised treatment.

As with other sympathomimetic agents, caution should be exercised in patients with prostatic enlargement or bladder dysfunction.

In severe hepatic or renal dysfunction a single dose of Actifed Compound Linctus should be given initially and the response to it used as a guide to the patient's requirement for further administration of the product.

The antibacterial agent furazolidone is known to cause a progressive inhibition of monoamine oxidase and although there are no reports of hypertensive crises having occurred, it should not be administered concurrently with Actifed Compound Linctus.

May cause drowsiness. Patients should not drive a vehicle or operate machinery until they have determined their own response. In some patients the drowsiness induced by antihistamines may be potentiated by alcohol or other central sedatives.

Side- and adverse effects: In some patients, pseudoephedrine may occasionally cause insomnia. Triprolidine may cause drowsiness. Fixed drug eruption due to pseudoephedrine taking the form of nummular patches and lichenoid skin eruption due to triprolidine have been reported but these are rare events.

Use in pregnancy and lactation: No data are available on the use of Actifed Compound Linctus during pregnancy nor on the excretion of it or its metabolites in human milk.

Toxicity and treatment of overdose: Probable symptoms include drowsiness, inco-ordination, weakness, palpitation, irritability, hypertension, convulsions and difficulty in micturition. In severe cases there may be respiratory depression due to the codeine component. Gastric lavage and supportive measures for respiration and circulation should be performed if indicated. Convulsions should be controlled with an anticonvulsant. Catheterisation of the bladder may be necessary. Alpha-adrenergic blockade may be required to treat hypertensive crises and beta-adrenergic blockade for the control of supra-ventricular dysrhythmias. Pseudoephedrine has a renal excretion half-life of approximately seven hours and if desired the elimination can be accelerated by acid diuresis or by dialysis.

Pharmaceutical precautions Store below 25°C. Protect from light.

Legal category P.

Package quantities Bottles of 100 ml and 2 litres.

Further information Nil.

Product licence number 0003/5005.

ACTIFED* EXPECTORANT

Presentation Each 5 ml of clear orange syrup contains 1.25 mg Triprolidine Hydrochloride BP, 30 mg Pseudoephedrine Hydrochloride BP and 100 mg Guaiphenesin BP.

Uses Conditions where an expectorant and upper respiratory tract decongestant are required.

Dosage and administration

Adults and children over 12 years: 10 ml three times a day

Children 6–12 years: 5 ml three times a day

Children 1–6 years: 2.5 ml three times a day

Actifed Expectorant may be diluted with Syrup BP.

Pharmacology: Pseudoephedrine has direct and indirect sympathomimetic activity and is an orally effective upper respiratory tract decongestant. Pseudoephedrine is substantially less potent than ephedrine in producing both tachycardia and elevation in systolic blood pressure and considerably less potent in causing stimulation of the central nervous system. On the basis of widespread and

long established clinical use, guaiphenesin is recognised as an expectorant in bronchitis. Triprolidine provides antihistamine activity by antagonising H₁ receptors.

Contra-indications, warnings, etc

Contra-indications: Contra-indicated in patients with known hypersensitivity to pseudoephedrine, triprolidine or guaiphenesin. Contra-indicated in persons under treatment with monoamine oxidase inhibitors and within 2 weeks of stopping such treatment.

Precautions: Although pseudoephedrine causes virtually no pressor effect in patients with normal blood pressure, Actifed Expectorant should be used with caution in patients with cardiovascular disorders, including hypertension. The effect of anti-hypertensive agents that modify sympathetic activity may be partially reversed by Actifed Expectorant.

Also caution should be exercised in patients taking other sympathomimetic agents, such as decongestants, appetite suppressants and amphetamine-like psycho stimulants. The effects of a single dose on the blood pressure of these patients should be observed before recommending repeated or unsupervised treatment.

As with other sympathomimetic agents caution should be exercised in patients with prostatic enlargement or bladder dysfunction.

In severe hepatic or renal dysfunction a single dose of Actifed Expectorant should be given and the patient's response used as a guide to the dosage requirement for further administration.

The antibacterial agent furazolidone is known to cause a progressive inhibition of monoamine oxidase and although there are no reports of a hypertensive crisis having occurred, it should not be administered concurrently with Actifed Expectorant.

May cause drowsiness. Patients should not drive a vehicle or operate machinery until they have determined their own response. In some patients the drowsiness induced by antihistamines may be potentiated by alcohol or other central sedatives.

Side- and adverse effects: In some patients, pseudoephedrine may occasionally cause insomnia. Triprolidine may cause drowsiness. Fixed drug eruption due to pseudoephedrine taking the form of nummular patches and lichenoid skin eruption due to triprolidine have been reported but these are rare events.

Use in pregnancy and lactation: No data are available on the use of Actifed Expectorant in human pregnancy, or on the excretion of it or its metabolites in human milk.

Toxicity and treatment of overdose: Probable symptoms may comprise drowsiness, inco-ordination, weakness, palpitations, irritability, hypertension, convulsions and difficulty in micturition. Gastric lavage and supportive measures for respiration and circulation should be performed if indicated. Convulsions should be controlled with an anticonvulsant. Catheterisation of the bladder may be necessary. Alpha-adrenergic blockade may be required to treat hypertensive crisis and beta-adrenergic blockade for the control of supraventricular dysrhythmias.

Pseudoephedrine has a renal excretion half-life of approximately 7 hours and if desired the elimination can be accelerated by acid diuresis or by dialysis.

Pharmaceutical precautions Store below 25°C. Do not refrigerate. Protect from light.

Legal category P.

Package quantities Bottles of 100 ml. Bottles of litre.

Further information Nil.

Product licence number 0003/0152.

ACTIFED* TABLETS AND SYRUP

Presentation Each tablet contains 2.5 mg Triprolidine hydrochloride BP and 60 mg Pseudoephedrine Hydrochloride BP. Scored and coded Wellcome M2A. White colour.

Each 5 ml of clear, golden-yellow syrup contains .25 mg Triprolidine Hydrochloride BP and 30 mg Pseudoephedrine Hydrochloride BP, and has a pleasant flavour.

Uses Decongestant and antihistamine.

For decongestion of the upper respiratory tract including the sinuses, antra and Eustachian tubes in the common cold, hay fever, allergic and vasomotor rhinitis and aerotitis (otitis barotrauma).

Dosage and administration *Adults:* 1 tablet or 10 ml three times a day.

Children: Over 12 years: As for adults.

6-12 years: 7.5 ml three times a day.

1-6 years: 5 ml three times a day.

3-12 months: 2.5 ml three times a day.

Actifed Syrup may be diluted with Syrup BP.

Pharmacology: Pseudoephedrine has direct and indirect sympathomimetic activity and is an orally effective upper respiratory tract decongestant. Pseudoephedrine is substantially less potent than ephedrine in producing both bradycardia and elevation in systolic blood pressure and considerably less potent in causing stimulation of the central nervous system. Triprolidine provides antihistamine activity by antagonising H₁ receptors.

Contra-indications, warnings, etc

Contra-indications: Contra-indicated in patients with known hypersensitivity to pseudoephedrine or triprolidine.

Contra-indicated in persons under treatment with monoamine oxidase inhibitors, and within two weeks of stopping such treatment.

Precautions: Although pseudoephedrine causes virtually no pressor effect in patients with normal blood pressure, it should be used with caution in patients with cardiovascular disorders, including hypertension. The effect of antihypertensive agents which modify sympathetic activity may be partially reversed by Actifed.

Caution should also be exercised in patients taking other sympathomimetic agents, such as decongestants, appetite suppressants and amphetamine-like psychostimulants. The effects of a single dose on the blood pressure of these patients should be observed before recommending repeated or unsupervised treatment.

As with other sympathomimetic agents, caution should be exercised in patients with prostatic enlargement or bladder dysfunction.

In severe hepatic or renal dysfunction a single dose of Actifed should be given initially and the response to it used as a guide to the patient's requirement for further administration of the product.

The antibacterial agent furazolidone is known to cause

a progressive inhibition of monoamine oxidase and although there are no reports of hypertensive crises having occurred, it should not be administered concurrently with Actifed.

May cause drowsiness. Patients should not drive a vehicle or operate machinery until they have determined their own response. In some patients the drowsiness induced by antihistamines may be potentiated by alcohol or other central sedatives.

Side- and adverse effects: In some patients, pseudoephedrine may occasionally cause insomnia. Triprolidine may cause drowsiness. Fixed drug eruption due to pseudoephedrine taking the form of nummular patches and lichenoid skin eruption due to triprolidine have been reported but these are rare events.

Use in pregnancy and lactation: No data are available on the use of Actifed during pregnancy nor on the excretion of it or its metabolites in human milk.

Toxicity and treatment of overdose: Probable symptoms include drowsiness, inco-ordination, weakness, palpitation, irritability, hypertension, convulsions and difficulty in micturition. Gastric lavage and supportive measures for respiration and circulation should be performed if indicated. Convulsions should be controlled with an anticonvulsant. Catheterisation of the bladder may be necessary. Alpha-adrenergic blockade may be required to treat hypertensive crises and beta-adrenergic blockade for the control of supra-ventricular dysrhythmias.

Pseudoephedrine has a renal excretion half-life of approximately seven hours and if desired the elimination can be accelerated by acid diuresis or by dialysis.

Pharmaceutical precautions *Tablets and syrup:* Store below 25°C in a dry place. Protect from light.

Legal category P.

Package quantities Bottles of 100 and 500 tablets. Pack of 12 tablets. Bottles of 100 ml, 500 ml and 2 litres syrup.

Further information Nil.

Product licence numbers

Tablets 0003/5003

Syrup 0003/5004

ALCOPAR* DISPERSIBLE GRANULES

Presentation 5 g of the dispersible yellow-green granules contain the equivalent of 2.5 g bephenium (base) as Bephenium Hydroxynaphthoate BP.

Uses For the treatment of hookworm infestation by *Ancylostoma duodenale* (but not *Necator americanus*). Also concurrent ascariasis (roundworm infection) and trichostrongyliasis.

Dosage and administration The required dose of Alcopar should be mixed in water or in a flavoured drink and swallowed immediately.

Adults: The contents of 1 sachet.

Children: Over 2 years: The contents of 1 sachet.

Under 2 years or under 10 kg body weight: Half the contents of 1 sachet.

In the presence of heavy infestations it is recommended that treatment be repeated after three days.

No purgation or dietary restriction is necessary.

Contra-indications, warnings, etc

Contra-indications: Alcopar should not be given to patients with persistent vomiting.

Side- and adverse effects: No serious side-effects have been reported. Nausea, vomiting, abdominal discomfort and diarrhoea have occasionally been observed.

Use in pregnancy and lactation: Alcopar can be administered during pregnancy, and to the lactating mother.

Toxicity and treatment of overdosage: No data available. When administered orally, only a small fraction is absorbed from the gastro-intestinal tract. Thus symptoms are likely to be similar to those listed under side- and adverse effects. Gastric lavage followed by symptomatic and general supportive therapy is recommended.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Box of 25 × 5 g sachets.

Further information Nil.

Product licence number 0003/5007.

ALKERAN* TABLETS AND INJECTION

Presentation *Alkeran Tablets:* 2 mg Melphalan BP coloured pink with a white core and coded Wellcome A2A.

5 mg Melphalan BP coloured pink with a white core and coded Wellcome B2A.

Alkeran Injection: Each vial contains the equivalent of 100 mg sterile anhydrous Melphalan BP. 1 ml ampoule of Wellcome Acid-Alcohol Solvent and 9 ml ampoule of Wellcome Diluent are included in the unit pack.

Uses Cytotoxic agent. Alkylating agent.

Alkeran tablets are indicated in the treatment of multiple myeloma and advanced ovarian adenocarcinoma. Alkeran has a significant therapeutic effect in a proportion of patients suffering from advanced breast cancer and polycythaemia vera. Alkeran has been used as an adjuvant to surgery in the management of breast carcinoma.

Alkeran injection is indicated in the treatment of localised malignant melanoma of the extremities and localised soft tissue sarcoma of the extremities, when treated by regional perfusion.

Dosage and administration

Adults: The absorption of Alkeran after oral administration is variable and in some patients it is poorly absorbed. Dosage may need to be cautiously increased until myelosuppression is seen, in order to ensure that potentially therapeutic levels have been reached.

Multiple myeloma: The administration of Alkeran and prednisone is more effective than Alkeran alone. The combination is usually given on an intermittent basis, although the superiority of this technique over continuous therapy is not established. A typical dosage schedule is 0.15 mg/kg bodyweight/day in divided doses for 4 days together with 40 mg prednisone daily for 4 days, repeated at intervals of six weeks. Numerous regimes have been used and the literature should be consulted for details. Prolonging treatment beyond one year in responders does not appear to improve results.

Ovarian adenocarcinoma: The usual regime is 0.2 mg/kg bodyweight/day, given orally in divided doses, three times daily, for 5 days. This is repeated every 4–8 weeks,

provided the bone marrow has recovered. Similar results have been reported following a single intravenous infusion of 1 mg/kg bodyweight over 8 hours every weeks.

Advanced carcinoma of the breast: Alkeran may be given orally at a dose of 0.2–0.3 mg/kg bodyweight daily 6 mg/m² body surface area daily for 4–6 days at repeated every 3–6 weeks.

Malignant melanoma: Regional perfusion with Alkeran has been used as an adjuvant to surgery for early malignant melanoma and as palliative treatment for advanced but localised disease. The literature should be consulted for details of perfusion technique and dosage.

Soft tissue sarcoma: Regional perfusion with Alkeran has been used in the management of all stages of localised soft tissue sarcoma, usually in combination with surgery. Alkeran has frequently been given with actinomycin D and the literature should be consulted for details of dose regimes.

Polycythaemia vera: For remission induction the usual dose is 6–10 mg daily for 7–10 days, the maintenance dose is 2–4 mg daily. During maintenance careful haematological control is essential with dosage adjustment according to the results of frequent blood counts.

Children: Alkeran is very rarely indicated in children and dosage guidelines cannot be stated.

Administration of injection: Alkeran is unstable in infusion fluids. It should not be given in dextrose solutions. Infusions may be given with saline but, at room temperature, the same solution should not be used for more than 8 hours. Alternatively, Alkeran may be injected into the tubing of a fast running infusion.

When using Alkeran Injection precautions should be taken to avoid contact with it. The wearing of protective gloves is essential and eye protection is advised.

Preparation of Alkeran Melphalan Injection: 1 ml Wellcome Acid-Alcohol Solvent should be added to the vial containing 100 mg anhydrous melphalan. The vial should be shaken at once and the melphalan will dissolve immediately. When it has dissolved, 9 ml Wellcome Diluent should be added to give a resulting solution with a pH of about seven which will remain clear for some time. The solution should be prepared as required and injected within 15 to 30 minutes.

Contra-indications, warnings, etc

Contra-indications: In view of the seriousness of the indications there are no absolute contra-indications.

Precautions: Alkeran is an active cytotoxic agent for use only under the direction of physicians experienced in the administration of such agents.

Careful attention should be paid to the monitoring of blood counts to avoid the possibility of excessive myelosuppression and the risk of irreversible bone marrow aplasia.

The main side-effect of Alkeran treatment is bone marrow depression, leading to leucopenia and thrombocytopenia. Blood counts may continue to fall after treatment is stopped, so at the first sign of an abnormally large fall in leukocyte or platelet counts treatment should be temporarily interrupted.

Alkeran should not be given to patients who have recently received radiotherapy or other cytotoxic agents.

In patients with moderate to severe renal impairment the initial dose of the intravenous preparation should be reduced by 50%. Subsequent dosage should be determined according to haematological response. Currently

ailable pharmacokinetic data does not justify an solute recommendation on dosage reduction when ministering the oral preparation to these patients, but may be prudent to use a reduced dose initially.

Patients with renal impairment should be closely served as they may have uraemic marrow suppression. mporary significant elevation of the blood urea has en seen in the early stages of Alkeran therapy in reloma patients with renal damage.

Alkeran is mutagenic in animals and chromosome errations have been observed in patients being treated th the drug.

The evidence is growing that Alkeran in common with her alkylating agents may be leukaemogenic in man. ere have been reports of acute leukaemia occurring ter prolonged Alkeran treatment for diseases such as nyloid, malignant melanoma, macroglobulinaemia, ld agglutinin syndrome and ovarian cancer.

A comparison of patients with ovarian cancer who ceived alkylating agents with those who did not owed that the use of alkylating agents, including keran, significantly increased the incidence of acute ukaemia. The leukaemogenic risk must be balanced jainst the potential therapeutic benefit when consid- ing the use of Alkeran.

Alkeran causes suppression of ovarian function in emenopausal women resulting in amenorrhoea in a nificant number of patients.

Side- and adverse effects: The most common side-effect bone marrow depression.

Gastro-intestinal effects such as nausea and vomiting cur in up to 30 per cent of patients receiving Alkeran. iarrhoea and stomatitis may occasionally occur. Gastro- testinal disturbance is usually mild and occurs less equently than with combination cytotoxic therapy.

Alopecia has been reported but is uncommon. Macu- papular rashes and pruritus have occasionally been oted. There have also been case reports of pulmonary rosis and haemolytic anaemia occurring after mel- halan treatment.

A life-threatening immediate allergic reaction has been ported after intravenous administration.

Use in pregnancy and lactation: Although there are no ata available the possibility that melphalan may be ratogenic should be borne in mind because of its imilarity to other alkylating agents which are potentially ratogenic.

The use of Alkeran should be avoided whenever ossible during pregnancy, particularly during the first imester. In any individual case the potential hazard to e foetus must be balanced against the expected benefit o the mother.

Mothers receiving Alkeran should not breastfeed.

Toxicity and treatment of overdose: The principal toxic ffect is on the bone marrow and as there is no known ntidote the blood picture should be closely monitored or two weeks.

General supportive measures, together with appropri- te blood transfusion, should be instituted if necessary.

Pharmaceutical precautions *Alkeran Tablets:* Store elow 25°C in a dry place.

Alkeran Injection: Store below 25°C. Protect from light.

Legal category POM.

Package quantities *Tablets 2 mg:* Bottle of 25.

Tablets 5 mg: Bottle of 25.

Unit Pack: 1 vial containing the equivalent of Melphalan BP 100 mg; 1 ampoule of 1 ml Wellcome Acid-Alcohol Solvent for Alkeran; 1 ampoule of 9 ml Wellcome Diluent for Alkeran.

Further information Alkeran has the general phar- macological properties of nitrogen mustard compounds. It is well absorbed by the oral route, both in animals and in man.

Product licence numbers

Tablets 2 mg 0003/5008

Tablets 5 mg 0003/5009

Injection 0003/5010

ALMEVAX* RUBELLA VACCINE, LIVE BP

Presentation A live attenuated Wistar RA 27/3 rubella virus strain, propagated in human diploid cells, and freeze-dried.

0.5 ml of the reconstituted vaccine contains not less than 1,000 TCID₅₀ (tissue culture infective dose, 50).

This vaccine contains not more than 2 i.u. neomycin sulphate and 5 i.u. polymyxin B sulphate per 0.5 ml reconstituted vaccine.

Uses For active immunisation against rubella. Vaccination may be carried out at any age; preferably, however, it should be postponed beyond the first year of life since, below one year, the presence of maternal antibodies may impair the immune response. It should be noted that a past history of clinical rubella is an unreliable guide to immune status.

As with any other live attenuated virus vaccine, vaccination does not always result in seroconversion of 100% of susceptible subjects.

Dosage and administration *Adults:* 0.5 ml of the reconstituted vaccine.

Children: As for adults.

A single dose constitutes a full immunising course.

0.5 ml of the reconstituted vaccine is injected subcu- taneously. If the injection site is swabbed, only acetone, ether or isopropyl alcohol should be used and allowed to dry before the injection is made.

Method of use: For reconstitution, use only the special sterile diluent. Almevax diluent has been tested to ensure that it does not inhibit the live attenuated virus.

Use only sterile disposable syringes and needles which are free from traces of disinfectants or spirits. Use a fresh syringe and needle for each injection.

To ensure satisfactory reconstitution add the diluent slowly. The reconstituted vaccine should be colourless to light pink. See *Pharmaceutical Precautions* for handling of reconstituted vaccine.

Do not attempt to obtain more than the stated number of doses from the vial.

Reconstitution: *Pack size – volume of special sterile diluent required for reconstitution of vaccine.*

One-dose: The contents of the diluent container.

Ten-dose: The contents of the diluent container.

Contra-indications, warnings, etc

Contra-indications: Pregnant women must not be vac- cinated. Vaccination should not be carried out within four weeks of other live vaccines or within six weeks following administration of human immune serum glob- ulin, whole blood or plasma.

The vaccine should not be given to persons suffering from febrile conditions, intercurrent infections, malignant

disease, severe chronic disease, gamma-globulin deficiency or to those with impaired immune responsiveness, whether idiopathic or as a result of treatment with steroids, radiotherapy, cytotoxic drugs or other agents. Vaccination of subjects with thrombocytopenia should be avoided. The vaccine should not be administered to a subject who has experienced a serious reaction (e.g. anaphylaxis) to a previous dose of this vaccine or who is known to be hypersensitive to any component thereof. The vaccine contains a small amount of neomycin and polymyxin and should not be given to individuals known to be sensitive to either of them.

Precautions: Attenuated rubella virus vaccine may temporarily depress tests for cell-mediated immunity.

Rubella virus has been implicated as a possible aetiological factor in juvenile rheumatoid arthritis and, on that basis, it is suggested that children with rheumatoid arthritis should not be routinely immunised with rubella virus vaccine. Although anaphylaxis is rare, facilities for its management should always be available during vaccination.

Side- and adverse effects: Side-effects are uncommon, but mild symptoms may occur about the ninth day after vaccination. Symptoms relate to those seen following natural infection, but in the majority of cases are slight and transient. They include lymphadenopathy, rash, malaise, sore throat, mild fever, headache and occasionally temporary arthralgia, infrequently associated with signs of inflammation. Marked joint symptoms are more often seen in adult females than in children or adolescents. Nevertheless, even in adults, joint symptoms do not usually interfere with normal activities. Local pain and, rarely, erythema at the site of injection may occur.

Falls in platelet counts, unassociated with symptoms, have been described after vaccination. Neurological symptoms have been reported following vaccination. However, a cause and effect relationship has not been established.

Use in pregnancy and lactation: There is a possibility that live attenuated virus administered during pregnancy could infect and damage the foetus, producing congenital abnormalities. Therefore, *pregnant women must not be vaccinated* and pregnancy should be excluded before vaccination is undertaken. This danger to the developing foetus equally applies in the case of a pregnancy conceived within three months following vaccination. Women of childbearing age must be warned that, for at least three months after vaccination, they must take strict contraceptive precautions. If there is any possibility that they may become pregnant within this period, they should not be vaccinated.

Toxicity and treatment of overdose: Not applicable.

Pharmaceutical precautions Store at 2–8°C. Use special Almevax diluent for reconstitution. After reconstitution the vaccine should be kept cool (2–20°C), protected from light, and used within one hour.

Legal category POM.

Package quantities Ampoule of 1 dose, with container of special diluent.

Rubber-capped vial of 10 doses, with container of special diluent.

Further information Rubella vaccination policy differs from country to country. In the UK the vaccine is offered routinely to all girls between their 11th and 14th

birthdays and to susceptible adult females of childbearing age, including post-partum women.

Product licence number 0003/5123.

ANTEPAR* TABLETS AND ELIXIR

Presentation Each tablet contains Piperazine Phosphate BP equivalent to 500 mg Piperazine Hydrate B coloured yellow and scored, with the word Antep embossed on the reverse side.

The elixir is a pineapple-flavoured clear, orange coloured syrup containing a stable combination Piperazine Hydrate BP and Piperazine Citrate BP equivalent to 750 mg Piperazine Hydrate BP in each 5 ml.

Uses For the treatment of enterobiasis (pinworm threadworm infection) and ascariasis (roundworm infection).

Antepar Elixir is especially suitable for administration to infants and children.

Dosage and administration The tablets should be chewed.

Enterobiasis: The dose should be calculated according to age or weight and given once daily for seven days.

Age (years)	Approx. weight	Elixir	Tablets
Adults	Over 55 kg	15 ml	4
Children:			
Over 12	Over 40 kg	15 ml	4
5–12	17–40 kg	10 ml	3
2–4	13–16 kg	5 ml	1½
Under 2	Under 13 kg	50–75 mg piperazine hydrate/kg bodyweight	

It may be necessary to repeat the course after a week interval.

No special dietary regimen is needed.

Attention to general cleanliness is essential in order to prevent reinfection.

Owing to the facility with which pinworm infection is transmitted, it is advisable to examine all other members of a household once one is known to be infected. Treatment of all positive cases should be carried out simultaneously.

Ascariasis: A single dose taken preferably in the morning will usually produce complete clearance of worms from the gut.

Age (years)	Approx. weight	Elixir	Tablets
Adults	Over 55 kg	30 ml	8
Children:			
Over 10	Over 34 kg	30 ml	8
6–10	21–33 kg	20 ml	6
5–6	17–20 kg	15 ml	4½
2–4	13–16 kg	10 ml	3
Under 2	Under 13 kg	120 mg piperazine hydrate/kg bodyweight	

Contra-indications, warnings, etc

Contra-indications: Patients with a history of piperazine hypersensitivity or patients with renal failure.

Precautions: Caution should be exercised in treating

ients with renal or significant hepatic impairment, or tonic disorders of the central nervous system.

Recipitation of grand mal attacks in patients with a own history of epilepsy has been reported.

Care should be taken in administration of piperazine to ients receiving phenothiazines as it has been suggested that piperazine potentiates the extrapyramidal acts of chlorpromazine in man and animals.

fe- and adverse effects: These are uncommon when tepar is given at the recommended dosage but the lowing reactions have been reported:

Gastro-intestinal: nausea, vomiting, colic and irrhoea.

Central nervous system: transient headache and ziness. More severe reactions, including ataxia, muscle hypotonia, clonic contractions, drowsiness and paired consciousness, seldom occur at the recommended dosage in individuals without a previous history neurological abnormalities or renal disease.

Hypersensitivity reactions: urticaria, bullous eruptions, edema, arthralgia, fever and tachycardia.

Case reports of purpura, a viral hepatitis-like disorder d acute haemolysis in a glucose-6-phosphate dehydrogenase deficient individual after piperazine administration, appear in the medical literature.

se in pregnancy and lactation: The safety of Antepar use during pregnancy has not been established but etal toxicity studies in animals and extensive clinical perience have not revealed evidence that its use is sociated with a risk to the foetus. Unless symptoms arant immediate treatment it is advisable to postpone ministration of Antepar until after parturition. No ormation is available on the excretion of piperazine or metabolites in breast milk.

toxicity and treatment of overdosage: Symptoms of erdosage are likely to be similar in character to the fe-effects listed above. These may be expected to solve spontaneously. Gastric lavage should be carried t only if Antepar has been recently ingested. Adequate ids and routine supportive measures should be given, cluding the administration of anti-convulsants when cessary.

armaceutical precautions *Tablets:* Store below 10°C. Keep dry. Protect from light.

Elixir: Antepar Elixir may be diluted with Syrup BP. Store low 25°C. Protect from light.

gal category P.

ckage quantities *Tablets:* Strip pack of 28.

Elixir: Bottles of 100 ml, 500 ml.

urther information Nil.

duct licence numbers

Elixir 0003/5015

Tablets 0003/5016

RILVAX* YELLOW FEVER VACCINE, VE BP

**(7D strain live freeze-dried)
(el/Vac)**

resentation A specially stabilised freeze-dried preparation of the living attenuated 7D strain of yellow fever virus which is avirulent for man. The strain of virus used in this preparation is free of avian leucosis viruses and is opagated in leucosis-free chick embryos. The vaccine ifls the requirements of the World Health Organisation.

Each 0.5 ml dose of reconstituted vaccine contains the equivalent of not less than 1,000 mouse LD₅₀ units as defined by the World Health Organisation requirements, and not more than 2 i.u. of neomycin sulphate and 5 i.u. of polymyxin B sulphate.

The diluent consists of sterile water which has been specially tested to ensure that it does not inhibit the vaccine virus.

Uses For active immunisation of residents in yellow fever endemic areas and travellers to and from such areas, for the issue of an International Certificate of Vaccination, as required by the national health authorities of certain countries which consider these zones as infected areas (although the 'yellow-fever endemic zones' are in fact no longer included in the International Health Regulations). Yellow fever endemic areas are limited to the African and South American continents and Central America. The International Health Regulations define the form of certificate of vaccination to be used which, in the case of primary vaccination, is valid for a period of 10 years from the 10th day after vaccination. In the case of revaccination within 10 years, the certificate is valid at once.

Dosage and administration *Adults and children over age of 9 months:* The dose shall be the same for persons of all ages, 0.5 ml of reconstituted vaccine, given subcutaneously.

For reconstitution use only the special sterile diluent supplied.

Arilvax diluent has been tested to ensure that it does not inhibit the vaccine virus. Using a sterile syringe and needle inject the contents of the appropriate Arilvax diluent container into the vaccine vial and gently agitate to ensure reconstitution. The vaccine vial is sealed under vacuum to enhance stability and some users may prefer to break this vacuum to facilitate withdrawal of the vaccine solution. Any frothing will then subside.

See *Pharmaceutical precautions* for handling of reconstituted vaccine.

Use a fresh sterile disposable syringe and needle free from traces of spirit and disinfectants for each injection.

Do not attempt to obtain more than the stated number of doses from the vial.

Contra-indications, warnings, etc

Contra-indications: The vaccine should not be administered to a subject who has experienced a serious reaction (e.g. anaphylaxis) to a previous dose of this vaccine or who is known to be hypersensitive to any component thereof. It is advisable to avoid vaccination during an acute infection. Since the vaccine is prepared in chick embryos and contains small quantities of neomycin and polymyxin, it should not be administered to individuals who are hypersensitive to egg or chick protein or to these antibiotics.

The vaccine should not be given to those with impaired immune responsiveness, whether idiopathic or as a result of treatment with steroids, radiotherapy, cytotoxic drugs or other agents.

Precautions: The vaccine is not recommended for use in children under the age of 9 months. The decision to vaccinate infants under this age must depend on the anticipated risk of exposure to the disease, since the small number of cases of encephalitis that have been reported have nearly all occurred in infants under this age.

It is advisable to avoid administration of the vaccine within 6 weeks following the administration of immune

globulin on general principles. Similarly, on theoretical grounds it is advisable to avoid the administration of immune globulin within 2–3 weeks following vaccination. Although anaphylaxis is rare, facilities for its management should always be available during vaccination.

Side- and adverse effects: Reactions to the vaccine are extremely rare. Occasionally some redness and swelling may occur at the site of injection, and headache has been reported.

Use in pregnancy and lactation: On theoretical grounds the vaccine should not be administered during pregnancy.

Toxicity and treatment of overdosage: Not applicable.

Pharmaceutical precautions The freeze-dried vaccine should be stored at temperatures below 8°C and protected from light. Diluent should not be frozen but should be stored upright in a cool place (below 15°C).

After reconstitution the vaccine should be kept cool, protected from light and used within one hour.

Legal category POM.

Package quantities Freeze-dried vaccine in packs of 10 × 1-dose vials with separate diluent; 10 × 5-dose vials with separate diluent; 10 × 10-dose vials with separate diluent.

Further information It is recommended that when both yellow fever and smallpox vaccines need to be given, there should be an interval of at least three weeks between the two procedures.

If this is not feasible, the two vaccines may be given at the same time, but at separate sites. This is preferable to shortening the interval between the two procedures because of the possibility of interference between the two vaccines.

Product licence number 0003/0100.

BANOCIDE* TABLETS

Presentation Each tablet contains 50 mg Diethylcarbamazine Citrate BP. Each tablet is scored, coded 'Wellcome S2A' and is white in colour.

Uses For the treatment of filarial infections due to: *Wuchereria bancrofti*, *Brugia malayi*, *Onchocerca volvulus*, *Loa loa*.

For the prophylaxis of bancroftian and malayan filariasis and loiasis.

Dosage and administration **Adults: Treatment:** 6 mg/kg body weight daily in 3 divided doses for three weeks. In order to reduce the incidence and severity of allergic manifestations (see below), an initial dose of 1 mg/kg body weight, gradually increased over three days, is recommended.

Prophylaxis: Bancroftian and malayan filariasis – 50 mg monthly.

Loiasis – 4 mg/kg for three successive days each month.

Children: As for adults.

Contra-indications, warnings, etc

Contra-indications: None.

Precautions: Onchocerciasis patients receiving diethylcarbamazine should be carefully monitored for eye changes.

Side- and adverse effects: Allergic reactions, arising from the destruction of microfilariae, are common and may be severe – particularly during treatment of onchocerciasis and malayan filariasis. They take the form of generalised pruritus and conjunctival congestion and may be modified by the concurrent administration of antihistamines or corticosteroids.

Eye changes, including reduction in visual field, acuity, optic atrophy and optic disc leakage have been observed during administration of diethylcarbamazine for the treatment of onchocerciasis. The frequency, duration of the changes and the roles of the parasite and drug in their aetiology are, at present, unknown. Investigations have not shown eye changes during treatment of other filarial infections.

Use in pregnancy and lactation: In view of the severe reactions that may follow diethylcarbamazine administration, it is advisable to postpone treatment of pregnant women until after parturition. No information is available on the excretion of diethylcarbamazine in breast milk.

Toxicity and treatment of overdosage: Symptoms likely to be those of nausea, vomiting, headache, dizziness and drowsiness. In severe cases convulsions and coma may occur. Treatment by gastric lavage and supportive measures should be adequate. Anti-convulsants may be required in cases of convulsions and coma.

Pharmaceutical precautions Store below 25°C. Keep dry.

Legal category P.

Package quantities Bottle of 100 tablets.

Further information Nil.

Product licence number 0003/5018.

BRETYLATE* INJECTION

Presentation Each 2 ml ampoule contains 100 mg bretylium tosylate.

Uses Bretylate Injection may be of value in the treatment of patients with ventricular dysrhythmias resistant to conventional treatment. Its use should be limited to intensive care units in hospitals, where facilities for monitoring and treating patients with serious cardiac dysrhythmias are available. There is a delay of 20 minutes to 2 hours in the development of antidysrhythmic activity following administration. For this reason, quick-acting local anaesthetics remain the treatment of choice for patients with serious ventricular dysrhythmias. If they continue to recur despite conventional treatment, Bretylate Injection may be of value in restoring sinus rhythm.

Dosage and administration **Adults:** An initial dose of Bretylate Injection of 0.1 ml/kg body weight (equivalent to 5 mg bretylium tosylate/kg body weight) may be given by intramuscular injection, taking care to avoid important nerves. Further intramuscular injections of Bretylate may be given at intervals of six or eight hours. Individual doses should not exceed 0.1 ml/kg body weight.

Intravenous injection from a syringe should not be used because: (1) bolus injections may cause nausea and vomiting; (2) there is no evidence that antidysrhythmic activity is hastened by this mode of administration. Slow intravenous infusion (10 mg bretylium tosylate/kg body weight in 24 hours) does not cause nausea.

vomiting, but the clinical efficacy of this mode of administration is not known.

Idren: Not applicable.

Contra-indications, warnings, etc

Contra-indications: There is no evidence that prophylactic administration of Bretlylate Injection confers clinical benefit in patients with recent but uncomplicated myocardial infarction. Not to be used in the primary treatment of cardiac dysrhythmias.

Precautions: Bretlylate Injection, in the dose recommended, will cause adrenergic neurone blockade which may result in a fall of blood pressure. Patients should therefore remain recumbent throughout treatment. Tissue perfusion usually remains satisfactory despite falls of blood pressure. If, however, a fall in blood pressure raises concern, treatment should be stopped or subsequent doses reduced. If perfusion of a vital organ falls critically, it is recommended that blood volume be increased with the usual precautions.

Noradrenaline or sympathomimetic amines should not be administered.

Side- and adverse effects: Nausea with or without vomiting may occasionally follow intramuscular administration of Bretlylate Injection in the recommended dose. If this occurs, treatment should be stopped or subsequent doses reduced.

Use in pregnancy and lactation: No data are available on the use of Bretlylate in human pregnancy nor on the excretion of it or its metabolites in human milk.

Toxicity and treatment of overdose: The symptoms of acute overdose are likely to be marked hypotension and syncope.

Treatment is by means of general supportive measures such as intravenous infusion of plasma. Slow intravenous injection of noradrenaline or phenylephrine may be given under expert supervision.

Pharmaceutical precautions Store below 25°C. Do not freeze. Protect from light.

Legal category POM.

Package quantities Box of 5 ampoules.

Further information Nil.

Product licence number 0003/0038.

HOLERA VACCINE BP WELLCOME® (Chol/Vac)

Description Cholera vaccine contains heat-killed, phenol-preserved *Vibrio cholerae*, serotypes Inaba and Ogawa, at a concentration of not less than 8,000 million per ml.

Uses Immunisation against cholera including cholera Tor. Although this vaccine does not contain the El Tor serotypes of the classical Inaba and Ogawa serotypes, carefully controlled field studies have shown that the classical biotype equally protects against both classical and El Tor.

Dosage and administration Primary vaccination consists of two doses of vaccine given subcutaneously, intramuscularly, preferably separated by a period of over a month. This interval may be reduced even to seven days, though the response may be poorer, when rapid immunisation is necessary.

Age	First dose	All subsequent doses
1-5 years	0.1 ml	0.3 ml
5-10 years	0.3 ml	0.5 ml
Over 10 years	0.5 ml	1.0 ml

The container should on all occasions be well shaken before withdrawing material for injection.

Immunity is short-lived so that booster doses are required every six months under conditions of continued exposure. A single booster dose will suffice even if considerably longer than six months has elapsed since the last dose was administered.

For second and subsequent doses, particularly if there has been some reaction to a previous dose, it may be preferable to give the vaccine intradermally, in a volume of 0.1 ml where the subcutaneous dose is 0.5 ml or less, and 0.2 ml in other cases. However, it is possible that some countries may be unwilling to accept travellers who have not received the larger subcutaneous doses.

Travellers to or from certain countries which have reported cholera infection may be required to produce written evidence of cholera vaccination during the previous six months. A single dose normally meets these requirements and the International Certificate becomes valid six days after the first dose of vaccine was administered, but some countries may demand two doses. The certificate becomes valid immediately after a booster dose within six months of primary immunisation.

Contra-indications, warnings, etc

Contra-indications: The vaccine should not be administered to a subject who has experienced a serious reaction (e.g. anaphylaxis) to a previous dose of this vaccine or who is known to be hypersensitive to any component thereof. It is advisable to avoid vaccination during an acute infection.

Precautions: Repeated vaccination may result in the development of hypersensitivity to protein constituents of the vaccine. Although anaphylaxis is rare, facilities for its management should always be available during vaccination.

Cholera vaccine is not recommended for administration to infants under the age of one year as reactions are more frequent in this age group.

Intradermal administration of the first dose of a primary course is not recommended.

Side- and adverse effects: Local reactions consisting of pain, redness and swelling may develop within hours of vaccination resulting in discomfort at the site of injection for one or two days. They may be accompanied by fever, malaise and headache. Persons who have received numerous doses of cholera vaccine are particularly susceptible to such reactions even if many years have elapsed since the last vaccination was carried out. Occasionally delayed reactions occur. Serious reactions are uncommon but may include collapse, and rarely neurological symptoms such as neuritis, polyneuritis and various other manifestations of cerebral and meningeal involvement.

Use in pregnancy and lactation: This vaccine has been in wide use for many years without apparent ill consequence. However, as with any agent which may produce a systemic reaction, vaccination is, if possible, to be avoided in pregnancy.

Toxicity and treatment of overdose: Not applicable.

Pharmaceutical precautions Store at 2-8°C. Protect

from light. *Do not freeze.* When multidose containers are employed it is good practice to discard any partly used vaccine vials at the end of the vaccinating session.

This preparation on standing has a tendency to settle out in a gelatinous form. This is the nature of the organism in the vaccine and vigorous shaking as a rule will yield a homogenous suspension for injection. The container should on all occasions be well shaken before withdrawing material for injection.

Legal category POM.

Package quantities Vials of 1.5 ml and 10 ml.

Further information Nil.

Product licence number 0003/5126.

DARAPRIM* TABLETS

Presentation Each tablet contains 25 mg of Pyrimethamine BP. Scored and coded A3A and white in colour.

Uses Daraprim acts as a causal prophylactic and suppressive agent against malaria caused by *Plasmodium falciparum*. It also acts as a suppressant against *Plasmodium vivax* infections. In areas of known or suspected resistance to pyrimethamine or related compounds, another prophylactic should be used.

Dosage and administration *Adults:* 1 tablet regularly each week.

Children: Over 10 years: 1 tablet regularly each week.

5–10 years: $\frac{1}{2}$ tablet regularly each week.

Under 5 years: Formulation not applicable.

Daraprim is rapidly absorbed and therefore prophylactic cover can be expected shortly after the first dose. Prophylaxis should commence before arrival in an endemic area and be continued once weekly. On returning to a non-malarious area dosage should be maintained for a further four weeks.

Contra-indications, warnings, etc

Contra-indications: Daraprim should not be given to patients with a history of pyrimethamine sensitivity.

Precautions: The recommended dosage should not be exceeded.

Daraprim should be used with caution in patients with hepatic or renal disorders.

During pregnancy and in other conditions predisposing to folate deficiency, a folate supplement should be given.

Daraprim, by its mode of action, may further depress folate metabolism in patients receiving treatment with other folate inhibitors. Occasional reports suggest that individuals taking pyrimethamine as malarial prophylaxis at doses in excess of 25 mg weekly may develop megaloblastic anaemia if co-trimoxazole is prescribed concurrently.

The concurrent administration of lorazepam and Daraprim may induce hepatotoxicity.

Side- and adverse effects: At the recommended dose, side-effects are rare. Occasionally, rashes have been observed. Excessive doses may produce a macrocytic anaemia resembling that of folic acid deficiency.

Use in pregnancy and lactation: While there is a theoretical risk of foetal abnormality with all folate inhibitors given during pregnancy, no such adverse effects have been reported with Daraprim. A folate supplement should be given to pregnant women receiv-

ing Daraprim. The amount of pyrimethamine excreted in breast milk is insufficient to contra-indicate its use in lactating mothers.

Toxicity and treatment of overdosage: Symptoms reported have included vomiting, cyanosis, respiratory distress, convulsions and tachycardia. In less severe cases gastric lavage, adequate fluids and general supportive measures are recommended. In severe cases maintenance of a clear airway and control of convulsions are required, in addition. Fresh blood transfusions counteract blood dyscrasias should be available.

To counteract possible folate deficiency, calcium folinate 9 to 15 mg daily should be given until the signs of toxicity have subsided.

Pharmaceutical precautions Store below 25°C. Protect from light.

Legal category P.

Package quantities Strip pack of 30 tablets.

Further information When taken as directed Daraprim is an effective antimalarial, but it may be rendered ineffective by the development of drug resistance from time to time in certain regions. Local medical advice about the suitability of the product should, therefore, be obtained immediately on arrival in a malarious region.

Product licence number 0003/5026.

DIPHTHERIA VACCINE TAF, BP 1968 WELLCOME* (Dip/Vac/TAF)

Presentation This preparation is a suspension of the floccules that are formed when toxoid prepared from the toxin of *Corynebacterium diphtheriae* and its antitoxin obtained from horse serum are mixed. The amount of antitoxin in the mixture is equivalent to about 80% of the toxoid produced. Each dose of Toxoid-Antitoxin Floccules contains not less than 100 Lf of the original toxoid.

Phenol is added at a concentration of 0.5% as a preservative.

Uses For active immunisation against diphtheria.

Diphtheria vaccine TAF is used for inducing or reinforcing immunity to diphtheria in persons over the age of 10 years and who are known to be Schick positive.

Dosage and administration *Adults:* For primary immunisation it is necessary to give three intramuscular or deep subcutaneous injections of 0.5 ml at intervals of not less than four weeks. For reinforcement of immunity a single 0.5 ml dose is sufficient.

Children: Over 10 years: As above.

Diphtheria Vaccine TAF is not as potent an immunising agent against diphtheria as the adsorbed vaccine and therefore its use is reserved for individuals for whom the other preparations are unsuitable. Primary immunisation against diphtheria in children up to the age of 10 years is usually carried out by the administration of the more potent Diphtheria, Tetanus, Pertussis vaccine (DTPe/Vac, DTPe/Vac/Ads). Diphtheria and Tetanus vaccines (DT/Vac, DT/Vac/Ads) or adsorbed diphtheria vaccine (Dip/Vac/Ads) as appropriate.

The vial should be well shaken before withdrawing each dose.

Record the title, dose and lot number of all vaccine and date administered. Report any untoward reactions

Intra-indications, warnings, etc

Contra-indications: Contra-indicated in persons allergic to horse serum. The vaccine should not be administered to a subject who has experienced a serious reaction (e.g. anaphylaxis) to a previous dose of this vaccine or who is known to be hypersensitive to any component thereof. It is advisable to avoid vaccination during an acute infection.

Precautions: This vaccine contains antitoxin derived from horse serum and may, therefore, cause sensitisation. Although anaphylaxis is rare, facilities for its management should always be available during vaccination.

Side- and adverse effects: Reactions occur infrequently. They include swelling, redness or tenderness that may develop locally and usually subsides without treatment. Headache, malaise and pyrexia may occasionally occur.

Use in pregnancy and lactation: Accurate information is not available on the safety of the vaccine in pregnancy.

Toxicity and treatment of overdosage: Not applicable.

Pharmaceutical precautions Store at 2–8°C. Protect from light.

Do not freeze.

When multi-dose containers are employed, it is good practice to discard any partly used vaccine vials at the end of the vaccinating session.

Legal category POM.

Package quantities Vial of 5 ml.

Further information Nil.

Product licence number 0003/5129.

ADSORBED DIPHTHERIA VACCINE BP, WELLCOME* (Dip/Vac/Ads)

Presentation Adsorbed Diphtheria Vaccine is a suspension of highly purified toxoid prepared from the exotoxin of *Corynebacterium diphtheriae* adsorbed onto hydrated aluminium phosphate. The aluminium content does not exceed 1.25 mg/dose. Thiomersal BP is added as a preservative to a concentration of 0.01%.

Each 0.5 ml dose has an immunising potency of not less than 30 International Units (IU).

The immunising potency of this vaccine is now expressed in International Units in accordance with the requirements of the European and British Pharmacopoeias. These units measure the immunising activity of the vaccine whereas the previously used Lf units expressed the quantity of toxoid present. There is no simple numerical relationship between IU and Lf. No change has been made to the potency although it is now expressed in IU.

Uses For active immunisation against diphtheria.

Primary immunisation against diphtheria in infancy is usually carried out by the administration of combined adsorbed diphtheria and tetanus (DT/Vac/Ads) or Trivax* (DTPe/Vac) or Trivax-Ad* (DTPe/Vac/Ads). Primary immunisation against diphtheria alone for children under the age of 10 years may be carried out with adsorbed diphtheria vaccine. It may also be used in healthy positive adults and children over the age of 10 years who are at particular risk.

Dosage and administration The primary course of immunisation is two doses given by intramuscular or

deep subcutaneous injection separated by an interval of at least four weeks.

Adults and children over 10 years of age: Two doses of 0.2 ml.

Children under 10 years of age: Two doses of 0.5 ml.

A reinforcing dose of 0.5 ml should be administered at about five years of age to children immunised in infancy.

Oral Poliomyelitis Vaccine BP may be given at the same time as Diphtheria Vaccine.

Shake well before each dose is withdrawn. Record the title, dose and lot number of all vaccines and the date administered. Report any untoward reactions.

Contra-indications, warnings, etc

Contra-indications: Adsorbed diphtheria vaccine should not be administered intradermally. The vaccine should not be administered to a subject who has experienced a serious reaction (e.g. anaphylaxis) to a previous dose of this vaccine or who is known to be hypersensitive to any component thereof. It is advisable to avoid vaccination during an acute infection.

Precautions: Adsorbed Diphtheria Vaccine should not be administered to children over the age of 10 years or to adults without a preliminary Schick test, to avoid giving vaccine to persons who are already immune or to those who are hypersensitive, i.e. those who show a negative-or-pseudo-Schick reaction.

Although anaphylaxis is rare, facilities for its management should always be available during vaccination.

Side- and adverse effects: Local reactions consisting of swelling, redness and tenderness at the injection site may occur and occasionally may be severe. They may be more frequent and severe after the second than the first injection. Local reactions are uncommon in children under two years of age.

General reactions consisting of transient fever, malaise and headache may occur.

Allergic reactions, urticaria, pallor and dyspnoea have been reported following injection of adsorbed diphtheria vaccine.

A small painless nodule may form at the injection site but usually disappears without sequelae. However, persistent nodules at the injection site may occasionally follow the administration of this vaccine especially if the inoculation is introduced into the superficial layers of subcutaneous tissue.

Use in pregnancy and lactation: Accurate information is not available on the safety of the vaccine in pregnancy.

Toxicity and treatment of overdosage: Not applicable.

Pharmaceutical precautions Store at 2–8°C. Protect from light.

Do not freeze.

Legal category POM.

Package quantities Box of 5 × 0.5 ml ampoules.

Further information Nil.

Product licence number 0003/5128.

DIPHTHERIA AND TETANUS VACCINE BP, WELLCOME* (DT/Vac/FT)

Presentation Diphtheria and tetanus vaccine is a mixture of purified diphtheria and tetanus toxoids which are prepared by formalin detoxification of *Corynebacterium diphtheriae* and *Clostridium tetani* exotoxins.

Thiomersal BP is added as a preservative to a concentration of 0.01%. Each 0.5 ml dose contains 25 Lf diphtheria toxoid and 3.5 Lf tetanus toxoid.

The antigenic content and formulation of this vaccine has not been changed, although the labelled content of the tetanus component has been altered to conform with the flocculation equivalence of the new British reference antitoxin preparation.

Uses For reinforcement of immunity at five years or over in children who were immunised in infancy with either adsorbed diphtheria-tetanus vaccine (DT/Vac/Ads) or with Trivax* (DTPer/Vac) or Trivax-Ad* (DTPer/Vac/Ads) and who do not require continued immunisation against whooping cough.

The more potent antigen, Adsorbed Diphtheria and Tetanus Vaccine is preferred for primary immunisation against diphtheria and tetanus, but either preparation of combined diphtheria-tetanus vaccine may be used for reinforcement of immunity.

Simultaneous reinforcement of immunity to diphtheria and tetanus in adults and children over 10 years of age is rarely needed. Diphtheria-containing vaccines should not be given unless a Schick test has been carried out to avoid giving the vaccine to persons who are already immune or to those who are hypersensitive, i.e. those who show a negative-or-pseudo-Schick reaction.

Dosage and administration The vaccine is given by intramuscular or deep subcutaneous injection.

Children under 10 years: 0.5 ml.

Adults and children over 10 years: 0.2 ml.

In subjects who suffered a reaction to a previous dose of adsorbed vaccine it may be preferable to administer 0.1 ml of Diphtheria and Tetanus vaccine in Simple Solution intradermally. Oral Poliomyelitis Vaccine BP may be given at the same time as Diphtheria Tetanus Vaccine.

Shake well before withdrawing a dose. Record the title, dose and lot numbers of all vaccines and date administered. Report any untoward reactions.

Contra-indications, warnings, etc

Contra-indications: The vaccine should not be administered to a subject who has experienced a serious reaction (e.g. anaphylaxis) to a previous dose of this vaccine or who is known to be hypersensitive to any component thereof. It is advisable to avoid vaccination during an acute infection.

Precautions: Although anaphylaxis is rare, facilities for its management should always be available during vaccination.

Side- and adverse effects: Local reactions, swelling, redness and tenderness at the injection site, and general reactions, transient fever, malaise and headache may be caused by either or both component toxoids. Acute allergic reactions – anaphylaxis, urticaria, angioneurotic oedema, pallor and dyspnoea, serum sickness and peripheral neuropathy have been reported following administration of diphtheria or tetanus vaccines.

Transverse myelitis has been reported after simultaneous administration of diphtheria and tetanus vaccine and oral polio vaccine, but a cause and effect relationship has not been established.

Use in pregnancy and lactation: Since simultaneous vaccination against diphtheria and tetanus in adults is uncommon, there is no accurate information on the safety of this vaccine in pregnancy.

Toxicity and treatment of overdose: Not applicable.

Pharmaceutical precautions Store at 2–8°C. Protect from light.

Do not freeze.

When multi-dose containers are employed it is good practice to discard any partly used vaccine vials at the end of the vaccinating session.

Legal category POM.

Package quantities Vial of 5 ml.

Further information Nil.

Product licence number 0003/5130.

ADSORBED DIPHTHERIA AND TETANUS VACCINE BP, WELLCOME* (DT/Vac/Ads)

Presentation Adsorbed diphtheria and tetanus vaccine is a mixture of highly purified diphtheria and tetanus toxoids which are prepared by formalin detoxification of *Corynebacterium diphtheriae* and *Clostridium tetani* exotoxins. The toxoids are adsorbed onto aluminium hydroxide. The aluminium content does not exceed 1.25 mg/dose. Thiomersal BP is added as a preservative to a concentration of 0.01%. Each 0.5 ml dose contains not less than 30 i.u. diphtheria toxoid and 40 i.u. tetanus toxoid.

The immunising potency of this vaccine is not expressed in International Units in accordance with the requirements of the European and British Pharmacopoeias. These units measure the immunising activity of the vaccine whereas the previously used Lf unit expressed the quantity of toxoid present. There is no simple numerical relationship between IU and Lf. No change has been made to the potency although it is not expressed in IU.

Uses For active immunisation against diphtheria and tetanus.

Adsorbed diphtheria and tetanus vaccine is used principally for the primary immunisation of infants and children under ten years of age against tetanus and diphtheria where the use of pertussis-containing vaccines (DTPer/Vac, DTPer/Vac/Ads) is contra-indicated or not required. It is also given to reinforce immunity in children under 10 years of age immunised in infancy with diphtheria and tetanus vaccine. Trivax* or Trivax Ad* (DT/Vac/Ads, DTPer/Vac, DTPer/Vac/Ads).

Simultaneous primary immunisation or reinforcement of immunity to diphtheria and tetanus in adults and children over 10 years of age is rarely needed. Diphtheria containing vaccines should not be given to these subjects unless a Schick test has been carried out to avoid immunising persons who are already immune and/or hypersensitive, i.e., those who show a negative and/or-pseudo-Schick reaction.

Dosage and administration For primary immunisation two intramuscular or deep subcutaneous injections separated by an interval of at least four weeks are recommended.

Children under 10 years: Two doses of 0.5 ml.

Adults and children over 10 years: Two doses of 0.2 ml

A single dose of adsorbed tetanus vaccine should be administered 6 to 12 months after the second dose of the combined diphtheria and tetanus vaccine to complete the primary course of immunisation against tetanus.

A reinforcing dose of 0.5 ml of adsorbed or simple diphtheria and tetanus vaccines should be administered at about five years of age to children immunised in

nfancy with diphtheria and tetanus vaccine or combined diphtheria, tetanus and pertussis vaccine.

It may be preferable to administer 0.1 ml of Diphtheria and Tetanus vaccine in simple solution intradermally to adults and children who have suffered a reaction to a previous dose of adsorbed vaccine.

Poliomyelitis vaccine (oral) may be given at the same time as diphtheria and tetanus vaccine.

Shake thoroughly before withdrawing each dose. Record the title, dose and lot numbers of all vaccines and the date administered. Report any untoward reactions.

Contra-indications, warnings, etc

Contra-indications: Adsorbed Diphtheria and Tetanus vaccine should not be administered intradermally.

The vaccine should not be administered to a subject who has experienced a serious reaction (e.g. anaphylaxis) to a previous dose of this vaccine or who is known to be hypersensitive to any component thereof. It is advisable to avoid vaccination during an acute infection.

Precautions: Although anaphylaxis is rare, facilities for its management should always be available during vaccination.

Side- and adverse effects: Local reactions, swelling, redness and tenderness at the injection site, and general reactions, transient fever, malaise and headache may be caused by either or both component toxoids. Acute allergic reactions – anaphylaxis, urticaria, angioneurotic oedema, pallor and dyspnoea, serum sickness and peripheral neuropathy have been reported following administration of diphtheria or tetanus vaccines.

Persistent nodules at the injection site may occasionally follow administration of adsorbed vaccine, especially if the inoculation is into the superficial layers of subcutaneous tissue.

Transverse myelitis has been reported after simultaneous administration of diphtheria and tetanus vaccine and oral polio vaccine, but a cause and effect relationship has not been established.

Use in pregnancy and lactation: Since simultaneous vaccination against diphtheria and tetanus in adults is uncommon there is no accurate information on the safety of this vaccine in pregnancy.

Toxicity and treatment of overdosage: Not applicable.

Pharmaceutical precautions Store at 2–8°C. Protect from light.

Do not freeze.

It is good practice to discard any partly used vaccine vials at the end of the vaccinating session.

Legal category POM.

Package quantities Box of 5 × 0.5 ml ampoules. Vial of 5 ml.

Further information Nil.

Product licence number 0003/5131.

HUMOTET* ANTITETANUS IMMUNOGLOBULIN INJECTION BP

Presentation Purified immunoglobulin obtained from the sera of healthy human donors known to have high levels of tetanus antitoxin following active immunisation with tetanus vaccine.

Humotet is a clear, colourless, semi-viscous liquid containing thiomersal 0.01% as a preservative, and glycine 2.25%. Each vial contains 250 i.u. of tetanus antitoxin in 1.0 ml solution.

Uses For passive immunisation against tetanus, in conjunction with adsorbed tetanus vaccine as soon as practicable after a tetanus-susceptible person has sustained a wound. Also for the treatment of tetanus.

Dosage and administration *Prevention of tetanus following injury: Adults:* Humotet should be administered by intramuscular injection usually in a dose of 250 i.u. – see table on next page.

Persons not immunised, or inadequately immunised, with tetanus vaccine are susceptible to tetanus and all wounds are prone to tetanus infection. In cases of doubt a person should be regarded as inadequately immunised.

Administration of immunoglobulin does not obviate the need for debridement and wound cleansing, nor does it contra-indicate the use of antibiotics.

The prophylactic immunisation schedule against tetanus (see table) should be carried out as soon as possible after a person has sustained a wound. Passive immunisation with immunoglobulin should be accompanied by simultaneous active immunisation with adsorbed tetanus vaccine.

If more than 24 hours have elapsed since the wound was sustained or if there is a risk of heavy contamination with *Clostridium tetani* 2 ml (500 i.u.). Humotet should be given, irrespective of immunisation history.

Humotet and adsorbed tetanus vaccine should be administered with separate syringes and into separate sites. Tetanus vaccine in simple solution is unsuitable for administration concurrently with Humotet.

A single dose of Humotet usually provides a protective level of tetanus antitoxin, over 0.01 i.u. per ml serum, for

<i>Patient's history</i>	<i>Immediate action</i>		<i>Follow-up action</i>
<i>Previous record of receiving tetanus vaccine</i>	<i>Administer Humotet</i>	<i>Administer adsorbed tetanus vaccine</i>	<i>Administer tetanus vaccine (adsorbed or in simple solution)</i>
None or Not known	1.0 ml (250 i.u.)	0.5 ml	0.5 ml after 6–12 weeks and 6–12 months
One dose (during last 6 weeks)	1.0 ml (250 i.u.)	0.5 ml to be given 4–6 weeks after first dose of vaccine	0.5 ml 6–12 months after second dose
One dose (more than 6 weeks ago)	1.0 ml (250 i.u.)	0.5 ml	0.5 ml 6–12 months after second dose
Two doses	Nil	0.5 ml to be given if more than 6 weeks after second dose of vaccine	Nil
Three doses	Nil	0.5 ml if more than 1 year since third dose of vaccine	Nil

a period of four weeks. Long-term immunity against tetanus is conferred by giving further doses: see table.

Children: As for adults.

Treatment of tetanus: Adults: 30–300 i.u. per kilogram body weight given intramuscularly.

Children: As for adults.

Contra-indications, warnings, etc

Contra-indications: Humotet should not be given intravenously. The administration of immunoglobulin may be contra-indicated by a history of anaphylaxis resulting from administration of a previous dose of human gamma-globulin.

Precautions: Humotet should not be given concurrently with tetanus in simple solution.

Although anaphylaxis is rare, facilities for its management should always be available during vaccination.

Side- and adverse effects: A local reaction, consisting of a small area of inflammation and tenderness, may occur after administration of the immunoglobulin, but this rarely constitutes more than a temporary inconvenience. Constitutional upsets, and particularly anaphylactic reactions, are uncommon. Patients with antibody deficiency syndromes may be liable to have local reactions after administration of the immunoglobulin.

Use in pregnancy and lactation: Accurate information is not available on the safety of Humotet in pregnancy.

Toxicity and treatment of overdosage: Not applicable.

Pharmaceutical precautions Store at 2–8°C.

Do not freeze.

Legal category POM.

Package quantities Vial containing 250 i.u. in 1.0 ml.

Further information Nil.

Product licence number 0003/0087.

IMURAN* TABLETS AND INJECTION

Presentation Each tablet contains 50 mg Azathioprine BP coded 'Wellcome K7A' and is yellow. Each vial of injection contains the equivalent of 50 mg Azathioprine BP as its sodium salt, freeze-dried.

Uses Imuran (Tablets and Injection) facilitates the survival and function of organ transplants.

Imuran Tablets have a significant therapeutic effect in a proportion of patients suffering from chronic active hepatitis, severe rheumatoid arthritis, systemic lupus erythematosus (SLE), idiopathic thrombocytopenic purpura, acquired haemolytic anaemia, severe cases of specified dermatological diseases (pemphigus vulgaris, dermatomyositis, polyarteritis nodosa, pyoderma gangrenosa) when these conditions are: (a) refractory to corticosteroids or (b) when corticosteroids are contra-indicated or (c) controlled by corticosteroids in dosages which are producing severe side-effects. In patients with such side-effects, the aim of Imuran medication is to reduce the required maintenance dose of steroids.

In pemphigus and rheumatoid arthritis Imuran has been shown to have significant therapeutic activity when used without corticosteroids.

The risks associated with Imuran therapy should be considered against the severity of the patient's condition and the expected clinical effect.

The use of Imuran in other indications must be regarded as experimental.

Dosage and administration *Adults:* Imuran Tablets are given by mouth, but patients unable to take oral medication may be given Imuran Injection for a short period.

Transplantation: A loading dose of up to 5 mg/kg orally or intravenously is usually given. The dosage during the first three months after transplantation is usually 1.0–4.0 mg/kg body weight per day (median 2.4 mg/kg body weight per day). 1.0–2.5 mg/kg body weight per day may be given intravenously as a maintenance dose, but only if oral therapy is impracticable. Cessation of Imuran therapy, even after a period of years, carries a high risk of rejection within a few weeks.

Other conditions: for the treatment of the conditions listed under *Uses*, except for chronic active hepatitis, the dosage is usually between 2.0 and 2.5 mg/kg body weight per day. For the treatment of chronic active hepatitis the dosage is usually between 1.0 and 1.5 mg/kg body weight per day.

The dosage of Imuran and the duration of treatment may vary according to the condition, its severity and the clinical response obtained. A therapeutic response may not be evident for a few days or even weeks after initiation of Imuran therapy. If no discernible improvement occurs in the patient's condition within three months, consideration should be given to the withdrawal of the drug. Treatment is otherwise undertaken on a long-term basis unless the patient exhibits evidence of intolerance to the drug.

Administration by intravenous injection (in transplantation only): the contents of each vial should be dissolved in not less than 5 ml of sterile pyrogen-free water for injection. The solution is alkaline and very irritant and must, therefore, be given slowly (not less than one minute) and then flushed through with at least 50 ml of physiological saline or glucose saline. The solution should be prepared immediately before use and any remainder discarded. There are no data on the compatibility of Imuran Injection with other intravenous fluids.

Children: As for adults.

Contra-indications, warnings, etc

Contra-indications: Imuran hypersensitivity will generally be a contra-indication to continued use.

Precautions: There are potential hazards in the use of this preparation. Therefore, it should not be prescribed unless the patient can be adequately monitored for toxic effects throughout the duration of the therapy.

During the first eight weeks of therapy with Imuran complete blood counts, including platelet counts, must be performed at least weekly (and more frequently when higher dosages are used or in the presence of disturbed renal or hepatic function), and with decreasing frequency thereafter.

Imuran may be given long-term unless the patient cannot tolerate the preparation. Withdrawal of an effective dose in certain instances, e.g. SLE with nephritis, may result in a serious relapse of the condition. In other instances, such as rheumatoid arthritis and certain haematological conditions, treatment may be withdrawn after a suitable interval without any ill-effect. Withdrawal should always be a gradual process performed under close supervision.

In the presence of severe renal or hepatic impairment careful monitoring is initially required, since the dosage of Imuran may have to be reduced.

Severe secondary infections, often with uncommon organisms, are a hazard of immunosuppressive therapy

y in transplant recipients or other indications.

enic and has been shown ge in man. The clinical unclear since the damage withdrawal of Imuran.

hibitory effect on either depression of fertility ia is generally reversed accompanying azathioprine

gnant tumours especially l has been observed in i tumours that have ocve been primarily on sun-d be cautioned against skin should be examined s, however, as yet no increased incidence of subjects. In such patients e from that accompanying atment.

n a different pattern from our occurrence is much d latency, is seen mainly erapy, is less exclusively cur in those patients also

o/) therapy: When Imuran tantly only one quarter of uld be given since Zyloric metabolism.

s: Imuran should be used ing, or who have recently uppressive agents.

Maxants: There is clinical nises the effect of non-such as curare, d-tubo-perimental data confirm nuscular blockade caused that Imuran potentiates aused by succinylcholine.

e principal side-effect of ally reversible, depression xpressed as leucopenia, naemia.

ematological toxicity in galoblastic erythropoiesis

most frequently noted at rts of the late occurrence confirm the wisdom of veillance of patients even

stro-intestinal intolerance an is variable. It is mani-anorexia with occasional eems to be a dose-related interruption administration itstituted, at a lower dose. be taken with food. Other complications of therapy is is seen most commonly as also been reported in owel disease treated with

estinal haemorrhage and ration are complications

seen only after transplantation and it appears likely that they are due to concomitant steroid therapy.

Imuran may occasionally cause cholestatic, dose-related reversible hepatotoxicity. In such cases it is advisable to withdraw Imuran. A variety of possibly allergic manifestations has been reported. Drug fever, skin rash, myalgia and arthralgia are well documented though uncommon complications. There are also single case reports of possible Imuran-related effects including acute renal insufficiency, haemolytic anaemia, acute restrictive lung disease and unexplained meningitic reactions.

Use in pregnancy and lactation: The potential teratogenicity of Imuran should be borne in mind. Although it has been shown to be teratogenic in laboratory animals clinical evidence suggests that the risk is not appreciable in man. There is no doubt that Imuran and its metabolites cross the placenta. A temporary impairment of immune function has been noted following exposure *in utero* to Imuran combined with prednisone. The long-term consequences of these properties of Imuran are unknown, but many children exposed *in utero* have now completed the first decade of life without reported problems.

It has not been possible to detect Imuran or its metabolites in the breast milk of treated patients.

Toxicity and treatment of overdosage: The most likely side-effect of overdosage is bone marrow depression, which may not reach its maximum until 9–14 days later. A single large dose of Imuran is less likely to have a toxic effect than a chronic minor overdosage on prescription. Although the effects of overdosage may be delayed it is not uncommon for improvement to commence after day 12 provided that the patient has not had high doses during the intervening period. If overdosage occurs the blood picture and hepatic function in particular should be monitored. Imuran is known to be dialysable and dialysis may be used in severe cases.

Pharmaceutical precautions *Tablets:* Store below 25°C. Protect from light. Keep dry.

Injection: Store below 25°C. Protect from light. Keep dry.

Legal category POM.

Package quantities Bottle of 100 tablets. Single vials.

Further information Nil.

Product licence numbers

Tablets 0003/0036

Injection 0003/5043

INSULINS

NEUSULIN*

Neutral Insulin Injection BP WELLCOME*

Presentation Neusulin insulin is a clear neutral solution of purified crystalline insulin.

pH 7.3 ± 0.7 .

It is available in strengths of 40 and 80 units per ml.

This insulin is prepared from ox pancreas.

Uses For the management of diabetes mellitus. Wellcome purified insulin may be helpful in obviating or resolving problems sometimes encountered with standard insulin therapy; local skin reactions, lipatrophy, generalised insulin allergy, and insulin resistance/high daily dose requirement.

Dosage and administration *Adults and children:* The daily unit dosage of insulin is determined by the physician in accordance with the patient's requirements.

Neusulin is administered by subcutaneous, intramuscular or intravenous injection. The site of each injection should be changed according to a suitable routine.

Accidental intravascular injection should be avoided.

Subcutaneous: Onset of action occurs within 30–60 minutes, with an overall duration of action of approximately 6–8 hours. Consequently, 2 or 3 injections daily before meals may be appropriate if not used in combination with other insulins.

Intramuscular: Onset of action is more rapid and overall duration of action shorter than with the subcutaneous route, assuming adequate vascular perfusion.

Intravenous: Onset of action is most rapid and duration of action shortest with this route. It is usually reserved either for investigational purposes, or for the management of diabetic ketoacidosis. See literature for details of continuous low-dose insulin infusion.

Note: Insulin may adsorb to surfaces of the infusion apparatus and other infusion constituents.

Transfer from standard insulin: When patients treated with standard bovine insulin are transferred to Wellcome purified bovine insulin, there is no general decrease in dose requirement in the short term. Neusulin may therefore be conveniently given in similar unit dosage to the corresponding standard insulins, without risk of provoking sudden hypoglycaemia.

Contra-indications, warnings, etc

Contra-indications: Hypoglycaemia is an absolute contra-indication.

Precautions: Variation in lifestyle and other factors, e.g. infection and pregnancy, can affect insulin requirements.

Insulin dosage requirement may change if the species of origin, type, or purity of insulin is changed.

Hypoglycaemia can be enhanced by drugs including the following: aspirin, sulphonylureas and agents affecting them; certain steroids.

Hyperglycaemia can be enhanced by drugs including the following: triiodothyronine; thyroxine; various natural and synthetic steroids, including some oral contraceptives; diuretics, including thiazides; certain psychotherapeutic agents, including benzodiazepines; cyclophosphamide.

Certain β -blockers, especially propranolol, may affect insulin requirements and mask the signs of hypoglycaemia mediated by the sympathetic nervous system.

Monoamine oxidase (M.A.O.) inhibitors may potentiate the action of insulin.

Side- and adverse effects: The most important side-effect is hypoglycaemia.

Reduction of hyperglycaemia in newly diagnosed diabetics may alter visual refraction.

Local reactions at the injection site may include, among others, transient erythema, induration, urticaria and oedema. These usually resolve with continuing use of insulin.

True generalised hypersensitivity reactions approaching anaphylaxis are very rare.

Clinical evidence suggests that purified insulins are unlikely to cause localised lipodystrophies. However, at present this possibility cannot be totally excluded.

Use in pregnancy and lactation: It is essential to maintain continuous good control of the insulin-requiring diabetic patient throughout pregnancy. In the insulin-treated

(gestational or insulin-dependent) pregnant diabetic patient, the insulin requirements fall in the first trimester and increase during the second and third trimester.

Breast-feeding is probably best avoided in insulin-dependent diabetic mothers because of their metabolic instability.

Toxicity and treatment of overdosage: The symptoms and signs of hypoglycaemia depend on the patient's clinical state and on the rate and extent of the fall in blood glucose.

If possible, glucose, sucrose or rapidly available carbohydrate should be taken by mouth. Failing this, hypoglycaemia should be reversed as rapidly as possible by intravenous injection of glucose 50% solution. Alternative emergency treatments include the subcutaneous injection of up to 1 ml of adrenaline solution 1:1000, or the subcutaneous, intramuscular or intravenous injection of lyophilised glucagon 0.5–1.0 mg (1 unit = 1.0 mg). Both adrenaline and glucagon injections mobilise hepatic glycogen, but the effect is short-lived, and must be supplemented by freely available carbohydrate as soon as possible.

Pharmaceutical precautions Store at 2–8°C.

Do not freeze.

Avoid direct sunlight.

Legal category P.

Package quantities

40 units/ml vial of 10 ml

80 units/ml vial of 10 ml

Further information *Mixing in the syringe:* Neusulin insulin can be mixed with Neuphane or Neulente insulin. If, on medical advice, Neusulin insulin is to be mixed in the syringe with one of these long-acting purified insulins, the following procedure should be adopted:

1. Inject a volume of air equivalent to the dose into the bottle of long-acting insulin, without inverting the bottle or withdrawing the dose.

2. Inject the appropriate volume of air into the bottle of Neusulin insulin and withdraw the dose in the usual way.

3. Re-insert the needle into the long-acting insulin and withdraw the appropriate dose.

4. Inject the mixture immediately.

Mixing of purified with standard preparations is not recommended, since this would result in the loss of their special advantages.

Further information is available on request.

Product licence numbers

Neusulin 40 units/ml 0003/0137

Neusulin 80 units/ml 0003/0138

NEUPHANE*

Isophane Insulin Injection BP WELLCOME*

Presentation Neuphane insulin is a cloudy neutral suspension of an insulin (purified)/protamine complex. pH 7.2 ± 0.3

It is available in strengths of 40 and 80 units per ml.

This insulin is prepared from ox pancreas.

Uses For the management of diabetes mellitus. Wellcome purified insulins may be helpful in obviating or resolving problems sometimes encountered with standard insulin therapy; local skin reactions, lipodystrophy, generalised insulin allergy and insulin resistance/high daily dose requirement.

Dosage and administration *Adults and children:* The daily unit dosage of insulin is determined by the physician in accordance with the patient's requirements.

Neuphane insulin should be well mixed by inverting the vial several times before use. It is administered by subcutaneous or intramuscular injection.

The site of each injection should be changed according to a suitable routine.

Accidental intravascular injection should be avoided.

Subcutaneous: Onset of action occurs within 2 hours, with an overall duration of action which may extend to 20–24 hours.

Intramuscular: Onset of action is more rapid and overall duration of action shorter than with the subcutaneous route, assuming adequate vascular perfusion.

Neuphane insulin should not be given intravenously.

Transfer from standard insulin: When patients treated with standard bovine insulin are transferred to Wellcome purified bovine insulin, there is no general decrease in dose requirement in the short term. Neuphane may therefore be conveniently given in similar unit dosage to the corresponding standard insulin, without risk of provoking sudden hypoglycaemia.

Contra-indications, warnings, etc

Contra-indications: Hypoglycaemia is an absolute contra-indication.

Precautions: Variation in lifestyle and other factors, e.g. infection and pregnancy, can affect insulin requirements.

Insulin dosage requirement may change if the species of origin, type, or purity of insulin is changed.

Hypoglycaemia can be enhanced by drugs including the following: aspirin, sulphonylureas and agents affecting them; certain steroids.

Hyperglycaemia can be enhanced by drugs including the following: triiodothyronine; thyroxine; various natural and synthetic steroids, including some oral contraceptives; diuretics, including thiazides; certain psychotherapeutic agents, including benzodiazepines; cyclophosphamide.

Certain β -blockers, especially propranolol, may affect insulin requirements and mask the signs of hypoglycaemia mediated by the sympathetic nervous system.

Monoamine oxidase (M.A.O.) inhibitors may potentiate the action of insulin.

Side- and adverse effects: The most important side-effect is hypoglycaemia.

Reduction of hyperglycaemia in newly diagnosed diabetics may alter visual refraction.

Local reactions at the injection site may include, among others, transient erythema, induration, urticaria and oedema. These usually resolve with continuing usage of insulin.

True generalised hypersensitivity reactions approaching anaphylaxis are very rare.

Clinical evidence suggests that purified insulins are unlikely to cause localised lipodystrophies. However, at present this possibility cannot be totally excluded.

Use in pregnancy and lactation: it is essential to maintain continuous good control of the insulin-requiring diabetic patient throughout pregnancy. In the insulin-treated (gestational or insulin-dependent) pregnant diabetic patient, the insulin requirements fall in the first trimester and increase during the second and third trimester.

Breast-feeding is probably best avoided in insulin-dependent diabetic mothers because of their metabolic instability.

Toxicity and treatment of overdosage: The symptoms and signs of hypoglycaemia depend on the patient's clinical state and on the rate and extent of the fall in blood glucose.

If possible, glucose, sucrose or rapidly available carbohydrate should be taken by mouth. Failing this, hypoglycaemia should be reversed as rapidly as possible by intravenous injection of glucose 50% solution. Alternative emergency treatments include the subcutaneous injection of up to 1 ml of adrenaline solution 1:1000, or the subcutaneous, intramuscular or intravenous injection of lyophilised glucagon 0.5–1.0 mg (1 unit = 1.0 mg). Both adrenaline and glucagon injections mobilise hepatic glycogen, but the effect is short-lived and must be supplemented by freely available carbohydrate as soon as possible.

Pharmaceutical precautions Store at 2–8°C.

Do not freeze.

Avoid direct sunlight.

Legal category P.

Package quantities

40 units/ml vial of 10 ml

80 units/ml vial of 10 ml

Further information *Mixing in the syringe:* Neuphane insulin can be mixed with Neusulin insulin.

If, on medical advice, Neuphane insulin is to be mixed in the syringe with Neusulin insulin, the following procedure should be adopted:

1. Inject a volume of air equivalent to the dose into the bottle of Neuphane insulin without inverting the bottle or withdrawing the dose.

2. Inject the appropriate volume of air into the bottle of Neusulin insulin and withdraw the dose in the usual way.

3. Re-insert the needle into the Neuphane insulin and withdraw the appropriate dose.

4. Inject the mixture immediately.

Mixing of purified with standard preparations is not recommended, since this would result in the loss of their special advantages.

Further information is available on request.

Product licence numbers

Neuphane 40 units/ml 0003/0139

Neuphane 80 units/ml 0003/0140

NEULENTE*

Insulin Zinc Suspension BP WELLCOME*

Presentation Neulente insulin is a neutral suspension of purified insulin consisting of 3 parts Semilente and 7 parts Ultralente insulin.

Appearance is cloudy after shaking.

pH 7.2 ± 0.3

It is available in strengths of 40 and 80 units per ml.

This insulin is prepared from ox pancreas.

Uses For the management of diabetes mellitus. Wellcome purified insulins may be helpful in obviating or resolving problems sometimes encountered with standard insulin therapy; local skin reactions, lipodystrophy, generalised insulin allergy and insulin resistance/high daily dose requirement.

Dosage and administration *Adults and children:* The daily unit dosage of insulin is determined by the physician in accordance with the patient's requirements.

Neulente insulin should be well mixed by gently inverting the vial several times before use. It should be administered by subcutaneous or intramuscular injection.

The site of each injection should be changed according to a suitable routine.

Accidental intravascular injection should be avoided.

Subcutaneous: Onset of action occurs within 2 hours, with an overall duration of action which may extend to 24–28 hours.

Intramuscular: Onset of action is more rapid and overall duration of action shorter than with the subcutaneous route, assuming adequate vascular perfusion.

Neulente insulin should not be given intravenously.

Transfer from standard insulin: When patients treated with standard bovine insulin are transferred to Wellcome purified bovine insulin, there is no general decrease in dose requirement in the short term, Neulente may therefore be conveniently given in similar unit dosage to the corresponding standard insulin, without risk of provoking sudden hypoglycaemia.

Contra-indications, warnings, etc

Contra-indications: Hypoglycaemia is an absolute contra-indication.

Precautions: Variation in lifestyle and other factors, e.g. infection and pregnancy, can affect insulin requirements.

Insulin dosage requirement may change if the species of origin, type, or purity of insulin is changed.

Hypoglycaemia can be enhanced by drugs including the following: aspirin, sulphonylureas and agents affecting them; certain steroids.

Hyperglycaemia can be enhanced by drugs including the following: triiodothyronine; thyroxine; various natural and synthetic steroids including some oral contraceptives; diuretics, including thiazides; certain psychotherapeutic agents, including benzodiazepines; cyclophosphamide.

Certain β -blockers, especially propranolol, may affect insulin requirements and mask the signs of hypoglycaemia mediated by the sympathetic nervous system.

Monoamine oxidase (M.A.O.) inhibitors may potentiate the action of insulin.

Side- and adverse effects: The most important side-effect is hypoglycaemia.

Reduction of hyperglycaemia in newly diagnosed diabetics may alter visual refraction.

Local reactions at the injection site may include, among others, transient erythema, induration, urticaria and oedema. These usually resolve with continuing usage of insulin.

True generalised hypersensitivity reactions approaching anaphylaxis are very rare.

Clinical evidence suggests that purified insulins are unlikely to cause localised lipodystrophies. However, at present this possibility cannot be totally excluded.

Use in pregnancy and lactation: It is essential to maintain continuous good control of the insulin-requiring diabetic patient throughout pregnancy. In the insulin-treated (gestational or insulin-dependent) pregnant diabetic patient, the insulin requirements fall in the first trimester and increase during the second and third trimester.

Breast-feeding is probably best avoided in insulin-dependent diabetic mothers because of their metabolic instability.

Toxicity and treatment of overdosage: The symptoms and signs of hypoglycaemia depend on the patient's

clinical state and on the rate and extent of the fall in blood glucose.

If possible, glucose, sucrose or rapidly available carbohydrate should be taken by mouth. Failing this hypoglycaemia should be reversed as rapidly as possible by intravenous injection of glucose 50% solution. Alternative emergency treatments include the subcutaneous injection of up to 1 ml of adrenaline solution 1:1000, or the subcutaneous, intramuscular or intravenous injection of lyophilised glucagon 0.5–1.0 mg (1 unit = 1.0 mg). Both adrenaline and glucagon injections mobilise hepatic glycogen, but the effect is short lived and must be supplemented by freely available carbohydrate as soon as possible.

Pharmaceutical precautions Store at 2–8°C.

Do not freeze.

Avoid direct sunlight.

Legal category P.

Package quantities

40 units/ml vial of 10 ml

80 units/ml vial of 10 ml

Further information *Mixing in the syringe:* Neulente insulin can be mixed with Neusulin insulin. If, *on medical advice*, Neulente insulin is to be mixed in the syringe with Neusulin insulin, the following procedure should be adopted:

1. Inject a volume of air equivalent to the dose into the bottle of Neulente insulin, without inverting the bottle or withdrawing the dose.

2. Inject the appropriate volume of air into the bottle of Neusulin insulin and withdraw the dose in the usual way.

3. Re-insert the needle into the Neulente insulin and withdraw the appropriate dose.

4. Inject the mixture immediately.

Mixing of purified with standard preparations is not recommended, since this would result in the loss of their special advantages.

Further information is available on request.

Product licence numbers

Neulente 40 units/ml 0003/0141

Neulente 80 units/ml 0003/0142

SOLUBLE

Insulin Injection BP WELLCOME*

Presentation Soluble Insulin Injection BP is a clear acidic solution of crystalline insulin in strengths of 20, 40 and 80 units per ml.

This insulin is prepared from ox pancreas

Uses For the management of diabetes mellitus.

Dosage and administration *Adults and children* The daily unit dosage of insulin is determined by the physician in accordance with the patient's requirements.

It is administered by subcutaneous, intramuscular or intravenous injection. The site of each injection should be changed according to a suitable routine.

Accidental intravascular injection should be avoided.

Subcutaneous: Onset of action occurs within 30–60 minutes, with an overall duration of action of approximately 6–8 hours. Consequently, 2 or 3 injections daily before meals may be appropriate if not used in combination with other insulins.

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It is essential to maintain insulin-requiring diabetic r. In the insulin-treated dent) pregnant diabetic s fall in the first trimester l and third trimester. best avoided in insulin- cause of their metabolic

rdosage: The symptoms depend on the patient's and extent of the fall in

se or rapidly available y mouth. Failing this, sed as rapidly as possible glucose 50% solution.

Alternative emergency treatments include the subcutaneous injection of up to 1 ml of adrenaline solution 1:1000, or the subcutaneous, intramuscular or intravenous injection of lyophilised glucagon 0.5–1.0 mg (1 unit=1.0 mg). Both adrenaline and glucagon injections mobilise hepatic glycogen, but the effect is short-lived and must be supplemented by freely available carbohydrate as soon as possible.

Pharmaceutical precautions Store at 2–8°C.

Do not freeze.

Avoid direct sunlight.

Legal category P.

Package quantities 20, 40 and 80 units per ml: bottles of 10 ml.

Further information *Mixing in the syringe:* Soluble insulin may be mixed in the syringe, *on medical advice*, with isophane or globin insulin if required. Mixing of standard with purified insulin preparations is not recommended since this would result in the loss of the latter's special advantages.

Product licence numbers

Soluble insulin	20 units/ml	0003/5044
	40 units/ml	0003/5045
	80 units/ml	0003/5046

SEMILENTE*

Insulin Zinc Suspension (Amorphous) BP

WELLCOME*

ULTRALENTE*

Insulin Zinc Suspension (Crystalline) BP

WELLCOME*

Presentation Semilente insulin is a neutral suspension containing amorphous insulin with zinc in acetate buffer, in strengths of 40 and 80 units per ml.

Ultralente insulin is a neutral suspension containing crystalline insulin with zinc in acetate buffer in strengths of 40 and 80 units per ml.

These insulins are prepared from ox pancreas.

Uses For the management of diabetes mellitus.

Dosage and administration *Adults and children:* The daily unit dosage of insulin is determined by the physician in accordance with the patient's requirements.

It should be administered by subcutaneous or intramuscular injection.

The site of each injection should be changed according to a suitable routine.

Accidental intravascular injection should be avoided.

The insulin zinc suspensions should be shaken gently in the bottle before use.

Transfer to purified insulin: When patients treated with standard bovine insulin are transferred to Wellcome purified bovine insulin, there is no general decrease in dose requirement in the short term.

Contra-indications, warnings, etc

Contra-indications: Hypoglycaemia is an absolute contra-indication.

Precautions: Variation in lifestyle and other factors, e.g. infection and pregnancy, can affect insulin requirements.

Insulin dosage requirement may change if the species of origin, type, or purity of insulin is changed.

Hypoglycaemia can be enhanced by drugs including the following: aspirin, sulphonylureas and agents affecting them; certain steroids.

Hyperglycaemia can be enhanced by drugs including the following: triiodothyronine, thyroxine, various natural and synthetic steroids including some oral contraceptives, diuretics, including thiazides, certain psychotherapeutic agents, including benzodiazepines, cyclophosphamide.

Certain β -blockers, especially propranolol, may affect insulin requirements, and mask the signs of hypoglycaemia mediated by the sympathetic nervous system.

Monoamine oxidase (M.A.O.) inhibitors may potentiate the action of insulin.

Side- and adverse effects: The most important side-effect is hypoglycaemia.

Reduction of hyperglycaemia in newly diagnosed diabetics may alter visual refraction.

Local reactions at the injection site may include, among others, transient erythema, induration, urticaria and oedema. These usually resolve with continuing usage of insulin.

True generalised hypersensitivity reactions approaching anaphylaxis are very rare.

Use in pregnancy and lactation: It is essential to maintain continuous good control of the insulin-requiring diabetic patient throughout pregnancy. In the insulin-treated (gestational or insulin-dependent) pregnant diabetic patient, the insulin requirements fall in the first trimester and increase during the second and third trimester.

Breast-feeding is probably best avoided in insulin-dependent diabetic mothers because of their metabolic instability.

Toxicity and treatment of overdosage: The symptoms and signs of hypoglycaemia depend on the patient's clinical state and on the rate and extent of the fall in blood glucose.

If possible, glucose, sucrose or rapidly available carbohydrate should be taken by mouth. Failing this, hypoglycaemia should be reversed as rapidly as possible by intravenous injection of glucose 50% solution. Alternative emergency treatments include the subcutaneous injection of up to 1 ml of adrenaline solution 1:1000, or the subcutaneous, intramuscular or intravenous injection of lyophilised glucagon 0.5–1.0 mg (1 unit = 1.0 mg). Both adrenaline and glucagon injections mobilise hepatic glycogen, but the effect is short-lived and must be supplemented by freely available carbohydrate as soon as possible.

Pharmaceutical precautions Store at 2–8°C.

Do not freeze.

Avoid direct sunlight.

Legal category P.

Package quantities Semilente and Ultralente insulin zinc suspension 40 and 80 units per ml: bottles of 10 ml.

Further information *Mixing in the syringe:* Semilente, and Ultralente insulin may be mixed in the syringe, on medical advice, with each other but not with protamine, isophane or soluble insulin. Mixing of standard with purified insulin preparations is not recommended since this would result in the loss of the latter's special advantages.

Product licence numbers

Semilente	40 units/ml	0003/5151
	80 units/ml	0003/5252
Ultralente	40 units/ml	0003/5253
	80 units/ml	0003/5254

GLOBIN

Zinc Insulin Injection BP WELLCOME® PROTAMINE

Zinc Insulin Injection BP WELLCOME®

Presentation Globin zinc insulin is a clear, solution containing insulin with globin and a percentage of zinc, in a strength of 80 units per ml.

Protamine zinc insulin is a neutral suspension of protamine, zinc and insulin, in strengths of 40 units per ml.

These insulins are prepared from ox pancreas.

Uses For the management of diabetes mellitus.

Dosage and administration *Adults and children:* The daily unit dosage of insulin is determined by the physician in accordance with the patient's requirements.

Administered subcutaneously. It should not be given intravenously.

The site of each injection should be changed according to a suitable routine.

Accidental intravascular injection should be avoided.

Protamine zinc insulin should be shaken gently before use.

Transfer to purified insulins: When patients treated with standard bovine insulin are transferred to Wellcome purified bovine insulin, there is no general decrease in requirement in the short term.

Contra-indications, warnings, etc

Contra-indications: Hypoglycaemia is an absolute contra-indication.

Precautions: Variation in lifestyle and other factors, such as infection and pregnancy, can affect insulin requirements.

Insulin dosage requirement may change if the origin, type, or purity of insulin is changed.

Hypoglycaemia can be enhanced by drugs including the following: aspirin, sulphonylureas and agents which inhibit insulin action; certain steroids.

Hyperglycaemia can be enhanced by drugs including the following: triiodothyronine; thyroxine; various natural and synthetic steroids, including some oral contraceptives; diuretics, including thiazides; certain psychotherapeutic agents, including benzodiazepines, cyclophosphamide.

Certain β -blockers, especially propranolol, may affect insulin requirements and mask the signs of hypoglycaemia mediated by the sympathetic nervous system.

Monoamine oxidase (M.A.O.) inhibitors may potentiate the action of insulin.

Side- and adverse effects: The most important side-effect is hypoglycaemia.

Reduction of hyperglycaemia in newly diagnosed diabetics may alter visual refraction.

Local reactions at the injection site may include, among others, transient erythema, induration, urticaria and oedema. These usually resolve with continuing usage of insulin.

True generalised hypersensitivity reactions approaching anaphylaxis are very rare.

Use in pregnancy and lactation: It is essential to maintain continuous good control of the insulin-requiring diabetic patient throughout pregnancy. In the insulin-treated (gestational or insulin-dependent) pregnant diabetic patient, the insulin requirements fall in the first trimester and increase during the second and third trimester.

Breast-feeding is probably best avoided in insulin-dependent diabetic mothers because of their metabolic instability.

Toxicity and treatment of overdosage: The symptoms and signs of hypoglycaemia depend on the patient's clinical state and on the rate and extent of the fall in blood glucose.

If possible, glucose, sucrose or rapidly available carbohydrate should be taken by mouth. Failing this, hypoglycaemia should be reversed as rapidly as possible by intravenous injection of glucose 50% solution. Alternative emergency treatments include the subcutaneous injection of up to 1 ml of adrenaline solution 1000, or the subcutaneous, intramuscular or intravenous injection of lyophilised glucagon 0.5–1.0 mg (unit = 1.0 mg). Both adrenaline and glucagon injections mobilise hepatic glycogen, but the effect is short-acted and must be supplemented by freely available carbohydrate as soon as possible.

Pharmaceutical precautions Store at 2–8°C.

Do not freeze.

Avoid direct sunlight.

Legal category P.

Package quantities *Globin Zinc Insulin Injection BP:* 10 units per ml; bottle of 10 ml.

Protamine Zinc Insulin Injection BP: 40 and 80 units per ml; bottles of 10 ml.

Further information *Mixing in the syringe:* Globin and protamine insulin may be mixed in the syringe, on medical advice, with soluble or neutral insulin if required. However, because of a variable diminution of immediate effect, the combination of protamine with either soluble or neutral insulin is not recommended. Mixing of standard with purified insulin preparations is not recommended since this would result in the loss of the latter's special advantages.

Product licence numbers

Protamine 80 units/ml 0003/5050

Protamine 40 units/ml 0003/5051

80 units/ml 0003/5052

EMADRIN* TABLETS AND INJECTION

Representation *Tablets:* Each white tablet containing 10 mg Procyclidine Hydrochloride BP is scored and coded 'Wellcome S3A'.

Injection: Each 2 ml ampoule contains 10 mg Procyclidine Hydrochloride BP.

Uses Kemadrin is indicated in all forms of Parkinson's disease: idiopathic (paralysis agitans), postencephalitic and arteriosclerotic.

Symptoms often responding well to Kemadrin include: rigidity, akinesia, tremor, speech and writing difficulties, sialorrhoea and drooling, sweating, oculogyric crises and depressed mood.

Kemadrin is also used to control troublesome extrapyramidal symptoms induced by neuroleptic drugs including pseudo-parkinsonism, acute dystonic reactions and akathisia.

Dosage and administration The variation in optimum dosage from one patient to another should be taken into consideration by the physician. Treatment is usually started at 2.5 mg three times a day, increasing by 2.5–5 mg daily at intervals of two or three days until the optimum clinical response is achieved. The usual maximum total daily dose is 30 mg. However, at the discretion of the attending physician where appropriate this total may be as high as 60 mg.

The daily dosage used in the control of neuroleptic-induced extrapyramidal symptoms is usually not more than 20 mg daily. After a period of 3–4 months, Kemadrin should be stopped and the patient observed to see if the neuroleptic-induced extrapyramidal symptoms recur. Cessation of treatment periodically is to be recommended even in patients who appear to require the drug for longer periods.

Kemadrin may be combined with levodopa or amantadine in patients who are inadequately controlled on a single agent.

In acute dystonia 5 mg Kemadrin intravenously is frequently effective within 5 minutes. An occasional patient may need 10 mg or more and may require up to half an hour to obtain relief.

Pharmacology: Procyclidine is a synthetic anticholinergic agent which blocks the excitatory effects of acetylcholine at the muscarinic receptor.

Idiopathic Parkinson's disease is now thought to result from degeneration of neurones in the substantia nigra whose axons project and inhibit cells in the corpus striatum. Blockade by neuroleptic drugs of the dopamine released by these terminals produces a similar clinical picture. The cell bodies in the corpus striatum also receive cholinergic innervation which is excitatory. Relief of the parkinsonian syndrome can be achieved either by potentiation of the dopaminergic system or blockade of the cholinergic input by anticholinergics. It is by a central action of this latter type that procyclidine exerts its effect.

Procyclidine is adequately absorbed from the gastrointestinal tract and disappears rapidly from the tissues. After intravenous administration it acts within 5 to 20 minutes with a duration of up to 4 hours. No information is available on its metabolic fate and excretion.

Contra-indications, warnings, etc

Contra-indications: There are no known contra-indications to the use of Kemadrin.

Precautions: As with all anticholinergics such as Kemadrin, cautious prescribing is indicated in patients predisposed to glaucoma, obstructive disease of the gastro-intestinal tract and those with urinary symptoms associated with prostatic hypertrophy.

In a proportion of patients undergoing neuroleptic treatment, tardive dyskinesias will occur. While anticholinergic agents do not cause this syndrome, when given in combination with neuroleptics they may reduce the threshold at which dyskinesias appear in patients predisposed to this abnormality. In such individuals subsequent adjustment of neuroleptic therapy is indicated.

Use in pregnancy and lactation: The safety of using Kemadrin during pregnancy has not been established. However, extensive clinical use has not given any evidence that in any way compromises the normal course of pregnancy. No data are available on the excretion of this drug in breast milk.

Side- and adverse effects: The main side-effects are those to be expected from any anticholinergic agent. Dry mouth, blurring of vision and constipation are most commonly recorded. At higher doses dizziness, mental confusion and hallucinations may occur. The unwanted anticholinergic effects are easily reversed by reducing the dosage.

Toxicity and treatment of overdosage: Reports of overdosage are relatively rare. Symptoms of overdosage are agitation, restlessness and confusion with severe sleeplessness lasting up to 24 hours or more. Visual and

occasionally auditory hallucinations are likely. Most subjects are euphoric but the occasional patient may be anxious and aggressive. The pupils are widely dilated and unreactive to light. In recorded cases, the disorientation has lasted 1 to 4 days and ended in recuperative sleep.

If procyclidine has been ingested within the previous hour or two (or possibly longer in view of its likely effects on gastric motility) then gastric lavage is probably indicated. Other active measures such as the use of cholinergic agents or haemodialysis are extremely unlikely to be of clinical value, although if convulsions occur they should be controlled by injections of diazepam.

Pharmaceutical precautions *Tablets and injection:* Store below 25°C.

Legal category POM.

Package quantities Bottles of 100 and 500 tablets. Ampoule of 10 mg in 2 ml. Box of 5 ampoules.

Further information Drowsiness and depressed mood are not a problem and several patients in a study had considerably less fatigue and more energy and drive when transferred from other anticholinergic agents to Kemadrin.

Product licence numbers

Tablets 0003/5255

Injection 0003/5256

LANOXIN* TABLETS

LANOXIN-125* TABLETS

LANOXIN-PG* TABLETS

LANOXIN* INJECTION

LANOXIN-PG* ELIXIR

Presentation Lanoxin tablets each contain 250 mcg (0.25 mg) of Digoxin BP, scored and coded Wellcome X3A, white in colour.

Lanoxin-125 Tablets each contain 125 mcg (0.125 mg) of Digoxin BP coded Wellcome Y3B, white in colour.

Lanoxin-PG (Paediatric/Geriatric) Tablets each contain 62.5 mcg (0.0625 mg) of Digoxin BP, coloured blue and coded Wellcome U3A.

Lanoxin Injection contains 250 mcg (0.25 mg) of Digoxin BP per ml in each 2 ml ampoule.

Lanoxin-PG (Paediatric/Geriatric) Elixir contains 50 mcg (0.050 mg) of Digoxin BP in each ml. Clear bright yellow in colour and lime flavoured.

Uses Lanoxin is indicated whenever digitalis therapy is required. It is of particular value in congestive heart failure and in certain cardiac arrhythmias, especially in atrial fibrillation.

Dosage and administration The suggested doses are intended only as a guide, as doses will have to be adjusted for each individual patient. Larger doses are necessary for the control of flutter and fibrillation than to improve the contractility of a failing heart still in sinus rhythm. Lanoxin Injection can be administered undiluted, either by intravenous or intramuscular route, but the latter should only be employed when no other route of administration is available, as it is likely to prove painful, and absorption may be unpredictable. Subcutaneous injection is not recommended as it causes intense local irritation.

When given intravenously, it may be diluted with Sodium Chloride 0.9% Injection BP or Dextrose 5% Injection BP, or Sodium Chloride 0.18%+Dextrose 4% Injection BP. The injection should be given slowly. The intramuscular route provides a similar rate of absorption to that of the oral route. Lanoxin-PG Elixir should be given undiluted.

Adults:

1. Rapid oral digitalisation: 0.75–1.5 mg followed by 0.25 mg at six-hourly intervals until optimal therapeutic effect has been obtained, or in cases of atrial fibrillation the ventricular rate lies between 70–80 beats per minute. The appearance of toxic symptoms before any therapeutic response is apparent must call for a review of the clinical situation.

2. Slow oral digitalisation: 0.25–0.75 mg daily, clinical improvement usually being seen in one to three weeks.

3. Emergency parenteral digitalisation: 0.5–1.0 mg intravenously (slowly) followed by 0.5 mg usually given and repeated, if necessary, after a few hours. It may be given undiluted intramuscularly with intervals of four to five hours between doses.

4. Maintenance (all routes): 0.25–0.5 mg daily as required. Best given in divided doses. It is recommended that digitalis therapy in elderly patients be carried out gradually, and with smaller doses, except in an emergency.

Peritoneal and haemo-dialyses remove only a very small percentage of digoxin and patients receiving such therapy should not require any adjustment to the maintenance dosage.

Children over 10 years: As for adults.

Infants and children under 10 years:

1. Digitalisation (all routes): 0.01–0.02 mg/kg body weight repeated six-hourly until therapeutic result obtained, 2–4 doses usually being sufficient.

2. Maintenance: 0.01–0.02 mg/kg body weight daily for a few days, after which the dose can be adjusted as necessary.

Contra-indications, warnings, etc

Contra-indications: The only absolute contra-indication to Lanoxin is toxicity due to cardiac glycosides. ventricular paroxysmal tachycardia or ventricular fibrillation Lanoxin is indicated only in refractory cases not induced by digitalis intoxication and where heart failure has developed.

Precautions: When digoxin is administered intravenously there is an element of risk that it may cause cardiac dysrhythmia with a possibly fatal result, and this must be weighed against the gravity of the emergency. The risk is greatly increased if the patient is already or has recently been receiving a cardiac glycoside. A smaller dose of Lanoxin should be given initially and as maintenance renal clearance is reduced (as in the elderly or in patients with moderate or severe renal disease). The doses suggested may produce evidence of toxicity in patients with acute myocardial infarction, severe pulmonary disease, advanced heart failure and in premature infants and elderly patients. Disturbances in electrolyte balance may occur as a result of the use of diuretics and other agents. The change in electrolyte balance may influence the response to digoxin. In hypokalaemia and hypomagnesaemia, the dose of Lanoxin should be reduced until the deficiencies are corrected. Disturbances in calcium levels may also modify the response to digoxin. Hypothyroid patients generally require less Lanoxin and

fluctuating states in thyroid function will call for adjustments in Lanoxin dosage.

Cardiac surgery and cardioversion may be associated with an enhanced liability to post-operative arrhythmias in the presence of digoxin plasma levels which would otherwise be considered normal. Lanoxin should therefore be withdrawn for 72 hours prior to such procedures whenever possible.

Plasma digoxin concentrations rise when quinidine is given concomitantly. Lithium treatment may potentiate the effects of digoxin. Some antacid constituents affect the bioavailability of digoxin if taken simultaneously. Digoxin activities are potentiated when the extracellular potassium levels are decreased, as occurs frequently with concomitant diuretic therapy.

de- and adverse effects: Side-effects are principally associated with signs of overdosage and usually disappear within a few hours of withdrawing the drug, and may include anorexia, nausea, vomiting, headache, fatigue and visual disturbances. There may be arrhythmias and bradycardia. Gynaecomastia occurs infrequently. Allergy, though very rare, does occur.

use in pregnancy and lactation: Lanoxin has been available since 1929 and there have been no reports to date of any teratogenic effects. A recent paper showed that digoxin is excreted in breast milk but not in clinically significant amounts.

Toxicity and treatment of overdosage: Common symptoms include nausea and vomiting. Supraventricular rhythmias with heart block and bradycardia have often been reported. Mild to pronounced hyperkalaemia is likely to be present. With chronic poisoning ventricular ectopic beats and other dysrhythmias are common.

Treatment of overdosage is by means of gastric lavage and ECG monitoring. For hypokalaemia give potassium. For hyperkalaemia give glucose and insulin. For bradycardia give atropine. For tachycardia and dysrhythmias give lignocaine and/or propranolol.

pharmaceutical precautions *Tablets:* Store below 5°C.

Elixir: Store below 25°C. Protect from light.

Injection: Store below 25°C. Protect from light.

legal category POM.

package quantities *Lanoxin tablets:* Bottles of 500 and 1,000; container of 5,000.

Lanoxin-125 Tablets: Bottle of 500.

Lanoxin Injection: Ampoule of 2 ml; box of 5 ampoules.

Lanoxin-PG Elixir: Bottle of 60 ml.

Lanoxin-PG Tablets: Bottles of 100 and 500.

further information Absorption of Lanoxin digoxin is uniform and almost complete. Duration of action is short. These characteristics improve control during digitalisation and offer an increased measure of safety.

product licence numbers

Tablets	0003/0090
25 Tablets	0003/0102
5 Tablets	0003/0091
5 Elixir	0003/5260
Injection	0003/5259

ANVIS* TABLETS

presentation Each pale greenish yellow biconvex tablet, scored and coded Wellcome U3B, contains 40 mg thioguanine.

Uses Cytotoxic agent.

The main indication is acute myeloblastic leukaemia, but it has also been used in acute lymphoblastic and chronic granulocytic (myelocytic, myeloid, myelogenous) leukaemia.

Cross-resistance exists between Lanvis and Puri-Nethol (6-mercaptopurine) and it is not to be expected that patients who no longer respond to Puri-Nethol will respond to Lanvis or vice versa.

Dosage and administration The dosage and duration of its administration must be carefully adjusted to obtain optimum benefit without undue toxic effects.

Adults: The usual dosage of Lanvis is between 2.0 and 2.5 mg/kg body weight/day, the total daily doses being calculated to the nearest multiple of 20 mg and given at one time. The duration of drug administration will depend on the nature and dosage of other antineoplastic drugs administered with thioguanine, the patient's condition and whether early signs of toxicity occur. For induction therapy thioguanine is usually administered as one of a number of drugs for periods of 5–20 days according to the regimen adopted and the patient's tolerance.

For maintenance therapy, the usual dosage of thioguanine is 2.0 mg/kg body weight/day, but the patient must be monitored for bone-marrow toxicity, particularly if other cytotoxic drugs are given conjointly.

Children: As for adults.

Contra-indications, warnings, etc

Contra-indications: In view of the seriousness of the indications there are no absolute contra-indications.

Precautions: Lanvis is an active cytotoxic agent for use only under the direction of physicians experienced in the administration of such agents.

Since Lanvis is strongly myelosuppressive, full blood counts must be taken daily during remission induction. Patients must be carefully monitored during therapy.

The main side-effect of treatment with Lanvis is bone marrow suppression leading to leucopenia and thrombocytopenia. The leucocyte and platelet counts continue to fall after treatment is stopped, so at the first sign of an abnormally large fall in the counts, treatment should be temporarily interrupted. Bone marrow suppression is readily reversible if the drug is withdrawn early enough. During remission induction in acute myelogenous leukaemia the patient may frequently have to survive a period of relative bone marrow aplasia and it is important that adequate supportive facilities are available.

Patients on myelosuppressive chemotherapy are particularly susceptible to a variety of infections.

During remission induction, particularly when rapid cell lysis is occurring, adequate precautions should be taken to avoid hyperuricaemia and/or hyperuricosuria and the risk of uric acid nephropathy.

In view of its action on cellular DNA, Lanvis is potentially mutagenic and carcinogenic, and consideration should be given to the theoretical risk of carcinogenesis when Lanvis therapy is given. It is advised that care be taken when handling or halving these tablets not to contaminate hands or to inspire drug.

Side- and adverse effects: Gastro-intestinal intolerance has been reported. Similar intolerance has been noted with Lanvis but individual patients may tolerate either Lanvis or Puri-Nethol better than the other. At high doses gastro-intestinal symptoms may be more apparent and stomatitis has also been reported. Intestinal necrosis and perforation has been reported in patients who received combination chemotherapy including Lanvis.

Liver function abnormalities and jaundice have been reported during treatment with Lanvis and may be reversible if therapy is withdrawn. There has been a report of veno-occlusive disease of the liver occurring in patients who received combination chemotherapy including Lanvis.

Use in pregnancy and lactation: Lanvis like other cytotoxic agents is potentially teratogenic. Its use should be avoided whenever possible during pregnancy, particularly during the first trimester. In any individual case the potential hazard to the foetus must be balanced against the expected benefit to the mother. There have been isolated cases where men who have received combinations of cytotoxic agents including Lanvis have fathered children with congenital abnormalities and consideration should be given to this potential risk when treating male patients.

Mothers receiving Lanvis should not breast feed.

Toxicity and treatment of overdose: The principal toxic effect is on the bone marrow and haematological toxicity is likely to be more profound with chronic overdose than with a single ingestion of Lanvis. As there is no known antidote the blood picture should be closely monitored and general supportive measures instituted together with appropriate blood transfusion if necessary.

Pharmaceutical precautions Store below 25°C. Protect from light. Keep dry.

Legal category POM.

Package quantities Bottle of 25 tablets.

Further information The concomitant use of Zyloric* (allopurinol) to inhibit uric acid formation does not necessitate reduction of the dosage of Lanvis as is necessary with Puri-Nethol* (6-mercaptopurine) and Imuran* (azathioprine).

Product licence number 0003/0083.

LEUKERAN* TABLETS

Presentation *Leukeran Tablets:* 2 mg Chlorambucil BP, coded Wellcome C2A. Coloured yellow with white core.

5 mg Chlorambucil BP, coded Wellcome H2A. Coloured yellow with white core.

Uses Cytotoxic agent.

Leukeran is indicated in the treatment of Hodgkin's disease, certain forms of non-Hodgkin's lymphoma, chronic lymphocytic leukaemia, Waldenstrom's macroglobulinaemia and advanced ovarian adenocarcinoma. Leukeran has a significant therapeutic effect in a proportion of patients with breast cancer.

Dosage and administration *Adults: Hodgkin's disease:* Used as a single agent a typical dosage is 0.2 mg/kg/day for 4–8 weeks. Leukeran is usually included in combination therapy and a number of regimes have been used. Leukeran has been used as an alternative to nitrogen mustard with a reduction in toxicity but similar therapeutic results.

Non-Hodgkin's lymphoma: Used as a single agent the usual dosage is 0.1–0.2 mg/kg/day for 4–8 weeks initially; maintenance therapy is then given either by a reduced daily dosage or intermittent courses of treatment. Leukeran is useful in the management of patients with advanced diffuse lymphocytic lymphoma and those who have relapsed after radiotherapy. There is no

significant difference in the overall response rate obtained with chlorambucil as a single agent and combination chemotherapy in patients with advanced non-Hodgkin's lymphocytic lymphoma.

Chronic lymphocytic leukaemia: Treatment with Leukeran is usually started after the patient has developed symptoms or when there is evidence of impaired bone marrow function (but not marrow failure) as indicated by the peripheral blood count. Initially Leukeran is given at a dosage of 0.15 mg/kg/day until the total leucocyte count has fallen to 10,000 per μ l. Treatment may be resumed 4 weeks after the end of the first course and continued at a dosage of 0.1 mg/kg/day. In a proportion of patients, usually after about 2 years of treatment, the blood leucocyte count is reduced to the normal range, enlarged spleen and lymph nodes become palpable and the proportion of lymphocytes in the bone marrow is reduced to less than 20 per cent. Patients with evidence of bone marrow failure should first be treated with prednisolone and evidence of marrow regeneration should be obtained before commencing treatment with Leukeran. Intermittent high dose therapy has been compared with daily Leukeran but no significant difference in therapeutic response or frequency of side effect was observed between the two treatment groups.

Waldenstrom's macroglobulinaemia: Leukeran is a treatment of choice in this indication. Starting doses of 6–12 mg daily until leucopenia occurs are recommended followed by 2–8 mg daily indefinitely.

Ovarian carcinoma: Used as a single agent a typical dosage is 0.2 mg/kg/day for 4–6 weeks. A dosage of 0.3 mg/kg/day has been given until leucopenia has been induced. Maintenance dosage of 0.2 mg/kg/day has been given aiming to keep the total leucocyte count below 4,000/mm³. In practice, maintenance courses tend to last 2–4 weeks with intervals of 2–6 weeks between each course.

Advanced breast cancer: Used as a single agent a typical dosage is 0.2 mg/kg bodyweight per day for 6 weeks. Leukeran may be given in combination with prednisolone at a dose range of 14–20 mg daily, regardless of bodyweight, over 4–6 weeks provided there is no serious haemopoietic depression. Leukeran may be given in combination with methotrexate, 5-fluorouracil, and prednisolone at a dosage of 5 to 7.5 mg/m²/day.

Children: Leukeran may be used in the management of Hodgkin's disease and non-Hodgkin's lymphomas in children. The dosage regimens are similar to those used in adults.

Contra-indications, warnings, etc

Contra-indications: In view of the seriousness of the indications there are no absolute contra-indications.

Precautions: Leukeran is an active cytotoxic agent; use only under the direction of physicians experienced in the administration of such agents.

Since Leukeran is capable of producing irreversible bone marrow suppression, blood counts should be closely monitored in patients under treatment.

At therapeutic dosage Leukeran depresses lymphocytes and has less effect on neutrophils and platelet counts and on haemoglobin levels. Discontinuation of Leukeran is not necessary at the first sign of a fall in neutrophils but it must be remembered that the fall may continue for 10 days or more after the last dose.

Leukeran should not be given to patients who have recently undergone radiotherapy or received other cytotoxic agents.

of the bone marrow is myeloplastic, the daily dose is reduced to 25 mg.

Impaired renal function as they are prone to be associated with azotaemia. still under investigation. In dose reduction in action.

It causes chromatin development of acute myeloid leukaemia. However, it was not a part of the natural chemotherapy was the

In ovarian cancer who those who did not, ting agents, including the incidence of acute

has been reported in a young Leukeran as long-term cancer.

It is balanced against the risk of considering the use

Impression of ovarian function reported following

It was as a result of therapy. It was stated that a total dose

It is spermatogenesis have been reported in lymphoma following doses of 410–2,600 mg. The most common side-effect though this frequently Leukeran is withdrawn due to bone marrow failure

Such as nausea and ulceration occur infrequently. It can be encountered but the usual dosage has been

Leukemia has occasionally been reported in chronic lymphocytic leukaemia therapy. However, the use of Leukeran. have been reported after

Side effects include fever, skin rash, interstitial pneumonia,

Children with nephrotic syndrome and dose-related focal

As with other cytotoxic drugs, it is teratogenic. The use of it is never possible during the first trimester. In any case, the foetus must be protected. It should not be breast fed.

Dosage: Reversible pancytopenia, inadvertent overdoses ranging from agitated

behaviour and ataxia to multiple grand mal seizures has also occurred. As there is no known antidote the blood picture should be closely monitored and general supportive measures should be instituted, together with appropriate blood transfusion if necessary.

Pharmaceutical precautions Store at 2–8°C in a dry place.

Legal category POM.

Package quantities 2 mg: Bottle of 25 tablets. 5 mg: Bottle of 25 tablets.

Further information Leukeran has the pharmacological properties of the nitrogen mustard compounds. The drug is only partly radiomimetic, affecting chiefly the lymphoid tissues. Experimental studies have shown that chlorambucil is well absorbed and well tolerated by the oral route.

Product licence numbers

Tablets 2 mg 0003/5264

Tablets 5 mg 0003/5265

LINCTIFED* EXPECTORANT

LINCTIFED* EXPECTORANT PAEDIATRIC

Presentation Linctified Expectorant contains:

Tripolidine Hydrochloride BP	1.25 mg
Pseudoephedrine Hydrochloride BP	20 mg
Codeine Phosphate BP	7.5 mg
Guaiphenesin BP	100 mg

in each 5 ml of orange-coloured syrup. It has an aromatic flavour.

Linctified Expectorant Paediatric contains:

Tripolidine Hydrochloride BP	0.6 mg
Pseudoephedrine Hydrochloride BP	12 mg
Codeine Phosphate BP	3 mg
Guaiphenesin BP	50 mg

in each 5 ml of red-coloured syrup. It has a sweet, fruity flavour.

Uses Expectorant.

To aid expectoration in bronchitis and other conditions where tenacious mucoid secretions are a problem.

Dosage and administration *Linctified Expectorant:*

Adults: 10 ml three times a day.

Children: Over 12 years: 10 ml three times a day.

Under 12 years: Linctified Expectorant Paediatric is recommended.

Linctified Expectorant Paediatric: Children: 6–12 years: 10 ml three times a day.

1–6 years: 5 ml three times a day.

May be diluted with Syrup BP.

Pharmacology: Pseudoephedrine has direct and indirect sympathomimetic activity and is an orally effective upper respiratory tract decongestant. Pseudoephedrine is substantially less potent than ephedrine in producing both tachycardia and elevation in systolic blood pressure and considerably less potent in causing stimulation of the central nervous system. On the basis of widespread and long established clinical use, guaiphenesin is recognised as an expectorant in bronchitis. Tripolidine provides antihistamine activity by antagonising H₁ receptors whilst codeine provides analgesic and antitussive actions, decreasing cough frequency but not totally suppressing it.

Contra-indications, warnings, etc

Contra-indications: Contra-indicated in patients with known hypersensitivity to any of the constituents.

Contra-indicated in persons under treatment with monoamine oxidase inhibitors and within two weeks of stopping such treatment.

Precautions: Although pseudoephedrine causes virtually no pressor effect in patients with normal blood pressure, Linctifed should be used with caution in patients with cardiovascular disorders, including hypertension. The effect of antihypertensive agents which modify sympathetic activity may be partially reversed by Linctifed.

Caution should also be exercised in patients taking other sympathomimetic agents, such as decongestants, appetite suppressants and amphetamine-like psychostimulants. The effects of a single dose on the blood pressure of these patients should be observed before recommending repeated or unsupervised treatment.

As with other sympathomimetic agents, caution should be exercised in patients with prostatic enlargement or bladder dysfunction.

In severe hepatic or renal dysfunction a single dose of Linctifed Expectorant or Linctifed Expectorant Paediatric should be given initially and the response to it used as a guide to the patient's requirement for further administration of the product.

The antibacterial agent furazolidone is known to cause a progressive inhibition of monoamine oxidase and although there are no reports of hypertensive crises having occurred, it should not be administered concurrently with Linctifed Expectorant or Linctifed Expectorant Paediatric.

May cause drowsiness. Patients should not drive a vehicle or operate machinery until they have determined their own response. In some patients the drowsiness induced by antihistamines may be potentiated by alcohol or other central sedatives.

Use in pregnancy and lactation: No data are available on the use of Linctifed Expectorant during pregnancy nor on the excretion of it or its metabolites in human milk.

Toxicity and treatment of overdose: Probable symptoms include drowsiness, inco-ordination, weakness, palpitation, irritability, hypertension, convulsions and difficulty in micturition. In severe cases there may be respiratory depression due to the codeine component. Gastric lavage and supportive measures for respiration and circulation should be performed if indicated. Convulsions should be controlled with an anticonvulsant. Catheterisation of the bladder may be necessary. Alpha-adrenergic blockade may be required to treat hypertensive crises and beta-adrenergic blockade for the control of supra-ventricular dysrhythmias. Pseudoephedrine has a renal excretion half-life of approximately seven hours and if desired the elimination can be accelerated by acid diuresis or by dialysis.

Pharmaceutical precautions Store below 25°C. Protect from light.

Legal category P.

Package quantities *Linctifed Expectorant:* Bottles of 500 ml and 2 litres.

Linctifed Expectorant Paediatric: Bottles of 500 ml and 2 litres.

Further information Nil.

Product licence numbers

Expectorant 0003/5266

Expectorant Paediatric 0003/5267

MALOPRIM* TABLETS

Presentation *Tablets:* Each white tablet is scored a contains 12.5 mg Pyrimethamine BP and 100 mg Dapsone BP, coded Wellcome H9A.

Uses Maloprim is effective as a causal prophylactic and suppressive agent against malaria caused by *Plasmodium falciparum* and probably other malaria parasites notably *P. vivax*. Since potentiation takes place between its two active constituents Maloprim is recommended particularly when resistance to pyrimethamine or other anti-folate preparations is known or suspected. It is effective in chloroquine-resistant areas.

Note: Maloprim should not be used for treatment of acute attack.

Dosage and administration *Adults:* 1 tablet each week.

Children: Over 10 years: 1 tablet each week.

5-10 years: ½ tablet each week.

Under 5 years: Formulation not applicable.

The constituents are rapidly absorbed and prophylactic cover can be expected shortly after taking the first dose. Prophylaxis should commence before arrival in endemic area and be continued once weekly. On returning to a non-malarious area dosage should be maintained for a further four weeks.

Contra-indications, warnings, etc

Contra-indications: Maloprim should not be given to individuals with a known history of sensitivity to sulphonamides or sulphones or pyrimethamine.

Precautions: The recommended dose should not be exceeded.

Maloprim should be used with caution in patients with hepatic or renal disorders.

During pregnancy and in the presence of other conditions predisposing to folate deficiency a folic acid supplement should be given.

Maloprim, through its mode of action, may further depress folate metabolism in patients already receiving treatment with other folate inhibitors, including combinations of trimethoprim and sulphonamides.

Side- and adverse effects: No significant side-effects caused by Maloprim at recommended dosage have been reported apart from rare instances of cyanosis attributed to methaemoglobinemia.

Excessive doses over a prolonged period may produce megaloblastic or haemolytic anaemia.

Acute haemolysis may also occur in individuals with glucose-6-phosphate dehydrogenase deficiency.

Rare idiosyncratic reactions include agranulocytosis and skin sensitivity reactions.

Use in pregnancy and lactation: While there is theoretical risk of foetal malformation with all folate inhibitors given during pregnancy, no such adverse effects have been reported with Maloprim. A folic acid supplement should be given to pregnant women receiving Maloprim. The amount of the components of Maloprim excreted in breast milk is insufficient to contraindicate its use in lactating mothers.

Toxicity and treatment of overdose: Symptoms are likely to be nausea, vomiting, hyperexcitability, methaemoglobinemia and haemolytic anaemia. Convulsions may be apparent and megaloblastic anaemia may ensue. Gastric lavage, adequate fluids and general supportive measures are recommended. Maintenance of a clear

way and control of convulsions may be required. Division should be made for fresh blood transfusions. To counteract possible folate deficiency calcium folinate 15 mg daily should be administered. Methaemoglobinemia should be treated with ascorbic acid, 200 mg three times daily, or, except in patients with G-6-PD deficiency, by intravenous administration of methylene blue, 2 mg/kg body weight.

Pharmaceutical precautions Store below 25°C. Protect from light.

Legal category POM.

Package quantities Strip pack of 30 tablets.

Further information Nil.

Product licence number 0003/5117.

IGRIL* TABLETS

Presentation Migril Tablets each contain 2 mg Ergotamine Tartrate BP, 50 mg Cyclizine Hydrochloride BP and 100 mg Caffeine Hydrate BP. Scored and coded Wellcome A4A, Coloured white with pink core.

Uses For relief of the acute migraine attack.

Dosage and administration *Adults:* The usual initial dose is 1 or 2 tablets, which should be swallowed *at the start of an attack*. Half or 1 tablet at half-hourly intervals may then be given, but not more than 4 tablets could be taken for any single attack. The smallest effective dose should be used. Not more than 6 tablets could be taken in any one week.

Children: Not applicable.

Contra-indications, warnings, etc

Contra-indications: Migril should not be used for prophylaxis.

The contra-indications to Migril are the same as for ergotamine, i.e. peripheral vascular disease, coronary disease, kidney and liver diseases, thyrotoxicosis, anaemia and during pregnancy.

Precautions: In very rare cases and certain febrile conditions a patient may be unduly sensitive to ergotamine. Unexpected coldness in the extremities is a sign that the drug should be withdrawn.

Side- and adverse effects: Side-effects include abdominal pain or fatigue of the limbs.

Indiscriminate use of products containing ergotamine may precipitate, upon discontinuation of the drug, withdrawal symptoms amongst which headaches feature prominently.

Prolonged abuse of such products may lead to chronic ergotism.

In common with other antihistamines, cyclizine may cause sedation, although this is rarely marked. Patients should be cautioned, therefore, not to drive motor vehicles or operate machinery if drowsiness occurs.

Use in pregnancy and lactation: See Contra-indications section concerning pregnancy. It is wise for the mother to refrain from breast feeding whilst taking ergotamine preparations.

Toxicity and treatment of overdosage: Symptoms may comprise: excitement, weakness, pyrexia and vomiting with tremors and convulsions. Peripheral vasoconstriction and abdominal colic. Shivering and paraesthesia. Bradycardia and hypotension. Respiratory depression, hypoxia and coma.

Treatment of overdosage is by means of gastric lavage, amyl nitrite inhalations, general supportive measures.

Sodium nitroprusside may be given as an intravenous infusion (50–120 micrograms per min) to produce vasodilation.

Pharmaceutical precautions Store below 25°C in a dry place.

Legal category POM.

Package quantities Bottle of 100 tablets.

Further information The Migril combination not only relieves the pain, but also the nausea and vomiting which are part of the migraine syndrome.

Product licence number 0003/5114.

MYLERAN* TABLETS

Presentation *Myleran Tablets:* 0.5 mg Busulphan BP, coded Wellcome F2A. Coloured white with yellow core. 2.0 mg Busulphan BP, coded Wellcome K2A. Coloured white with yellow core.

Uses Cytotoxic agent. Myleran is indicated for the treatment of chronic granulocytic leukaemia. Myleran has been shown to be superior to splenic irradiation when judged by survival times, control of spleen size and maintenance of haemoglobin levels. Although not curative, Myleran reduces the total granulocyte mass, relieves symptoms of disease, and improves the clinical state of the patient. Myleran is not useful once blast transformation has occurred. Myleran is also effective in producing remission in polycythaemia vera. It is especially useful in cases resistant to radiophosphorous (32p) therapy and where there is marked thrombocytosis. Myleran may be useful in selected cases of essential thrombocythaemia and myelofibrosis.

Dosage and administration *Adults: Chronic Granulocytic Leukaemia: Remission induction:* The dosage is 0.06 mg/kg daily with a maximum daily dose of 4 mg which may be given as a single dose.

Administration of Myleran should be discontinued when the white blood cell count has fallen to between 20–25,000/cu mm or earlier if the platelet count falls below 100,000/cu mm otherwise there is a considerable risk of causing irreversible bone marrow aplasia since the counts may continue to fall for some time after treatment is stopped. The blood count should be monitored at least weekly during the induction phase and the dose should be increased only if the response after three weeks is inadequate.

Maintenance therapy: Although the white count may be controlled without further therapy for long periods after induction therapy, most clinicians use some form of maintenance treatment.

Dosage is usually between 0.5–2 mg per day but individual requirements may be much less. The aim is to maintain a white blood count of 10–15,000/cu mm and blood counts should be performed at least every four weeks.

Polycythaemia vera and essential thrombocythaemia: **Remission induction:** The dosage is 4–6 mg daily. The total dose required to produce remission varies so that very careful haematological control is essential. **Maintenance therapy:** The dosage is approximately half the induction dose but the exact amount must be assessed individually for each patient. Prolonged treatment is

necessary, requiring close supervision and frequent blood counts.

Myelofibrosis: The usual dosage is 2–4 mg per day, with a lower dose for maintenance. Very careful haematological control is required because of the great sensitivity of the bone marrow in this condition.

Children: Very rarely indicated.

Contra-indications, warnings, etc

Contra-indications: In view of the seriousness of the indications, there are no absolute contra-indications.

Precautions: Careful attention should be paid to the monitoring of blood counts to avoid the possibility of excessive myelosuppression and the risk of irreversible bone marrow aplasia.

The main side-effect of Myleran treatment is bone marrow depression, particularly thrombocytopenia. Special care must be taken when the initial platelet count is low and when the count falls during treatment. Administration of Myleran should be stopped immediately at any stage of treatment if there is a sharp fall in the platelet count or if purpura develops.

Myleran should not be given to patients who have recently received radiotherapy or other cytotoxic drugs.

Hyperuricaemia and/or hyperuricosuria are not uncommon in untreated patients with chronic granulocytic leukaemia and should be corrected before starting therapy with Myleran. During treatment hyperuricaemia and the risk of uric acid nephropathy should be prevented by adequate prophylaxis.

Various chromosome aberrations have been noted in cells from patients receiving Myleran. Widespread epithelial dysplasia has been reported.

The possibility that Myleran is carcinogenic should be borne in mind. A number of malignant tumours have been reported in patients receiving busulphan.

Ovarian suppression and amenorrhoea with menopausal symptoms commonly occur in pre-menopausal patients.

Busulphan interferes with spermatogenesis in experimental animals and there have been clinical reports of sterility, azoospermia and testicular atrophy in man.

Side- and adverse effects: The most common side-effect is bone marrow depression. Gastro-intestinal effects such as nausea, vomiting and diarrhoea have been reported rarely. Such intolerance is not a significant problem and can be controlled by giving the daily treatment in divided doses.

Hyperpigmentation is the most common skin reaction and occurs in 5–10% of patients, particularly those with a dark complexion. In a few cases a clinical syndrome resembling adrenal insufficiency and characterised by weakness, severe fatigue, anorexia, weight loss, nausea and vomiting, and hyperpigmentation of the skin has developed after prolonged busulphan therapy. The syndrome has sometimes resolved when busulphan has been withdrawn.

Diffuse pulmonary fibrosis with progressive dyspnoea and a persistent non-productive cough has occurred rarely, usually after prolonged treatment over a number of years. In a single case pulmonary ossification also occurred. The lung pathology may be complicated by superimposed infections. It is possible that subsequent radiotherapy can augment subclinical lung injury caused by Myleran. Lens changes, and cataracts which may be bilateral, have been reported during Myleran therapy.

Other reported adverse reactions include urticaria, erythema multiforme, erythema nodosum, alopecia, por-

phyria cutanea tarda, excessive dryness and fragility of the skin with complete anhidrosis, dryness of the or mucous membranes and cheilosis, gynaecomastia, cholestatic jaundice, endocardial fibrosis and myasthenia gravis. Most of these are single case reports and in many a clear cause and effect relationship with Myleran has not been demonstrated.

Use in pregnancy and lactation: Myleran is potential teratogenic and embryotoxic, although there have been a number of reported cases where apparently normal children have been born after busulphan treatment during pregnancy, Myleran should be avoided during pregnancy, particularly during the first trimester. In each case, the potential benefit to the mother must be weighed against the risk to the foetus.

Mothers receiving Myleran should not breast feed.

Toxicity and treatment of overdosage: The principal toxic effect is on the bone marrow. Survival after a single large dose has been reported but haematological toxicity is likely to be more profound with chronic overdosage. As there is no known antidote the blood picture should be closely monitored and general supportive measures together with appropriate blood transfusion, instituted necessary.

Pharmaceutical precautions Store below 25°C in dry place.

Legal category POM.

Package quantities 0.5 mg: Bottle of 25 tablets
2.0 mg: Bottle of 25 tablets.

Further information Myleran is more selective than nitrogen mustard or the folic acid antagonists in its effect on the myeloid cells and may be somewhat safer in use in certain patients have received daily doses of 4 mg for as long as a year.

Product licence numbers

Tablets 0.5 mg 0003/5113
Tablets 2.0 mg 0003/5112

PENTOSTAM* INJECTION

Presentation Pentostam is a sterile faintly straw coloured solution of Sodium Stibogluconate BP containing the equivalent of 100 mg pentavalent antimony per ml.

Uses Pentostam is indicated in the following infection caused by Leishmania organisms:

Visceral leishmaniasis (kala-azar)

Cutaneous leishmaniasis (oriental sore) – both dry and moist forms, but excluding diffuse leishmaniasis.

American muco-cutaneous leishmaniasis (espundia).

Dosage and administration *Visceral leishmaniasis (kala-azar):* Adults: 6 ml daily for 7–10 days by intramuscular or intravenous injection. Two or three further courses, separated by an interval of 10 days, may be necessary.

Children: 0.1 ml/kg body weight for 21 days or 0.2 ml/kg body weight for 12–14 days by intravenous or intramuscular injection up to a maximum of 6 ml in a day.

Inadequate treatment may lead to relapse. Therefore a full course of treatment should be given where possible. All patients should be re-examined regularly for two years after treatment.

Cutaneous leishmaniasis (oriental sore): The dosage

me outlined for visceral leishmaniasis is recommended. Alternatively Pentostam can be infiltrated and the edge of the lesions in a dosage of *not more* 12 ml at any one time.

co-cutaneous leishmaniasis (espundia): Improvement or complete resolution may occur after a course of 1 Pentostam daily for 10 days given intravenously or amulsularly. A similar course can be repeated, if necessary, on two occasions at monthly intervals.

travenous injections should be administered very slowly and discontinued immediately if coughing, vomiting, or substernal pain occurs. In such cases extreme care should be taken if Pentostam is readministered by route.

ntra-indications, warnings, etc

ntra-indications: Pentostam is contra-indicated in pneumonia, myocarditis, hepatitis and nephritis.

cautions: Very rarely anaphylactic shock may develop during treatment for which Adrenaline Injection BP and appropriate supportive measures should be given immediately.

accumulation of antimony in the cardiac conducting system may give rise to disturbances in cardiac rhythm. In such circumstances further treatment with Pentostam may be contra-indicated.

care should be taken in the administration of Pentostam to patients who have recently received other antimonial drugs.

Side- and adverse effects: Documented side-effects include anorexia, substernal pain, coughing, vomiting and weakness.

Use in pregnancy and lactation: Although no effects on the foetus have been reported, Pentostam should be withheld during pregnancy unless the potential benefits to the patient outweigh the possible risk to the foetus.

No information is available on the excretion of Pentostam in breast milk.

Toxicity and treatment of overdose: Main symptoms of antimony poisoning are gastro-intestinal disturbances (nausea, vomiting and severe diarrhoea). Haemorrhagic enteritis and hepatitis may also occur. After oral ingestion gastric lavage should be carried out.

There is only limited information on the use of chelating agents in the treatment of intoxication with antimony compounds. Dimercaprol has been reported to be active. A dose of 200 mg by intramuscular injection, every six hours until recovery is complete, is suggested.

Pharmaceutical precautions Store below 25°C and protect from light.

Pharmaceutical category POM.

Package quantities Rubber-capped bottle of 100 ml.

Further information Nil.

Product licence number 0003/5105.

PHYSEPTONE® INJECTION PHYSEPTONE® TABLETS PHYSEPTONE® LINCTUS

Presentation Physeptone Injection contains 10 mg methadone Hydrochloride BP in each ml.

Physeptone Tablets each contain 5 mg Methadone hydrochloride BP, scored, coded Wellcome L4A and white in colour.

Physeptone Linctus contains 2 mg Methadone Hydro-

chloride BP, in each 5 ml and is a clear orange-brown syrup.

Uses 1. **Analgesic:** In conditions where morphine would make a reasonable alternative, particularly for the relief of pain of visceral origin. It is not recommended for use in ambulant patients.

2. **Cough suppressant:** For the control of severe cough where diamorphine linctus would be a reasonable alternative.

Dosage and administration **Analgesic use: Adults:** Usual single dose 5–10 mg by mouth, subcutaneous or intramuscular injection.

Owing to its long plasma half-life caution with repeated dosage should be observed in the very ill or elderly. The usual initial dose should be 5–10 mg, 6–8 hourly, later adjusted to the degree of pain relief obtained.

Children: Not suitable.

Anti-tussive use: Adults: 5 ml every 3–4 hours.

Children: Dilute 1 volume of linctus with 7 volumes Syrup BP. Doses of diluted preparation are:

Children over 10 years: 10 ml every 4 hours.

Children under 10 years: 5 ml every 4 hours.

Where the drug is given by mouth for the control of pain associated with a chronic condition it is wise to restrict the dose to the smallest amount which adequately controls the symptoms.

Physeptone has less hypnotic effect than morphine.

If it is necessary to give a patient a potent analgesic for a prolonged period, some increase in dose may be found necessary; in such circumstances it is probably sound practice to change to another drug (codeine, morphine, pethidine) for a time. Physeptone may then be resumed in diminished doses.

Contra-indications, warnings, etc

Contra-indications: Respiratory depression, obstructive airways disease. Concurrent administration with monoamine oxidase inhibitors, or within 2 weeks of discontinuation of treatment with them. Obstetric use is not recommended.

Precautions: Children are very sensitive to the depressant effects.

The possibility of addiction cannot be excluded and patients should be reminded of the necessity of adhering to the prescribed dosage.

Side- and adverse effects: Euphoria, dizziness, drowsiness, vomiting or nausea, and respiratory depression may occur in some patients. In rare cases a hypersensitive subject may react with a sudden transient fall in blood pressure; this is short-lived and self-terminating. Side-effects are more common and more severe in ambulant patients. Nausea and vomiting appear to be more frequent after oral administration than after injection.

In known drug addicts, Physeptone has produced withdrawal symptoms but these are mild. Tolerance and dependence of the morphine type may occur.

Use in pregnancy and lactation: There is no, or inadequate, evidence of safety in human pregnancy but the drug has been widely used for many years without apparent ill-consequence and animal studies have not shown any hazard. From theoretical considerations methadone is likely to be excreted in breast milk.

Toxicity and treatment of overdose: Toxic doses of methadone cause unconsciousness, pin-point pupils, slow, shallow respiration, cyanosis and weak pulse. Often there is a 2–3 hour delay between ingestion and

the appearance of symptoms. Lavage, dialysis and CNS stimulation are contra-indicated. Intravenous naloxone should be given and repeated at 5–10 minute intervals to attain full benefit.

Acidification of the urine will increase the rate of elimination of the drug via the kidney.

Pharmaceutical precautions *Tablets:* Store below 25°C.

Linctus: Store below 25°C, protect from light.

Injection: Store below 25°C, protect from light.

Physeptone Linctus may be diluted with Syrup BP.

Legal category POM, MDA.

Package quantities *Physeptone Injection:* 10 mg in 1 ml ampoules. Boxes of 5 and 100 ampoules.

Physeptone Tablets: Bottle of 100 tablets.

Physeptone Linctus: Bottle of 500 ml.

Further information Nil.

Product licence numbers

Injection 0003/5100

Tablets 0003/5099

Linctus 0003/5232

POLIOMYELITIS VACCINE, LIVE (ORAL) BP WELLCOME® TRIVALENT (SABIN TYPE, MONKEY KIDNEY CELL CULTURE) (Pol/Vac (Oral))

Presentation This vaccine is a stabilised sterile aqueous suspension of suitable live attenuated strains of poliomyelitis virus, types 1, 2 and 3, grown in cultures of monkey kidney tissue cells.

The attenuated vaccine strain of each type of poliovirus has antibody-inducing characteristics similar to its virulent counterpart. Extensive studies have shown that there is little risk of Sabin attenuated virus reverting to a virulent condition.

The vaccine may vary in colour from clear to light pink.

Use For active immunisation against poliomyelitis.

Dosage and administration *Dosage: Adults and children:* Three drops constitute one dose. The primary course consists of three doses of poliomyelitis vaccine at intervals of not less than four weeks.

Administration: For oral use only. The container should be shaken. To ensure the correct drop size is obtained, the container should be held vertically with the nozzle pointing downwards. Although between batches of containers the drop size, and hence the fill volume, may vary, the virus dose provided remains constant.

In the United Kingdom, oral polio vaccine is usually given in infancy at the same time as routine immunisation against diphtheria, tetanus and pertussis. Thereafter it is recommended that all immunised children be given a single reinforcing dose of oral poliomyelitis vaccine at school entry at the time they receive their reinforcing dose of diphtheria/tetanus vaccine, and again at 15 to 19 years of age or on leaving school. Further reinforcing doses are given to adults if they are likely to be exposed to special risk of contracting the disease.

Administration of oral poliomyelitis vaccine induces circulating antibodies and local antibody responses in the intestine. However, one type of poliovirus in the vaccine may inhibit another from establishing immunity.

Thus, when only a single dose of trivalent oral p vaccine is given successful immunisation against three types of poliovirus may not occur. Therefore in primary course the vaccine is administered on at least three occasions to ensure that each type of vaccine poliovirus is given an opportunity of establishing immunity. Record the title, dose and lot numbers of all vaccine and the date administered.

Contra-indications, warnings, etc

Contra-indications: Oral poliomyelitis vaccine may contain up to 4.5 i.u. of polymyxin, 0.06 i.u. of neomycin, 3.7 mcg kanamycin, 0.004 i.u. penicillin and 3.7 n streptomycin per dose. Patients with an established hypersensitivity to any of these antibiotics should not be vaccinated. In arriving at a decision to withhold administration of vaccine in an individual case, the vaccinating physician should decide whether the hazards of a hypersensitivity reaction outweigh the benefits of vaccination.

The efficacy of the vaccine may be impaired if given while the subject has diarrhoea or vomiting. In combination with other live vaccines, it should not be administered to subjects with an acute febrile illness or impaired immune responsiveness whether idiopathic, or as a result of treatment with steroids, radiotherapy, cytotoxic drugs or other agents.

Vaccinees, parents and other household contacts should be made aware of the possible risk of recipient and contact paralysis prior to vaccination.

Side- and adverse effects: Vaccine-related paralysis in recipients or contacts may occur on very rare occasions.

Use in pregnancy and lactation: The vaccine should not be administered to pregnant women, unless they are known to be at an increased risk of contracting poliomyelitis.

Toxicity and treatment of overdosage: Not applicable.

Pharmaceutical precautions If stored between 2 and 4°C oral poliomyelitis vaccine can be expected to retain its potency for six months. If stored at or just below 25°C, oral poliomyelitis vaccine can be expected to retain its potency for one week. When tubes of vaccine have been opened there is a risk of contamination with bacteria and moulds which may result in a reduction of vaccine potency. It is good practice, therefore, to discard vaccine remaining in opened tubes at the end of the vaccinating session.

Legal category POM.

Package quantities Polythene dropper tubes of 10 doses.

Product licence number 0003/5270.

POLYTRIM® EYE DROPS

Presentation A clear, colourless, sterile, aqueous solution containing in each ml: Trimethoprim BP 10 mg, Polymyxin B Sulphate BP 10,000 units, Thiomersal F (0.05 mg per ml) is included as a preservative.

Uses Antibacterial agent. For the treatment of a prophylaxis of external bacterial infections of the eye including conjunctivitis, keratitis, corneal ulcerative ulcerative blepharitis with associated conjunctivitis, acute chronic dacryocystitis. Prophylactically, it is used following removal of foreign bodies, and before and after ophthalmic surgery to help provide and maintain a sterile field.

sage and administration *Adults:* 1 drop in the affected eye four times daily. *Children:* As for adults. More frequent administration may be required, depending on the severity of the condition. Treatment should normally be continued for at least forty-eight hours after the eye has apparently returned to normal.

Contra-indications, warnings, etc

Contra-indications: Contra-indicated in individuals who have a history of hypersensitivity to trimethoprim or to polymyxins.

cautions: As with all antibacterial preparations, prolonged use may result in the overgrowth of non-susceptible organisms including fungi.

e- and adverse effects: Polyttrim is isotonic with tears and is well tolerated in the eye. No local adverse effects are to be expected, except rarely, a hypersensitivity reaction. If one is suspected during treatment, administration should be discontinued.

Toxicity and treatment of overdosage: Not applicable.

Pharmaceutical precautions Do not use if the container seal has been broken. Use within one month of opening container. Store in a dry place, below 25°C, and protect from light. Not suitable for injection.

Legal category POM.

Package quantities Screw-capped plastic dropper bottle containing 5 ml.

Further information There is *in vitro* evidence of synergy between trimethoprim and polymyxin. The combination is effective against a wide variety of Gram-positive and Gram-negative bacterial ocular pathogens, including *Pseudomonas aeruginosa*.

Product licence number 0003/0153.

IO-ACTIDIL* TABLETS

Presentation Each tablet contains 10 mg of Triprolidine Hydrochloride BP divided between three layers to give a rapid onset of action, followed by a sustained release of the drug to give a therapeutic effect lasting up to 24 hours in most patients. Each tablet is coded with Wellcome M4A and is white with blue core and pink outer layer.

Uses Prolonged action antihistamine.

In allergic dermatoses, urticaria, seborrhoeic eczema, allergic rhinitis, conjunctivitis, vasomotor rhinitis, hay fever, particularly nocturnal and early morning attacks.

Dosage and administration *Adults:* 1 tablet swallowed whole with a little water in the early evening, or 1 to 2 tablets before retiring. A few patients with very severe symptoms may need two tablets during 24 hours.

Children: Over 10 years: 1 tablet a day.

Under 10 years: It is recommended that Actidil Elixir is used.

Contra-indications, warnings, etc

Contra-indications: Contra-indicated in patients with known hypersensitivity to triprolidine.

Precautions: Caution in severe hepatic or renal dysfunction.

May cause drowsiness. Patients should not drive a vehicle or operate machinery until they have determined their own response. In some patients the drowsiness

induced by antihistamines may be potentiated by alcohol or other central sedatives.

Side- and adverse effects: Triprolidine may cause drowsiness. Lichenoid skin eruptions due to triprolidine have rarely been reported.

Use in pregnancy and lactation: No data are available on the use of Pro-Actidil in human pregnancy nor on the excretion of it or its metabolites in human milk.

Toxicity and treatment of overdosage: Drowsiness, dizziness, inco-ordination, weakness, convulsions and respiratory depression may occur.

Necessary measures should be taken to maintain and support respiration. Gastric lavage should be performed if indicated and convulsions controlled with diazepam. There are theoretical grounds for believing that the elimination of triprolidine and its metabolites could be accelerated by dialysis.

Pharmaceutical precautions Store below 15°C.

Legal category P.

Package quantities Bottle of 100 tablets.

Further information Nil.

Product licence number 0003/5228.

PURI-NETHOL* TABLETS

Presentation Each tablet contains 50 mg Mercaptopurine BP, fawn coloured, scored and coded Wellcome 04A.

Uses Cytotoxic agent.

Puri-Nethol is indicated for the treatment of acute leukaemia. It is of value in remission induction and is particularly indicated for maintenance therapy in acute lymphoblastic leukaemia and acute myelogenous leukaemia. Puri-Nethol is used in the treatment of chronic granulocytic leukaemia.

Dosage and administration For adults and children the usual dose is 2.5 mg/kg bodyweight per day, but the dose and duration of administration depend on the nature and dosage of other cytotoxic agents given in conjunction with Puri-Nethol. The dosage should be carefully adjusted to suit the individual patient. Puri-Nethol has been used in various combination therapy schedules for acute leukaemia and the literature should be consulted for details. Consideration should be given to reducing the dosage in patients with impaired hepatic or renal function. When Zyloric (Allopurinol) and Mercaptopurine are administered concomitantly it is essential that only a quarter of the usual dose of Mercaptopurine is given since Zyloric (Allopurinol) decreases the rate of catabolism of Mercaptopurine.

Contra-indications, warnings, etc

Contra-indications: In view of the seriousness of the indications there are no absolute contra-indications.

Precautions: Puri-Nethol is an active cytotoxic agent for use only under the direction of physicians experienced in the administration of such agents.

Since Puri-Nethol is strongly myelosuppressive full blood counts must be taken daily during remission induction. Patients must be carefully monitored during therapy.

Treatment with Puri-Nethol causes bone marrow suppression leading to leucopenia and thrombocytopenia.

The leucocyte and platelet counts continue to fall after treatment is stopped, so at the first sign of an abnormally large fall in the counts, treatment should be interrupted immediately.

Bone marrow suppression is reversible if Puri-Nethol is withdrawn early enough.

During remission induction in acute myelogenous leukaemia the patient may frequently have to survive a period of relative bone marrow aplasia and it is important that adequate supportive facilities are available.

Puri-Nethol is hepatotoxic and liver function tests should be monitored weekly during treatment. More frequent monitoring may be advisable in those with pre-existing liver disease or receiving other potentially hepatotoxic therapy. The patient should be instructed to discontinue Puri-Nethol immediately if jaundice becomes apparent.

During remission induction when rapid cell lysis is occurring, uric acid levels in blood and urine should be monitored as hyperuricaemia and/or hyperuricosuria may develop, with the risk of uric acid nephropathy.

Puri-Nethol in common with other antimetabolites is potentially mutagenic and chromosome damage has been reported in rats and man.

In view of its action on cellular deoxyribonucleic acid (DNA) mercaptopurine is potentially carcinogenic and consideration should be given to the theoretical risk of carcinogenesis with this treatment.

When Zyloric [allopurinol] and Puri-Nethol are administered concomitantly it is essential that only a quarter of the usual dose of Puri-Nethol is given since Zyloric decreases the rate of catabolism of Puri-Nethol.

Inhibition of the anticoagulant effect of warfarin, when given with Puri-Nethol, has been reported.

It is advised that care be taken when handling or inhaling these tablets not to contaminate hands or to inspire drug.

Side- and adverse effects: The main side-effect of treatment with Puri-Nethol is bone marrow suppression leading to leucopenia and thrombocytopenia. Puri-Nethol is hepatotoxic in animals and man. The histological findings in man have shown hepatic necrosis and biliary stasis. The incidence of hepatotoxicity varies considerably and can occur with any dose but more frequently when the recommended dose of 2.5 mg/kg bodyweight daily is exceeded. Monitoring of liver function tests may allow early detection of liver toxicity. This is usually reversible if Puri-Nethol therapy is stopped soon enough. However, irreversible liver damage leading to a fatal outcome has occurred.

Anorexia, nausea and vomiting have occasionally been noted.

Oral ulceration has been reported during Puri-Nethol therapy and rarely intestinal ulceration has occurred.

Rare complications are drug fever and skin rash.

Use in pregnancy and lactation: Puri-Nethol is embryotoxic in rats. This effect is dose dependent.

Normal offspring have been born after Puri-Nethol therapy during human pregnancy, but abortion, prematurity and malformation have been reported. The small numbers involved do not allow an evaluation of the degree of risk of Puri-Nethol therapy during pregnancy and the possible hazard to the foetus must be balanced against the expected benefit in individual cases.

Mothers receiving Puri-Nethol should not breast feed.

Toxicity and treatment of overdosage: The principal toxic effect is on the bone marrow and haematological toxicity is likely to be more profound with chronic overdosage

than with a single ingestion of Puri-Nethol. The risk of overdosage is also increased when Zyloric is being given concomitantly with Puri-Nethol. As there is no known antidote the blood picture should be closely monitored and general supportive measures, together with appropriate blood transfusion, instituted if necessary.

Pharmaceutical precautions Store below 2°C. Keep dry, protect from light.

Legal category POM.

Package quantities Bottle of 25 tablets.

Further information Puri-nethol is an analogue of adenine and hypoxanthine, and microbiological studies have shown it to be an antagonist of these; its mode of action differs thus from that of the folic acid antagonist.

Product licence number 0003/5227.

SCHICK TEST TOXIN BP AND SCHICK CONTROL BP WELLCOME*

Presentation Schick Test Toxin is the sterile dilute filtrate from a culture of *Corynebacterium diphtheriae*. The Control Fluid is the same material heated sufficiently to inactivate the toxin but not sufficiently to destroy more heat-stable bacterial proteins and their constituents.

Uses The Schick test is used to demonstrate whether or not a certain degree of immunity to diphtheria is present, either initially or after immunisation. The test produces a local skin reaction in those who are susceptible to the disease, while in those who are satisfactorily immune it is neutralised by the subject's antitoxin and no reaction results. The concurrent injection of Control Fluid at another, comparable site provides a means of distinguishing between true, positive reactions due to toxin and other reactions of an allergic nature due to non-specific constituents. During the first few months of life babies usually have maternally derived immunity. Those between 6 months and 8 years rarely suffer from untoward reactions after primary immunisation. Therefore, the Schick test is not usually given to infants or children up to 8 or even 10 years of age. In children over 10 years and adults, the state of immunity varies, so a preliminary Schick test should always be performed before injection of a vaccine, the main purpose being to detect those giving a negative and pseudo reaction, for they may experience a reaction after a dose of vaccine.

Dosage and administration *Technique:* A dose of 0.2 ml of the Toxin is injected intradermally into the anterior surface of the left forearm, and 0.2 ml of the Control Fluid into the corresponding position on the right forearm.

Separate syringes and needles should be used for the Toxin and Control Fluid. It is a practical advantage, when dealing with groups of subjects, to identify each syringe with a rubber band around the barrels of, say, those for the Control Fluid is suggested. Any unused portion of the container should be discarded.

Readings: Results may be read at 24-48 (possibly up to 72) hours, and again at five to seven days to detect late reactions and to reconsider earlier, doubtful readings. When comparing the appearance of the two arms it is possible to judge how far any reaction is due to the toxin and how

to the other constituents. Four types of result may be seen:

Negative (= immune). No reaction visible on either arm.

Negative-and-pseudo (= immune). Both arms show somewhat similar flushes which usually fade more rapidly than that of a true positive reaction. They are due to non-specific constituents and not to toxin.

Positive (= susceptible). The left arm shows a flush 10–50 mm in diameter; this fades and becomes brown and fine desquamation may occur. The staining persists for several weeks.

Positive-and-pseudo (= susceptible) (also called 'combined'). Both arms show a flush but the left is larger, deeper and more persistent than the right. The pseudo reaction develops more rapidly than any positive response and may be at its maximum at 24–72 hours. By the fifth sixth day, the pseudo effect has faded considerably or disappeared, whereas the positive reaction has increased in size and intensity.

Distinction must be made between those with a well-marked pseudo reaction, which may be slightly greater on the left arm, and those with a positive-and-pseudo reaction, which will be markedly greater on the left arm. The true positive-and-pseudo reaction is extremely rare in most subjects showing a large flush on both arms is immune, even if there is some difference between the two arms. Persons showing a well-marked pseudo reaction are almost invariably immune to diphtheria and could not be immunised further because they may react adversely to the vaccine.

The Schick test may be vitiated by the following: the timing of Schick tests performed from 12 hours before to four weeks after the administration of diphtheria, tetanus or of any other equine antitoxin or of convalescent human serum or gammaglobulin may be erroneous and should, if negative, be disregarded.

Contra-indications, warnings, etc

Contra-indications: Subjects with a history of hypersensitivity to previous doses of Schick Test materials or with known hypersensitivity to diphtheria vaccine should not be tested.

Precautions: Although anaphylaxis associated with the Schick Test is extremely rare, facilities for the management of anaphylaxis should be available during its administration.

The validity of the Schick Test may be impaired if the test is performed within 12 hours to 4 weeks following administration of any equine antitoxin or of human serum or gamma globulin. Negative results obtained during this period are not indicative of immunity to diphtheria and should be disregarded.

Use in pregnancy and lactation: The vaccine has been widely used for many years without apparent ill consequence.

Toxicity and treatment of overdose: Not applicable.

Pharmaceutical precautions Store at 2–8°C. Do not freeze.

Pharmaceutical category POM.

Package quantities Set of 1 ml.

Further information Nil.

Product licence number 0003/5139.

SEPTRIN® TABLETS SEPTRIN® DISPERSIBLE TABLETS SEPTRIN® FORTE TABLETS SEPTRIN® ADULT SUSPENSION SEPTRIN® PAEDIATRIC SUSPENSION SEPTRIN® PAEDIATRIC TABLETS

Presentation Septrin Tablets (Co-trimoxazole Tablets BP) each contain 80 mg Trimethoprim BP and 400 mg Sulphamethoxazole BP. Coded Septrin Y2B Wellcome. White in colour.

Septrin Dispersible Tablets (Dispersible Co-trimoxazole Tablets BP) each contain 80 mg Trimethoprim BP and 400 mg Sulphamethoxazole BP. Coded Septrin Y2B Wellcome. Orange in colour.

Septrin Forte Tablets (Co-trimoxazole Tablets BP) each contain 160 mg Trimethoprim BP and 800 mg Sulphamethoxazole BP. Scored and coded Septrin Forte O2C. White in colour.

Septrin Adult Suspension (Co-trimoxazole Mixture BP) contains 80 mg Trimethoprim BP and 400 mg Sulphamethoxazole BP in each 5 ml. Off-white in colour.

Septrin Paediatric Suspension (Paediatric Co-trimoxazole Mixture BP) contains 40 mg Trimethoprim BP and 200 mg Sulphamethoxazole BP in each 5 ml. Pale pink in colour.

Septrin Paediatric Tablets (Paediatric Co-trimoxazole Tablets BP) each contain 20 mg Trimethoprim BP and 100 mg Sulphamethoxazole BP. Scored and coded Wellcome H4B. White in colour.

Uses Antibacterial agent. Septrin is effective *in vitro* against a wide range of Gram-positive and Gram-negative organisms. It is not active against *Mycobacterium tuberculosis*, *Mycoplasma* or *Treponema pallidum*, *Pseudomonas aeruginosa* is usually insensitive.

Septrin is of value in the treatment of the following:

Respiratory tract: Acute and chronic bronchitis, bronchiectasis, lobar and broncho-pneumonia, *Pneumocystis carinii* pneumonitis, otitis media and sinusitis.

Genito-urinary tract: Urethritis, cystitis, pyelitis, pyelonephritis, and prostatitis. Male and female gonorrhoea.

Gastro-intestinal tract: Typhoid and paratyphoid fevers, chronic carriage of *Salmonella typhi* and *paratyphi*, cholera and shigellosis.

Skin infections: Pyoderma, abscesses and wound infections.

Other bacterial infections: Acute and chronic osteomyelitis, acute brucellosis, septicaemias and other infections caused by sensitive organisms.

Dosage and administration *Septrin Tablets* and *Septrin Dispersible Tablets – Adults:* Standard dosage: 2 twice daily.

For severe infections: 3 twice daily. For long-term treatment (more than 14 days): 1 twice daily.

Children over 12 years: As for adults.

6–12 years: 1 twice daily.

Septrin Dispersible Tablets should be taken in a little water or swallowed whole.

Septrin Forte Tablets – Adults: Standard dosage: 1 twice daily.

For severe infections: 1½ twice daily.

Children over 12 years: As for adults.

Children under 12 years: Not applicable.

Septrin Adult Suspension – Adults: Standard dosage: 10 ml twice daily.

For severe infections: 15 ml twice daily. For long-term treatment (more than 14 days): 5 ml twice daily.

Children over 12 years: As for adults.

Septrin Paediatric Suspension

Children 6–12 years: 10 ml twice daily.

6 months to 6 years: 5 ml twice daily.

6 weeks to 6 months: 2.5 ml twice daily.

Septrin Adult and Paediatric Suspensions may be diluted with Syrup BP.

Septrin Paediatric Tablets

Children 6–12 years: 4 twice daily.

2–6 years: 2 twice daily.

In acute infections, Septrin should be given for at least five days or until the patient has been symptom-free for two days.

In prostatitis and acute brucellosis, treatment at standard dosage should last for a period of at least four weeks.

Dosage in gonorrhoea: In uncomplicated gonorrhoea, 4 tablets every 12 hours for two days, or 5 tablets followed eight hours later by a further dose of 5 tablets, is recommended.

*Dosage in *Pneumocystis carinii* pneumonitis:* 20 mg trimethoprim, 100 mg sulphamethoxazole/kg/day in two divided doses for two weeks.

Dosage recommendations in renal impairment: If Septrin is given to patients with renal impairment then the following dosage scheme is suggested (no information is available for children with renal failure).

<i>Creatinine clearance (ml/min)</i>	<i>Serum creatinine (μmol/l)</i>	<i>Dosage</i>
Above 25	men < 265 women < 175	Standard dosage.
15–25	men 265–620 women 175–400	Standard dosage for a maximum of three days followed by half the standard dosage.
Below 15	men > 620 women > 400	Not to be administered unless haemodialysis facilities are available. Under this condition half the standard dosage may be given.

Measurements of plasma concentrations of sulphamethoxazole at intervals of two to three days are recommended in samples obtained 12 hours after administration of Septrin. If the concentration of total sulphamethoxazole exceeds 150 mcg/ml, then treatment should be interrupted until the value falls below 120 mcg/ml.

Contra-indications, warnings, etc

Contra-indications: Septrin should not be given to patients with a history of sulphonamide, trimethoprim or co-trimoxazole hypersensitivity.

Contra-indicated in patients showing marked liver parenchymal damage.

Except in certain circumstances it should not be given to patients with serious haematological disorders. The combination has been administered to patients receiving cytotoxic agents without evidence of an adverse effect on the bone marrow or peripheral blood.

Contra-indicated in severe renal insufficiency where

repeated measurements of the plasma concentration cannot be performed.

Septrin should not be given to premature babies nor full-term infants during the first six weeks of life. The drug should not be given during pregnancy. (See below)

Precautions: In cases with renal impairment a modified dosage schedule as described above is indicated. In such patients, measurements of the plasma concentration of the drug is advisable, and an adequate urinary output should be maintained.

A folate supplement should be considered when treating potentially folate deficient patients.

If Septrin treatment is prolonged, especially in patients with suspected impairment of folate metabolism, it is suggested that complete blood counts including thrombocytes be performed at monthly intervals.

The usual caution in prescribing any drug for women of child-bearing age should be exercised with Septrin.

Care should be taken when giving Septrin to patients receiving sulphonylurea hypoglycaemics, oral anticoagulants of the coumarin group or phenytoin as the action of these agents may be increased.

Patients receiving pyrimethamine in doses in excess of 25 mg weekly who are also receiving Septrin should have their blood pictures monitored because of the occasional report of megaloblastic anaemia apparently occurring in these circumstances.

Side- and adverse effects: Nausea, vomiting, diarrhoea, glossitis and skin rashes can occur. Pseudomembranous colitis has been reported rarely. Isolated cases of severe skin sensitivity reactions such as erythema multiforme, bullous (Stevens-Johnson syndrome) and toxic epidermal necrolysis (Lyell syndrome) have occurred.

As Septrin contains a sulphonamide, the possibility of blood dyscrasias like those associated with sulphonamides should be borne in mind. The changes reported with Septrin mainly consist of thrombocytopenia, purpura, leucopenia, neutropenia and very rarely agranulocytosis. They have usually proved to be reversible on withdrawal of the drug. Elderly patients are more susceptible to the blood changes. Septrin may induce haemolysis in certain susceptible glucose-6-phosphate dehydrogenase deficient patients.

There have been a few reports of subjective experiences such as headache, depression, dizziness or hallucinations but their relationship to therapy remain unproven.

During long-term therapy, isolated cases of megaloblastic changes in the bone marrow have been reported; these are reversible by folic acid therapy.

Use in pregnancy and lactation: The safety of Septrin in human pregnancy has not been established. Animal studies have shown teratogenic effects typical of a folate antagonist in rats but not rabbits at high doses; these were prevented by administration of dietary folate. Sulphonamide-containing products should not be administered in late pregnancy because of the risk of kernicterus.

Both sulphamethoxazole and trimethoprim may be found in breast milk but this does not contra-indicate the use of Septrin in lactating mothers.

Toxicity and treatment of overdose: Symptoms of acute overdose are likely to be nausea, vomiting, abdominal pain, dizziness and confusion. Treatment should consist of gastric lavage if within an hour of ingestion. Increased fluid intake will increase the elimination of sulphamethoxazole. Alkalinisation of the urine will also increase the elimination of sulphamethoxazole.

decrease that the trimethoprim. Calcium folinate 3–10 mg given orally or intramuscularly for five to seven days should counteract any bone-marrow effects of trimethoprim. General supportive measures are recommended.

Pharmaceutical precautions *Tablets*: Store below 25°C. Protect from light.

Injectable Tablets: Store below 25°C. Keep dry, protect from light.

Adult and Paediatric Suspension: Store below 25°C. Protect from light.

Legal category POM.

Package quantities *Septirin Tablets*: packs of 100 and 500 tablets.

Septirin Dispersible Tablets: packs of 100 and 500 tablets.

Septirin Forte Tablets: pack of 100 tablets.

Septirin Adult Suspension: bottle of 100 ml.

Septirin Paediatric Suspension: bottle of 100 ml.

Septirin Paediatric Tablets: pack of 100 tablets.

Further information Absorption by the oral route is rapid; significant plasma levels are obtained within an hour. Peak levels are reached between two and four hours and are maintained over a period of 12 hours.

In the treatment of tonsillo-pharyngitis due to Group A beta-haemolytic streptococci, eradication of these organisms from the oro-pharynx is less rapid than with many other antibiotics.

Trimethoprim may cause an apparent rise in serum creatinine levels due to (a) competition for the tubular resecretory mechanisms; (b) chemical interference with a visual auto-analyser method of estimating creatinine. Co-trimoxazole may cause a fall in peripheral thyroid hormone levels but the clinical significance requires confirmation.

Septirin for Infusion and Septirin Intra-muscular Injection are also available.

Product licence numbers

Tablets	0003/0109
Dispersible Tablets	0003/0099
Forte Tablets	0003/0121
Adult Suspension	0003/5223
Paediatric Suspension	0003/5222
Paediatric Tablets	0003/0108

SEPTIRIN* FOR INFUSION

Strong Sterile Co-trimoxazole Solution
to make Co-trimoxazole Intravenous Infusion BP.

Presentation Septirin for Infusion contains 80 mg trimethoprim BP and 400 mg Sulphamethoxazole BP in each 5 ml ampoule. The infusion is faintly yellow and contains 40 per cent propylene glycol together with nyl alcohol and a small amount of benzyl alcohol. It has a pH of approximately 10.

Uses Antibacterial agent. Septirin is effective *in vitro* against a wide range of Gram-positive and Gram-negative organisms. It is not active against *Mycobacterium tuberculosis*, *Mycoplasma* or *Trachomatis pallidum*. *Pseudomonas aeruginosa* is usually insensitive.

In general, the indications for the use of Septirin for infusion are the same as those for oral presentations. Septirin for Infusion is for use when oral dosage is not possible.

Clinical experience with oral Septirin indicates its value in the following:

Respiratory tract: Acute and chronic bronchitis, bronchiectasis, lobar and broncho-pneumonia, *Pneumocystis carinii* pneumonitis, otitis media and sinusitis.

Genito-urinary tract: Urethritis, cystitis, pyelitis, pyelonephritis and prostatitis. Male and female gonorrhoea.

Gastro-intestinal tract: Typhoid and paratyphoid fevers, chronic carriage of *Salmonella typhi* and *paratyphi*, cholera, and shigellosis.

Skin infections: Pyoderma, abscesses and wound infections.

Other bacterial infections: Acute and chronic osteomyelitis, acute brucellosis, septicaemias and other infections caused by sensitive organisms.

Dosage and administration

Adults and children over 12 years: Standard dosage: 10 ml twice daily, morning and evening.

For severe infections: 15 ml twice daily, morning and evening.

Children up to 12 years: The recommended dosage is approximately 6 mg trimethoprim and 30 mg sulphamethoxazole per kg body weight per 24 hours, divided into two equal doses. As a guide the following doses of Septirin for Infusion may be used:

6 weeks to 6 months: 1.25 ml twice daily.

6 months to 6 years: 2.5 ml twice daily.

6–12 years: 5.0 ml twice daily.

It is intended that Septirin for Infusion should be used only during such a period as the patient is unable to accept oral therapy. It is recommended that the dosage for severe infections, indicated above, should not be administered for more than three successive days. In general, administration is unlikely to be required for more than a few days.

Dosage in *Pneumocystis carinii* pneumonitis: The dosage is 15 to 20 mg trimethoprim, 75 to 100 mg sulphamethoxazole/kg/day in divided doses. The course is two weeks, but oral therapy should be substituted as soon as it is appropriate.

Dosage recommendations in renal impairment: If Septirin is given to patients with renal impairment then the following dosage scheme is suggested (no information is available for children with renal failure).

Creatinine Serum creatinine Dosage
clearance (μmol/l)
(ml/min)

Above 25	men < 265 women < 175	Standard dosage.
15–25	men 265–620 women 175–400	Standard dosage for a maximum of three days followed by half the standard dosage.
Below 15	men > 620 women > 400	Not to be administered unless haemodialysis facilities are available. Under this condition half the standard dosage may be given.

Measurements of plasma concentrations of sulphamethoxazole at intervals of two to three days are recommended in samples obtained 12 hours after

administration of Septrin. If the concentration of total sulphamethoxazole exceeds 150 mcg/ml then treatment should be interrupted until the value falls below 120 mcg/ml.

Administration: Septrin for Infusion must be given by the intravenous route **ONLY** and **MUST BE DILUTED** before administration, according to the following schedules:

One ampoule Septrin for Infusion (5 ml) to 125 ml infusion solution.

Two ampoules Septrin for Infusion (10 ml) to 250 ml infusion solution.

Three ampoules Septrin for Infusion (15 ml) to 500 ml infusion solution.

DILUTION SHOULD BE CARRIED OUT DIRECTLY BEFORE USE. After the addition of Septrin for Infusion to the infusion solution the mixture should be shaken to ensure thorough mixing. Should visible turbidity or crystallisation appear in the solution at any time before or during an infusion the mixture should be discarded.

Septrin for Infusion is known to be compatible, when diluted in accordance with the schedules above, with the following fluids:

Dextrose Injection BP 5% and 10%.

Laevulose Injection BP 5%.

Sodium Chloride Injection BP (0.9%).

Sodium Chloride (0.18%) and Dextrose (4%) Injection BP.

Dextran 70 Injection BP 6% in dextrose 5% or normal saline.

Dextran 40 Injection BP 10% in dextrose 5% or normal saline.

Ringer's Solution for Injection BPC 1959.

No other substance should be mixed with the infusion.

It is suggested that the duration of the infusion should be approximately one and a half hours, but this should be balanced against the fluid requirements of the patient.

Contra-indications, warnings, etc

Contra-indications: Septrin should not be given to patients with a history of sulphonamide, trimethoprim or co-trimoxazole hypersensitivity.

Contra-indicated in patients showing marked liver parenchymal damage.

Except in certain circumstances it should not be given to patients with serious haematological disorders. The combination has been administered to patients receiving cytotoxic agents without evidence of an adverse effect on the bone marrow or peripheral blood.

Contra-indicated in severe renal insufficiency where repeated measurements of the plasma concentration cannot be performed.

Septrin should not be given to premature babies nor to full-term infants during the first six weeks of life. The drug should not be given during pregnancy. (See below.)

Precautions: In cases with renal impairment a modified dosage schedule as described above is indicated. In such patients, measurement of the plasma concentration of the drug is advisable, and an adequate urinary output should be maintained.

A folate supplement should be considered when treating potentially folate deficient patients.

If Septrin treatment is prolonged, especially in patients with suspected impairment of folate metabolism, it is suggested that complete blood counts including thrombocytes be performed at monthly intervals.

The usual caution in prescribing any drug for women of child-bearing age should be exercised with Septrin.

Care should be taken when giving Septrin to patients receiving sulphonylurea hypoglycaemics, oral anticoagulants of the coumarin group or phenytoin as the action of these agents may be increased.

Patients receiving pyrimethamine in doses in excess of 25 mg weekly who are also receiving Septrin should have their blood pictures monitored because of the occasional report of megaloblastic anaemia apparent occurring in these circumstances.

Side- and adverse effects: Nausea, vomiting, diarrhoea, glossitis and skin rashes can occur. Pseudomembranous colitis has been reported rarely. Isolated cases of severe skin sensitivity reactions such as erythema multiforme bullosa (Stevens-Johnson syndrome) and toxic epidermal necrolysis (Lyell syndrome) have occurred.

As Septrin contains a sulphonamide, the possibility of blood dyscrasias like those associated with sulphonamides should be borne in mind. The changes reported with Septrin mainly consist of thrombocytopenia, purpuric leucopenia, neutropenia and very rarely agranulocytosis. They have usually proved to be reversible on withdrawal of the drug. Elderly patients are more susceptible to the blood changes. Septrin may induce haemolysis in certain susceptible glucose-6-phosphate dehydrogenase deficient patients.

There have been a few reports of subjective experiences such as headache, depression, dizziness or hallucinations but their relationship to therapy remain unproven.

During long-term therapy, isolated cases of megaloblastic changes in the bone marrow have been reported; these are reversible by folic acid therapy.

Use in pregnancy and lactation: The safety of Septrin in human pregnancy has not been established. Animal studies have shown teratogenic effects typical of a folate antagonist in rats but not rabbits at high doses; these were prevented by administration of dietary folate. Sulphonamide-containing products should not be administered in late pregnancy because of the risk of kernicterus.

Both sulphamethoxazole and trimethoprim may be found in breast milk, but this does not contra-indicate the use of Septrin in lactating mothers.

Toxicity and treatment of overdosage: Not applicable.

Pharmaceutical precautions Store below 25°C. Protect from light.

Legal category POM.

Package quantities Box of 10 ampoules.

Further information In the treatment of tonsillopharyngitis due to Group A beta-haemolytic streptococci eradication of these organisms from the oropharynx is less rapid than with some other antibiotics.

Trimethoprim may cause an apparent rise in serum creatinine levels due to (a) competition for the tubular secretory mechanisms; (b) chemical interference with the visual auto-analyser method of estimating creatinine.

Co-trimoxazole may cause a fall in peripheral thyroid hormone levels but the clinical significance requires confirmation.

Septrin is available also as: Tablets, Dispersible Tablets, Forte Tablets, Adult Suspension, Paediatric Suspension, Paediatric Tablets, and Intramuscular Injection.

Product licence number 0003/0095.

EPTRIN® INTRAMUSCULAR INJECTION

approved name: Co-trimoxazole

presentation Septrin IM Injection contains 160 mg rimethoprim BP and 800 mg Sulphamethoxazole BP in each 3 ml ampoule.

The sterile solution is faintly yellow and contains the cative substances in a 52 per cent v/v solution of lycofurol.

The pH of the solution is approximately 9.0–10.5.

Ises Antibacterial agent. Septrin is effective *in vitro* against a wide range of Gram-positive and Gram-negative organisms. It is not active against *Mycobacterium tuberculosis*, *Mycoplasma* or *Treponema pallidum*. *Pseudomonas aeruginosa* is usually insensitive.

In general, the indications for the use of Septrin intramuscular are the same as for oral presentations. Septrin Intramuscular should be used when the intramuscular route is considered preferable.

Clinical experience with oral Septrin indicates its value in the following:

Respiratory tract: Acute and chronic bronchitis, bronchiectasis, lobar and broncho-pneumonia, *Pneumocystis carinii* pneumonitis, otitis media and sinusitis.

Genito-urinary tract: Urethritis, cystitis, pyelitis, pyelonephritis and prostatitis. Male and female gonorrhoea.

Gastro-intestinal tract: Typhoid and paratyphoid fevers, chronic carriage of *Salmonella typhi* and *paratyphi*, cholera and shigellosis.

Skin infections: Pyoderma, abscesses and wound infections.

Other bacterial infections: Acute and chronic osteomyelitis, acute brucellosis, septicaemias and other infections caused by sensitive organisms.

Dosage and administration *Adults and children over 12 years:* Standard dosage: One 3 ml ampoule 12-hourly, morning and evening.

Maximum dosage (for severe infections): One and a half ampoules (4.5 ml) 12-hourly, morning and evening, or one 3 ml ampoule three times daily.

Children aged 6–12 years: The usual recommended dose is half an ampoule (1.5 ml) 12-hourly, morning and evening (this dose is based on an average of 6 mg trimethoprim plus 30 mg sulphamethoxazole per kg body weight daily).

Slight adjustment of this dose may be necessary for children whose body weights approach the extremes of the range for their height and age.

It is NOT recommended that Septrin Intramuscular Injection be given to children under the age of six years because of their small muscle mass.

It is intended that Septrin IM Injection should be used only during such a period as the patient is unable to accept oral therapy. It is recommended that the standard dosage (above) should not normally be administered for more than five successive days nor the maximum dosage (above) for more than three successive days.

Dosage in *Pneumocystis carinii* pneumonitis: Since the volume containing the suggested dose exceeds the maximum recommended, the use of Septrin Intramuscular is inappropriate. Septrin for Infusion should be administered if parenteral therapy is required.

Dosage recommendations in renal impairment: If Septrin is given to patients with renal impairment then the following dosage scheme is suggested (no information is available for children with renal failure).

<i>Creatinine clearance (ml/min)</i>	<i>Serum creatinine (μmol/l)</i>	<i>Dosage</i>
Above 25	men < 265 women < 175	Standard dosage.
15–25	men 265–620 women 175–400	Standard dosage for a maximum of three days followed by half the standard dosage.
Below 15	men > 620 women > 400	Not to be administered unless haemodialysis facilities are available. Under this condition half the standard dosage may be given.

Measurements of plasma concentration of sulphamethoxazole at intervals of two to three days are recommended in samples obtained 12 hours after administration of Septrin. If the concentration of total sulphamethoxazole exceeds 150 mcg/ml, then treatment should be interrupted until the value falls below 120 mcg/ml.

Administration: Septrin IM Injection must be given by this route ONLY and ONLY when an intramuscular formulation is indicated by the clinical condition.

The injection should be made deep into the upper and outer quadrant of the buttock, and injections should be given into each buttock alternately.

If the total contents of an ampoule are not used after opening then the remainder should be destroyed.

Contra-indications, warnings, etc

Contra-indications: Septrin should not be given to patients with a history of sulphonamide, trimethoprim or co-trimoxazole hypersensitivity.

Contra-indicated in patients showing marked liver parenchymal damage.

Except in certain circumstances it should not be given to patients with serious haematological disorders. The combination has been administered to patients receiving cytotoxic agents without evidence of an adverse effect on the bone marrow or peripheral blood.

Contra-indicated in severe renal insufficiency where repeated measurements of the plasma concentration cannot be performed.

Septrin should not be given to premature babies nor to full-term infants during the first six weeks of life. The drug should not be given during pregnancy. (See below.)

Precautions: In cases with renal impairment a modified dosage schedule as described above is indicated. In such patients, measurements of the plasma concentration of the drug is advisable, and an adequate urinary output should be maintained.

A folate supplement should be considered when treating potentially folate deficient patients.

The usual caution in prescribing any drug for women of child-bearing age should be exercised with Septrin.

If Septrin treatment is prolonged, especially in patients with suspected impairment of folate metabolism, it is suggested that complete blood counts including thrombocytes be performed at monthly intervals.

Care should be taken when giving Septrin to patients receiving sulphonylurea hypoglycaemics, oral anticoagulants of the coumarin group or phenytoin as the action of these agents may be increased.

Patients receiving pyrimethamine in doses in excess of 25 mg weekly who are also receiving Septrin should have their blood pictures monitored because of the occasional report of megaloblastic anaemia apparently occurring in these circumstances.

Side- and adverse effects: On the basis of animal experiments some local muscle damage is to be expected but experience has shown that this does not appear to be a clinical problem. Local reactions mainly vary from mild to moderate pain at the injection site; induration is uncommon.

Nausea, vomiting, diarrhoea, glossitis and skin rashes can occur. Pseudomembranous colitis has been reported rarely. Isolated cases of severe skin sensitivity reactions such as erythema multiforme bullosa (Stevens-Johnson syndrome) and toxic epidermal necrolysis (Lyell syndrome) have occurred.

As Septrin contains a sulphonamide, the possibility of blood dyscrasias like those associated with sulphonamides should be borne in mind. The changes reported with Septrin mainly consist of thrombocytopenia, purpura, leucopenia, neutropenia and very rarely agranulocytosis. They have usually proved to be reversible on withdrawal of the drug. Elderly patients are more susceptible to these blood changes. Septrin may induce haemolysis in certain susceptible glucose-6-phosphate dehydrogenase deficient patients.

There have been a few reports of subjective experiences such as headache, depression, dizziness and hallucinations but their relationship to therapy remains unproven.

During long-term therapy, isolated cases of megaloblastic changes in the bone marrow have been reported: those are reversible by folic acid therapy.

Use in pregnancy and lactation: The safety of Septrin in human pregnancy has not been established. Animal studies have shown teratogenic effects typical of a folate antagonist in rats but not rabbits at high doses; these were prevented by administration of dietary folates. Sulphonamide-containing products should not be administered in late pregnancy because of the risk of kernicterus.

Both sulphamethoxazole and trimethoprim may be found in breast milk, but this does not contra-indicate the use of Septrin in lactating mothers.

Toxicity and treatment of overdosage: Not applicable.

Pharmaceutical precautions Do not use if the injection solution is cloudy or if precipitation has occurred. Store below 25°C. Do not freeze. Protect from light.

Legal category POM.

Package quantities Box of 10 ampoules.

Further information In the treatment of tonsillopharyngitis to Group A beta-haemolytic streptococci, eradication of these organisms from the oropharynx is less rapid than with some other antibiotics.

Trimethoprim may cause an apparent rise in serum creatinine levels due to (a) competition for the tubular secretory mechanisms; (b) chemical interference with the visual auto-analyser method of estimating creatinine.

Co-trimoxazole may cause a fall in peripheral thyroid hormone levels but the clinical significance requires confirmation.

Septrin is available also as: Tablets, Dispersible Tablets,

Forte Tablets, Adult Suspension, Paediatric Suspension Paediatric Tablets and Septrin for Infusion.

Product licence number 0003/0124.

SYRAPRIM* TABLETS

Presentation White scored tablets coded 'Y3C' containing 300 mg Trimethoprim BP. White scored tablets coded Q9A containing 100 mg Trimethoprim BP.

Uses Antibacterial agent indicated for the treatment of infections due to trimethoprim-sensitive organisms, particularly those affecting the urinary and respiratory tracts. Also for the long-term prophylaxis of recurrent, or suppression of chronic, urinary tract infections caused by sensitive organisms.

Syraprim is active *in vitro* against a wide range of Gram-negative and Gram-positive organisms. It is not active against *Pseudomonas* spp., *Mycobacterium tuberculosis*, *Mycoplasma*, *Clostridia*, *Treponema pallidum* and anaerobes. It is relatively inactive against *Brucella* and *Neisseria*.

Dosage and administration *Urinary Tract Infections:*
Treatment:

Adults: 300 mg once daily.

Children over 12 years: as for adults.

6-12 years: 150 mg once daily.

Under 6 years: formulation inapplicable.

Prophylaxis:

Adults: 100 mg once daily.

Children over 12 years: as for adults.

6-12 years: 50 mg once daily.

Under 6 years: formulation inapplicable.

To ensure maximal urinary concentrations it may be advantageous to take the dose at bedtime.

Respiratory Infections:

Adults: 200 mg twice daily.

Children over 12 years: as for adults.

6-12 years: 100 mg twice daily.

6 months-6 years: 50 mg twice daily.

In acute infections, Syraprim should be given for at least five days or until the patient has been symptom-free for two days. Long-term administration may be continued for 3 to 12 months or more as appropriate.

Dosage recommendations in renal impairment: When creatinine clearance is below 15-20 ml/minute, trimethoprim levels should be monitored after approximately 3 days' treatment to provide guidance on the appropriate dosage reduction. When the clearance is below 10 ml/minute Syraprim should not be administered unless plasma concentrations can be estimated regularly and haemodialysis facilities are available.

Contra-indications, warnings, etc

Contra-indications: Syraprim should not be given to patients with a history of hypersensitivity to trimethoprim.

Contra-indicated in patients with severe impairment of renal function where repeated estimations of the plasma concentration, or haemodialysis, cannot be carried out.

Precautions: Care should be taken when giving the drug to patients with blood dyscrasias.

Caution should be exercised in the administration of Syraprim to patients with actual or potential folate deficiency and administration of a folate supplement should be considered.

Care should be taken if Syraprim and warfarin or phenytoin are co-administered as occasional potentiation of the effects of these agents may occur.

Patients receiving pyrimethamine in doses in excess of 25 mg weekly for malarial prophylaxis and who are given Syraprim should have their blood pictures monitored because of the possibility of megaloblastic anaemia developing.

During prolonged administration regular blood counts are advised. It is suggested that blood counts be performed at approximately monthly intervals.

Side- and adverse effects: Minor gastro-intestinal disturbances including nausea and vomiting, sore mouth/tongue, pruritus and skin rashes may occasionally occur. Although an effect on folate metabolism is possible, interference with haematopoiesis rarely occurs at the recommended dose. If any such change is seen, folic acid should reverse the effect. Elderly patients may be more susceptible and a lower dosage may be advisable.

Use in pregnancy and lactation: The safety of trimethoprim in human pregnancy has not been established. Animal studies have shown, at high doses, teratogenic effects typical of a folate antagonist in rats but not rabbits; these were prevented by administration of dietary folates. The benefit of using Syraprim in pregnancy should be weighed against the possible hazard.

Despite its excretion in breast milk the administration of Syraprim to a lactating woman represents a negligible risk to the suckling infant.

Toxicity and treatment of overdosage: Nausea, vomiting, abdominal pain, dizziness and confusion are likely symptoms of overdosage. Gastric lavage may be useful although absorption of trimethoprim from the gastro-intestinal tract is normally complete in approximately 2 hours. This may not be the case in gross overdosage. There is no specific antidote but calcium folinate 3–6 mg given for five to seven days should counteract any effect on the bone marrow. Acidification of the urine will increase the elimination of trimethoprim. General supportive measures are recommended.

Pharmaceutical precautions Store below 25°C and protect from light.

Legal category POM.

Package quantities

Bottle of 100 × 300 mg tablets.

Bottles of 28 and 100 × 100 mg tablets.

Further information Absorption by the oral route is rapid; significant plasma levels are obtained within half an hour; peak levels may be reached as early as one hour.

Excretion is predominantly in the urine in the form of unchanged drug. Urinary concentrations are generally well above the MIC of common pathogens for more than 24 hours after the last dose.

Trimethoprim may cause an apparent rise in serum creatinine levels due to (a) competition for the tubular secretory mechanisms; (b) chemical interference with the visual auto-analyser method of estimating creatinine.

Product licence numbers

300 mg tablets 0003/0148

100 mg tablets 0003/0147

SYRAPRIM® INJECTION

Presentation Syraprim Injection is a sterile aqueous solution of trimethoprim lactate equivalent to 20 mg trimethoprim base in 1 ml of water. Each ampoule contains 5 ml.

Uses Antibacterial agent indicated for the treatment of infections due to sensitive organisms, in particular for Gram-negative infections. Trimethoprim is effective *in vitro* against a wide range of Gram-negative and Gram-positive organisms. It is not active against *Pseudomonas* spp., *Mycobacterium tuberculosis*, *Mycoplasma*, *Clostridia*, *Treponema pallidum*, and anaerobes. It is relatively inactive against *Brucella* and *Neisseria*.

Dosage and administration *Dosage: Adults and children over 12 years:* 150–250 mg every 12 hours. *Children under 12 years:* The total daily dose should approximate to 6–9 mg/kg of body weight divided into two or three equal doses and administered either 12-hourly or 8-hourly.

The severely ill patient may require initially higher, or more frequent, doses as may a person considerably in excess of the average weight for his/her height. Total daily doses up to 20 mg/kg of body weight in divided doses have been well tolerated.

Dosage recommendations in renal impairment: When creatinine clearance is below 15–20 ml/minute, trimethoprim levels should be monitored after approximately 3 days' treatment to provide guidance on the appropriate dosage reduction. When the clearance is below 10 ml/minute Syraprim should not be administered unless plasma concentrations can be estimated regularly and haemodialysis facilities are available.

Administration: Syraprim Injection should be administered slowly as a bolus:

1. By direct intravenous injection, or
2. via the tubing (close to the vein) of an established intravenous infusion.

If it is necessary to add Syraprim Injection to the infusion fluid it is compatible with the following:

Dextrose Injection BP 5% w/v.

Laevulose Injection BP 5% w/v.

Sodium Lactate Injection BP.

Contra-indications, warnings, etc

Contra-indications: Syraprim should not be given to patients with a history of hypersensitivity to trimethoprim.

Contra-indicated in patients with severe impairment of renal function where repeated estimations of the plasma concentration, or haemodialysis cannot be carried out.

Precautions: Care should be taken when giving the drug to patients with blood dyscrasias.

Caution should be exercised in the administration of Syraprim to patients with actual or potential folate deficiency, and administration of a folate supplement should be considered.

Care should be taken if Syraprim and warfarin or phenytoin are co-administered as occasional potentiation of the effects of these agents may occur.

Patients receiving pyrimethamine in doses in excess of 25 mg weekly for malarial prophylaxis and who are given Syraprim should have their blood pictures monitored because of the possibility of megaloblastic anaemia developing.

Side- and adverse effects: Minor gastro-intestinal disturbances including nausea and vomiting, sore

mouth/tongue, pruritus and skin rashes may occasionally occur. An effect on folate metabolism is possible but rarely occurs. Interference with haematopoiesis may occur particularly if the daily dose exceeds 500 mg in adults. Folinic acid should reverse any such effect. Elderly patients may be more susceptible and a lower dosage may be advisable.

Nausea due to too rapid injection may occur and if so the time over which the injection is given should be prolonged.

Use in pregnancy and lactation: The safety of trimethoprim in human pregnancy has not been established. Animal studies have shown, at high doses, teratogenic effects typical of a folate antagonist in rats but not rabbits; these were prevented by administration of dietary folates. The benefit of using Syraprim in pregnancy should be weighed against its possible hazard.

Despite its excretion in breast milk the administration of Syraprim to a lactating woman represents a negligible risk to the suckling infant.

Toxicity and treatment of overdosage: Not applicable.

Pharmaceutical precautions Store below 25°C and protect from light.

Syraprim Injection should not be added to any chloride-containing infusion fluid.

Syraprim Injection is incompatible with solutions of sulphonamides and the two should not be mixed.

Legal category POM.

Package quantities Box of 10 ampoules.

Further information Excretion is predominantly in the urine in the form of unchanged drug.

Trimethoprim may cause an apparent rise in serum creatinine levels due to (a) competition for the renal tubular secretory mechanism, (b) chemical interference with the usual auto-analyser method of estimating creatinine.

Syraprim Injection may be given in conjunction with, but separately from, parenteral aminoglycosides, metronidazole, or sulphonamides depending on the organism responsible for the infection.

Product licence number 0003/0149.

TETANUS VACCINE BP (IN SIMPLE SOLUTION) WELLCOME* (Tet/Vac/FT)

Presentation Tetanus vaccine is prepared by formalin detoxification of *Clostridium tetani* exotoxin. Thiomersal BP is added as a preservative to a concentration of 0.01%. Each 0.5 ml dose contains 14Lf toxoid.

The antigenic content and formulation of this vaccine has not been changed, although the labelled content has been altered to conform with the flocculation equivalence of the new British reference antitoxin preparation.

Uses For active immunisation against tetanus.

Administration of the antigenically more potent adsorbed vaccine is usually preferred for all injections. Tetanus vaccine in simple solution is insufficiently antigenic to be used as the first immunising dose but may be used instead of adsorbed tetanus vaccine if necessary for the second, third or later reinforcing injections. Tetanus vaccine in simple solution is now often reserved for administration to patients who have had some reaction to a previous dose of adsorbed vaccine and who are not thought to be adequately protected against infection.

Dosage and administration The dose of tetanus vaccine in simple solution is 0.5 ml given by deep subcutaneous or intramuscular injection. When Tetanus vaccine in simple solution is used for second or third doses in an immunising course, intervals of 6 to 12 weeks and 6 to 12 months respectively are recommended between the first and second and the second and third doses.

The United Kingdom Department of Health and Social Security recommend the administration of reinforcing doses after five years and after a further 5 to 15 years with the administration of additional doses in the event of injuries which may give rise to tetanus. Tetanus vaccine should not be given to any patient who has received a booster dose in the preceding year.

A single dose of vaccine given several years after the completion of a primary course will rapidly stimulate the production of tetanus antitoxin in the circulation.

In subjects who have suffered a reaction to a previous dose of adsorbed vaccine it may be preferred to administer 0.1 ml of tetanus vaccine in simple solution intradermally.

Oral Poliomyelitis Vaccine BP may be given at the same time as tetanus vaccine.

Shake well before each dose is withdrawn. Record the title, dose and lot numbers of all vaccines and the date administered. Report any untoward reactions.

Contra-indications, warnings, etc

Contra-indications: The vaccine should not be administered to a subject who has experienced a serious reaction (e.g. anaphylaxis) to a previous dose of this vaccine or who is known to be hypersensitive to any component thereof. It is advisable to avoid vaccination during an acute infection. Tetanus vaccine in simple solution should not be given simultaneously with human tetanus immunoglobulin or tetanus antitoxin which may markedly depress its antigenicity.

Precautions: Although anaphylaxis is rare, facilities for its management should always be available during vaccination.

Side- and adverse effects: Local reactions consisting of swelling, redness and pain may develop at the injection site and persist for several days. Delays of up to 10 days before symptoms develop are reported. Local reactions are rare in children and the incidence increases with age and according to the number of previously administered doses. General reactions are uncommon but may include headache, lethargy, malaise, myalgia and pyrexia. Acute anaphylactic reactions, urticaria, angioneurotic oedema, serum sickness and peripheral neuropathy occasionally occur.

Use in pregnancy and lactation: In developing countries tetanus vaccines are widely administered during pregnancy to prevent neonatal tetanus without significant apparent adverse effects on pregnancy or foetal development.

Toxicity and treatment of overdosage: Not applicable.

Pharmaceutical precautions Store at 2–8°C. Protect from light. *Do not freeze.* When multidose containers are employed it is good practice to discard any partly used vaccine vials at the end of the vaccinating session.

Legal category POM.

Package quantities Pack of 5 × 0.5 ml ampoules. Vial of 5 ml.

Further information Persons of all ages are suscep-

able to tetanus unless they have been immunised with tetanus vaccine. Rarely, if ever, does natural immunity develop even in persons who have recovered from severe tetanus. Since most tetanus cases follow trivial wounds all persons should be actively immunised against the disease.

Product licence number 0003/5190.

ADSORBED TETANUS VACCINE BP WELLCOME* (Tet/Vac/Ads)

Presentation Adsorbed tetanus vaccine is a suspension of highly purified toxoid prepared by formalin detoxification of *Clostridium tetani* exotoxin. The toxoid is adsorbed onto aluminium hydroxide. Thiomersal BP is added as a preservative to a concentration of 0.01%. Each 0.5 ml dose has an immunising potency of not less than 40 International Units (IU).

The immunising potency of this vaccine is now expressed in International Units in accordance with the requirements of the European and British Pharmacopoeias. These units measure the immunising activity of the vaccine whereas the previously used Lf units expressed the quantity of toxoid present. There is no simple numerical relationship between IU and Lf. No change has been made to the potency although it is now expressed in IU.

Uses For active immunisation against tetanus.

Dosage and administration Primary immunisation consists of three deep subcutaneous or intramuscular doses of adsorbed vaccine each of 0.5 ml administered at intervals of 6 to 12 weeks and 6 to 12 months respectively. Adsorbed tetanus vaccine may be used for the routine anti-tetanus immunisation of persons of all ages although it is usual to employ plain or adsorbed combined diphtheria/tetanus/pertussis vaccine (DTPe/Vac or DTPe/Vac/Ads) or adsorbed diphtheria and tetanus vaccine (DT/Vac/Ads) for immunisation of infants.

The United Kingdom Department of Health and Social Security recommend the administration of reinforcing doses after five years and after a further 5 to 15 years with the administration of additional doses in the event of injuries which may give rise to tetanus. Tetanus vaccine should not be given to any patient who has received a booster dose in the preceding year.

A single dose of vaccine given several years after the completion of a primary course will rapidly stimulate the production of tetanus antitoxin in the circulation.

Adsorbed tetanus vaccine may be administered simultaneously with human tetanus immunoglobulin or tetanus antitoxin but must be given at separate sites. The antibody response of subjects to subsequent doses of vaccine is not significantly impaired by this procedure.

Oral Poliomyelitis Vaccine BP may be given at the same time as Tetanus Vaccine.

Shake well before each dose is withdrawn. Record the title, dose and lot numbers of all vaccines and the date administered. Report any untoward reactions.

Contra-indications, warnings, etc

Contra-indications: Adsorbed tetanus vaccine should not be administered intradermally.

The vaccine should not be administered to a subject who has experienced a serious reaction (e.g. anaphylaxis) to a previous dose of this vaccine or who is known to be hypersensitive to any component thereof. It is

advisable to avoid vaccination during an acute infection.

Precautions: Although anaphylaxis is rare, facilities for its management should always be available during vaccination.

Side- and adverse effects: Local reactions consisting of swelling, redness and pain may develop at the injection site and persist for several days. Delays of up to 10 days before symptoms develop are reported. Local reactions are rare in children and the incidence increases with age and according to the number of previously administered doses. General reactions are uncommon but may include headache, lethargy, malaise, myalgia and pyrexia. Acute anaphylactic reactions, urticaria, angioneurotic oedema, serum sickness and peripheral neuropathy occasionally occur.

Persistent nodules at the site of injection may occasionally follow administration of adsorbed vaccines especially if the inoculation is into the superficial layers of subcutaneous tissue.

Use in pregnancy and lactation: In developing countries tetanus vaccines are widely administered during pregnancy to prevent neonatal tetanus without significant apparent adverse effects on pregnancy or foetal development.

Toxicity and treatment of overdosage: Not applicable.

Pharmaceutical precautions Store at 2–8°C. Protect from light. *Do not freeze.* When multidose containers are employed it is good practice to discard any partly used vaccine vials at the end of the vaccinating session.

Legal category POM.

Package quantities Pack of 5 × 0.5 ml ampoules. Vial of 5 ml.

Further information Persons of all ages are susceptible to tetanus unless they have been immunised with tetanus vaccine. Rarely, if ever, is natural immunity developed even in persons who have recovered from severe tetanus. Since most tetanus cases follow trivial wounds all persons should be actively immunised against the disease.

Product licence number 0003/5191.

TINEAFAX* OINTMENT

Presentation Zinc Undecenoate BP 80 mg and zinc naphthenate solution 80 mg (10% zinc) in a non-greasy base. Cream in colour.

Uses To eradicate 'athlete's foot' and other ringworm infections of the skin.

Dosage and administration *Adults:* The affected parts must first be washed with soap and water and thoroughly dried. Dead or loose skin should be removed. The ointment is then rubbed into and around the lesions. This treatment is, at first, repeated night and morning then, as healing progresses, one treatment daily is sufficient. It is important to keep the feet free from moisture; a daily change of stockings is advisable.

Children: As for adults.

Contra-indications, warnings, etc

Contra-indications: No special comment.

Treatment of overdosage: Not applicable.

Pharmaceutical precautions Store below 25°C.

Legal category P.

Package quantities Tube of 25 g.

Further information Nil.

Product licence number 0003/5216.

TINEAFAX* POWDER

Presentation Zinc Undecenoate BP 100 mg per gram of white powder.

Uses Prophylactic against 'athlete's foot'.

Dosage and administration *Adults:* To avoid either initial infection or reinfection with the fungi responsible for 'athlete's foot', hosiery and shoes should be dusted inside with Tineafax Powder. The feet should be kept dry, and walking barefooted in public dressing rooms should be avoided.

Children: As for adults.

Contra-indications, warnings, etc

Contra-indications: No special comment.

Pharmaceutical precautions Store below 25°C.

Legal category GSL.

Package quantities Puffer pack of 50 g.

Further information Nil.

Product licence number 0003/5215.

TRIVAX* DIPHTHERIA, TETANUS AND PERTUSSIS VACCINE BP (DTPer/Vac)

Presentation Trivax is a sterile preparation consisting of a mixture of diphtheria and tetanus toxoids and killed whole *Bordetella pertussis*.

Each 0.5 ml of vaccine contains 25 Lf of purified diphtheria toxoid, 3.5 Lf of purified tetanus toxoid and not more than 20,000 million chemically killed *Bordetella pertussis* organisms with a potency of not less than 4 i.u., in an isotonic buffer solution. Organisms bearing all three pertussis agglutinogens are included. Vaccine of this composition has been shown to provide adequate immunising potency against each of the three diseases. Thiomersal is added as a preservative to a final concentration of 0.01%.

The antigenic content and formulation of this vaccine has not been changed, although the labelled content of the tetanus component has been altered to conform with the flocculation equivalence of the new British reference antitoxin preparation.

Uses For active immunisation against diphtheria, tetanus and whooping cough in infants and pre-school children. It is not recommended that pertussis-containing vaccines be used in older children except in areas where whooping cough is a serious problem.

Dosage and administration *Dosage: Adults:* Not recommended.

Children up to 5 years: Each dose is 0.5 ml, given by deep subcutaneous or intramuscular injection. The primary course consists of 3 doses of vaccine at intervals of not less than four weeks.

Administration: Shake well before withdrawing a dose. Record the title, dose and lot numbers of all vaccines

and the date administered. Report any untoward reactions.

Since whooping cough can often be a serious disease in the early months of life the primary course should preferably be started between the third and sixth month of life. It is believed that immune responses are better if the interval between the first and second dose is extended to six to eight weeks and the interval between the second and third dose is four to six months. It is not considered necessary to repeat the full course of immunisation if these intervals are exceeded.

Reinforcing doses: Where primary immunisation was completed during the first six to eight months of life one reinforcing dose of 0.5 ml should be given about 12 months later in order to boost immunity. Children over the age of five years do not normally require further immunisation with pertussis vaccine since whooping cough is rarely a problem in older children. However, reinforcement of immunity against diphtheria and tetanus is necessary. This can be achieved by giving 1 dose (0.5 ml) of Diphtheria and Tetanus Vaccine (DT/Vac/FT or DT/Vac/Ads) to five-year-old children and 1 dose (0.5 ml) of Tetanus Vaccine (Tet/Vac/Ads) at 15/19 years of age or on leaving school.

Contra-indications, warnings, etc

Contra-indications: The administration of pertussis-containing vaccine is contra-indicated in children with a personal or family history of epilepsy or other familial or hereditary diseases of the central nervous system. Administration of pertussis vaccine is also contra-indicated in children with a history of severe allergy, seizures, convulsions, cerebral irritation in the neonatal period, developmental neurological defect or other disorder of the central nervous system. Children with acute infection or illness, particularly those with respiratory symptoms should not be immunised until they are fully recovered. Any child exhibiting a severe local or significant general reaction to a previous dose of a pertussis-containing vaccine should not be given a further dose. However, protection against diphtheria and tetanus is advisable and can be accomplished by giving Adsorbed Diphtheria and Tetanus Vaccine.

Precautions: Since combined diphtheria, tetanus and pertussis vaccines are widely used in a population in which sudden illnesses of undefined origin are not uncommon, intercurrent illness bearing a temporal but not a causal relationship to vaccination may be expected.

Side- and adverse effects: Local reactions, particularly erythema at the site of injection, are commonly seen during the 24 hours following vaccination. They normally subside without treatment. A nodule may be found at the site of injection; this occurs less frequently and is less persistent following the administration of plain vaccine.

A transient rise in temperature, restlessness, irritability, crying or loss of appetite may sometimes occur a few hours after vaccination, but does not generally call for treatment. The incidence of these systemic reactions is lower following the administration of adsorbed vaccine. Allergic manifestations including pallor, dyspnoea and collapse have been observed rarely. Convulsions, infantile spasms and encephalopathy have been reported as rare complications after pertussis vaccination.

Convulsions may be precipitated by a febrile response to the pertussis component. In an individual case it may be difficult to distinguish between spontaneously occurring convulsions and those associated with vaccination.

Abnormal crying and persistent screaming have also

seen described as reactions which may be encountered after vaccination.

An increased incidence of reactions may occur due to failure to shake the container and re-suspend the vaccine before withdrawing a dose, to inadvertent intravenous administration or to an over-rapid injection.

Use in pregnancy and lactation: Since simultaneous vaccination against diphtheria and tetanus in adults is uncommon there is no accurate information on the safety of this vaccine in pregnancy.

Toxicity and treatment of overdosage: Not applicable.

Pharmaceutical precautions Store between 2°C and 8°C, protected from light. *Do not freeze.*

When multi-dose containers are employed, it is a good practice to discard any partly used vaccine vials at the end of the vaccinating session.

Legal category POM.

Package quantities Pack of 5 × 0.5 ml ampoules. Vial of 5 ml.

Further information Oral Poliomyelitis Vaccine BP may be given at the same time as Trivax.

Product licence number 0003/5192.

TRIVAX-AD* ADSORBED DIPHTHERIA, TETANUS AND PERTUSSIS VACCINE BP (DTPer/Vac/Ads)

Presentation Trivax-AD is a sterile preparation consisting of a mixture of diphtheria and tetanus toxoids and killed whole *Bordetella pertussis*.

Each 0.5 ml of vaccine has an immunizing potency of not less than 30 International units (IU) purified diphtheria toxoid and not less than 60 IU (mouse assay) purified tetanus toxoid, with not more than 20,000 million chemically killed *Bordetella pertussis* organisms with a potency of not less than 4 IU adsorbed onto aluminium hydroxide in an isotonic buffer solution. The aluminium content does not exceed 1.25 mg per dose. Organisms bearing all three pertussis agglutinogens are included. Vaccine of this composition has been shown to provide adequate immunizing potency against each of the three diseases. Thiomersal is added as a preservative to a final concentration of 0.01%.

The potency of this vaccine is now expressed in International Units in accordance with the requirements of the European and British Pharmacopoeias. These units measure the immunizing activity of the vaccine, whereas the previously used Lf units expressed the quantity of toxoid present. There is no simple numerical relationship between IU and Lf. No change has been made to the potency although it is now expressed in IU.

Uses For active immunisation against diphtheria, tetanus and whooping cough in infants and pre-school children. It is not recommended that pertussis-containing vaccines be used in older children except in areas where whooping cough is a serious problem.

Dosage and administration *Dosage: Adults:* Not recommended.

Children up to 5 years: Each dose is 0.5 ml, given by deep subcutaneous or intramuscular injection. The primary course consists of 3 doses of vaccine at intervals of not less than four weeks.

Administration: Shake well before withdrawing a dose.

Record the title, dose and lot numbers of all vaccines and the date administered. Report any untoward reactions.

Since whooping cough can often be a serious disease in the early months of life the primary course should preferably be started between the third and sixth month of life. It is believed that immune responses are better if the interval between the first and second dose is extended to six to eight weeks and the interval between the second and third dose is four to six months. It is not considered necessary to repeat the full course of immunisation if these intervals are exceeded.

Reinforcing doses: Where primary immunisation was completed during the first six to eight months of life one reinforcing dose of 0.5 ml should be given about 12 months later in order to boost immunity. Children over the age of five years do not normally require further immunisation with pertussis vaccine since whooping cough is rarely a problem in older children. However, reinforcement of immunity against diphtheria and tetanus is necessary. This can be achieved by giving 1 dose (0.5 ml) of Diphtheria and Tetanus Vaccine (DT/Vac/FT or DT/Vac/Ads) to five-year-old children and 1 dose (0.5 ml) of Tetanus Vaccine (Tet/Vac/Ads) at 15–19 years of age or on leaving school.

Contra-indications, warnings, etc

Contra-indications: The administration of pertussis-containing vaccine is contra-indicated in children with a personal or family history of epilepsy or other familial or hereditary diseases of the central nervous system. Administration of pertussis vaccine is also contra-indicated in children with a history of severe allergy, seizures, convulsions, cerebral irritation in the neonatal period, developmental neurological defect or other disorder of the central nervous system. Children with acute infection or illness, particularly those with respiratory symptoms should not be immunised until they are fully recovered. Any child exhibiting a severe local or significant general reaction to a previous dose of a pertussis-containing vaccine should not be given a further dose. However, protection against diphtheria and tetanus is advisable and can be accomplished by giving Adsorbed Diphtheria and Tetanus Vaccine.

Precautions: Since combined diphtheria, tetanus and pertussis vaccines are widely used in a population in which sudden illnesses of undefined origin are not uncommon, intercurrent illness bearing a temporal but not a causal relationship to vaccination may be expected.

Side- and adverse effects: Local reactions, particularly erythema at the site of injection, are commonly seen during the 24 hours following vaccination. They normally subside without treatment. A nodule may be found at the site of injection; this occurs less frequently and is less persistent following the administration of plain vaccine.

A transient rise in temperature, restlessness, irritability, crying or loss of appetite may sometimes occur a few hours after vaccination, but does not generally call for treatment. The incidence of these systemic reactions is lower following the administration of adsorbed vaccine. Allergic manifestations including pallor, dyspnoea and collapse have been observed rarely. Convulsions, infantile spasms and encephalopathy have been reported as rare complications after pertussis vaccination.

Convulsions may be precipitated by a febrile response to the pertussis component. In an individual case it may be difficult to distinguish between spontaneously occurring convulsions and those associated with vaccination.

Abnormal crying and persistent screaming have also been described as reactions which may be encountered after vaccination.

An increased incidence of reactions may occur due to failure to shake the container and re-suspend the vaccine before withdrawing a dose, to inadvertent intravenous administration, or to an over-rapid injection.

Use in pregnancy and lactation: Since simultaneous vaccination against diphtheria and tetanus in adults is uncommon there is no accurate information on the safety of this vaccine in pregnancy.

Toxicity and treatment of overdosage: Not applicable.

Pharmaceutical precautions Store between 2°C and 8°C, protected from light. *Do not freeze.*

When multi-dose containers are employed it is a good practice to discard any partly used vaccine vials at the end of the vaccinating session.

Legal category POM.

Package quantities Pack of 5 × 0.5 ml ampoules. Vial of 5 ml.

Further information Oral Poliomyelitis Vaccine BP may be given at the same time as Trivax-AD.

Product licence number 0003/5193.

TYPHOID VACCINE BP (MONOVALENT) WELLCOME* (Typhoid/Vac)

Presentation Typhoid (Monovalent) Vaccine contains heat-killed, phenol-preserved, *Salmonella typhi* organisms at a concentration of not less than 1,000 million organisms per ml.

Uses For active immunisation against typhoid fever.

Typhoid vaccine protects 70–90% of recipients against typhoid.

Dosage and administration

<i>Initial dose to be administered by deep subcutaneous or intramuscular injection</i>	<i>Time interval between administration of initial dose and second dose</i>	<i>Second dose</i>
Children 1–10 years 0.25 ml	4–6 weeks	0.25 ml by i.m. or s.c. injection or 0.1 ml by intradermal injection
Children over 10 years and adults 0.5 ml	4–6 weeks	0.5 ml by i.m. or s.c. injection or 0.1 ml by intradermal injection

Wellcome Typhoid Vaccine (Monovalent) may be administered subcutaneously, intramuscularly or intradermally. Subcutaneous or intramuscular injection should be used for the first dose but intradermal injection reduces systemic reactions and may therefore be preferred for the second dose, particularly for persons who have experienced reactions in the past.

Shake well before withdrawing dose. The interval between the first and second doses should be four to six weeks.

Although two doses of vaccine are recommended for primary immunisation, the results of field trials indicate

that one dose of typhoid vaccine is almost as effective for a short period, as two doses.

Reinforcing doses: Under conditions of continued or repeated exposure to infection a reinforcing dose of vaccine should be given at least every three years. When more than three years have elapsed since the last dose, a single dose is sufficient to boost immunity.

Contra-indications, warnings, etc

Contra-indications: The vaccine should not be administered to a subject who has experienced a serious reaction (e.g. anaphylaxis) to a previous dose of this vaccine or who is known to be hypersensitive to any component thereof. It is advisable to avoid vaccination during an acute infection.

Precautions: Typhoid vaccine produces in some people constitutional or local reactions. These are often more marked in adults over the age of 35 years, especially where there is a history of previous vaccination against typhoid.

It is prudent to avoid administering vaccine to subjects with acute infections or chronic illness.

Vaccination of children under 12 months of age is not advised because of the risk of adverse reactions, the relatively low incidence of typhoid in this age group and the relatively mild course of the disease in infants.

Although anaphylaxis is rare, facilities for its management should always be available during vaccination.

Side- and adverse effects: Local redness, swelling, pain and tenderness may appear in two or three hours.

Systemic reactions, such as malaise, nausea, headache, or pyrexia may occur, but usually disappear in 36 hours, when they are severe the patient is best kept in bed. The incidence of systemic reactions is considerably reduced by giving the vaccine intradermally, but local reactions may still occur.

Neurological complications including polyneuritis, neuritis, myelitis or various manifestations of cerebral and meningeal disease have been described following the administration of typhoid-containing vaccines.

Use in pregnancy and lactation: While no specific effects on the foetus have followed the administration of Typhoid Vaccine, it is not considered advisable to administer vaccines which may cause pyrexia during pregnancy.

Toxicity and treatment of overdosage: Not applicable.

Pharmaceutical precautions Store at 2–8°C. Protect from light. *Do not freeze.* When multi-dose containers are employed it is good practice to discard any partly used vaccine vials at the end of the vaccinating session.

Legal category POM.

Package quantities Vial of 1.5 ml.

Further information Nil.

Product licence number 0003/5195.

ZOVIRAX* I.V. for intravenous infusion ▼

Presentation Each vial contains the equivalent of 250 mg sterile acyclovir as the freeze-dried sodium salt. When reconstituted as directed, Zovirax I.V. has a pH of about 11.

Uses Zovirax I.V. is indicated in the treatment of infections caused by *Herpes simplex* virus in immuno-compromised patients.

Dosage and administration Patients with normal renal function should be treated with doses of 5 mg/kg every 8 hours. Each dose should be administered by slow intravenous infusion over one hour.

In patients with renal impairment, Zovirax I.V. should be administered with caution because the drug is excreted by the kidneys.

As transient rises in serum creatinine or urea have been reported during use of Zovirax, monitoring of renal function is recommended, particularly in patients with renal transplants where, should this occur, it could be confused with graft rejection.

The following modifications in dosage are recommended:

creatinine clearance	Dosage
5–50 ml/min	5 mg/kg every 12 hours
0–25 ml/min	5 mg/kg every 24 hours
(Anuric) – 10 ml/min	2.5 mg/kg every 24 hours or after dialysis

The dose in children should be calculated as for adults on the basis of bodyweight.

For acute infections with *Herpes simplex virus*, 5 days' treatment should be adequate. However, this should be judged in the light of the patient's illness, and the response to treatment.

Method of administration: In all cases the total dose should be administered slowly over a period of one hour. Zovirax I.V. must be given by the intravenous route only and must be reconstituted and used as directed.

Each vial (containing the equivalent of 250 mg cyclovir) should be reconstituted by the addition of 10 ml of either Water for Injections BP or Sodium Chloride Intravenous Infusion BP (0.9% w/v). The required dose/volume should be calculated on the basis of 25 mg per ml of reconstituted solution.

Zovirax I.V., after reconstitution, may be injected directly into a vein over 1 hour by a controlled rate infusion pump, or be further diluted for administration by infusion. For intravenous injection by controlled rate infusion pump, a solution containing 25 mg acyclovir/ml is used. For intravenous infusion, each vial of Zovirax I.V. should be reconstituted and then, wholly or in part according to dosage required, added to and mixed with at least 50 ml of infusion solution. The contents of two vials (500 mg of acyclovir) may therefore be added to 100 ml of infusion solution. Where the dose required or infusion is greater than 500 mg a second volume of infusion solution must be used.

Zovirax I.V., when diluted in accordance with the above schedules to give a concentration not greater than 1.5% w/v of acyclovir, is known to be compatible with the following infusion fluids and stable for up to 12 hours at room temperature (15–25°C).

Sodium Chloride Intravenous Infusion BP (0.45% and 0.9% w/v).

Sodium Chloride (0.18% w/v) and Dextrose (4% w/v) Intravenous Infusion BP.

Sodium Chloride (0.45% w/v) and Dextrose (2.5% w/v).

Intravenous Infusion BP.

Compound Sodium Lactate Intravenous Infusion BP.

(Hartmann's solution).

After addition of Zovirax I.V. to an infusion solution the mixture should be shaken to ensure thorough mixing.

Reconstitution or dilution should be carried out immediately before use and, as no preservative is included, any unused solution should be discarded. Should visible turbidity or crystallisation appear in the solution before or during the infusion, the mixture should be discarded. The solution should not be refrigerated.

Pharmacology: Zovirax is an antiviral agent which is highly active *in vitro* against *Herpes simplex* types I and II, and *Varicella zoster* viruses. Toxicity to mammalian host cells is low.

Zovirax is phosphorylated to the active triphosphate after entry into a herpes-infected cell. The first step in this process requires the presence of the HSV-coded thymidine kinase. Acyclovir triphosphate acts as an inhibitor of, and substrate for, the herpes-specified DNA polymerase, preventing further viral DNA synthesis without affecting normal cellular processes.

After intravenous administration, Zovirax is principally excreted as unchanged drug through the kidneys. Both glomerular filtration and tubular secretion contribute to its elimination in the urine. The plasma half-life of acyclovir in subjects with normal renal function is about 3 hours. The estimated half-life in an anuric patient is approximately 24 hours. A metabolite 9-carboxymethoxymethylguanine has been identified in the urine of patients treated with Zovirax I.V.

Contra-indications, warnings, etc

Contra-indications: Zovirax I.V. is contra-indicated in patients known to be previously hypersensitive to acyclovir.

Precautions: Care should be observed when administering Zovirax to patients with abnormal renal function (see above), in order to avoid accumulation. The drug should not be given as a bolus intravenous injection but by slow infusion over one hour.

Reconstituted Zovirax I.V. has a pH of approximately 11.0 and should not be administered by mouth.

Side- and adverse effects: Rapid reversible increases in blood urea and creatinine have occurred in a few patients given Zovirax intravenously. This is believed to be related to peak plasma levels and the state of hydration of the patient.

Adequate hydration of the patient should be maintained.

Severe inflammation sometimes leading to ulceration has occurred when Zovirax I.V. has been accidentally infused into extravascular tissues. Mechanical infusion pumps pose a greater risk than infusion by gravity feed.

The following events have been reported whilst patients have been receiving Zovirax I.V.: increased liver related enzymes, decreases in haematological indices, neurological reactions, and rashes. There is no evidence to suggest that these events are directly related to Zovirax therapy.

Use in pregnancy and lactation: Studies in animals with systemically administered Zovirax have not demonstrated an effect on the foetus. However, as there has been no clinical experience of the effects of Zovirax intravenous injection on human pregnancy, or the foetus, caution should be exercised in prescribing Zovirax to pregnant women. No information is available on levels of Zovirax which may appear in breast milk after administration of Zovirax I.V.

Drug interactions: Zovirax is not known to interact with any other drug.

Toxicity and treatment of overdosage: Single doses of up to 80 mg/kg have been accidentally administered with no adverse consequences. Zovirax I.V. is dialysable.

Two-generation studies in mice did not reveal any effect on fertility.

Pharmaceutical precautions Store below 25°C. The injection contains no preservative. Reconstitution and dilution should therefore be carried out immediately before use and any unused solution should be discarded. The reconstituted or diluted solution should not be refrigerated.

Legal category POM.

Package quantities Pack of 5 vials.

Further information Nil.

Product licence number 0003/0159.

ZOVIRAX* OPHTHALMIC OINTMENT ▼

Presentation White to pale yellow sterile ointment containing 3 per cent w/w acyclovir in a white soft paraffin base.

Uses Treatment of herpes simplex keratitis. Acyclovir is an antiviral agent which is highly active *in vitro* against herpes simplex (HSV) types I and II.

Dosage and administration *Adults:* 1 cm ribbon of ointment should be placed inside the lower conjunctival sac five times a day at approximately four hourly intervals. Treatment should continue for at least 3 days after healing is complete.

Children: As for adults.

Pharmacology: Acyclovir is phosphorylated to the active compound acyclovir triphosphate after entry into a herpes infected cell. The first step in this process requires the presence of the HSV coded thymidine kinase. Acyclovir triphosphate acts as an inhibitor of, and substrate for, the herpes specified DNA polymerase, preventing further viral DNA synthesis without affecting normal cellular processes. Acyclovir is rapidly absorbed through the corneal epithelium and superficial ocular tissues. In animals, it achieves antiviral concentrations in aqueous humor. It has not been possible by existing methods to detect acyclovir in the blood after topical

application to the eye. However, trace quantities may be measured in the urine. These levels are not clinically significant.

Contra-indications, warnings, etc *Contra-indications:* Patients with a known hypersensitivity to acyclovir.

Side- and adverse effects: For ophthalmic use only. Transient mild stinging immediately following administration occurs in a small proportion of patients. Superficial punctate keratopathy has been reported but has not resulted in patients being withdrawn from therapy, nor healing has occurred without apparent sequelae.

The results of a wide range of mutagenicity tests *in vitro* and *in vivo* indicate that acyclovir does not pose a genetic risk to man.

Acyclovir is not known to interact with any other drugs.

Use in pregnancy and lactation: No teratogenicity, embryotoxicity or effects on fertility have been demonstrated following systemic administration of acyclovir in animal studies.

The results of tests in animals indicate that Zovirax ophthalmic ointment does not affect human fertility. Two-generation mouse studies have shown no effects on fertility have been demonstrated.

No information is available on levels of acyclovir which may appear in breast milk after administration of Zovirax ophthalmic ointment.

Toxicity and treatment of overdosage: No untoward effects would be expected if the entire contents of the tube containing 135 mg of acyclovir were ingested orally. Single oral doses of 600 mg and daily doses of 1,000 mg have been administered to human volunteers without adverse effects.

Pharmaceutical precautions When stored below 25°C Zovirax ophthalmic ointment can be expected to have a shelf life of 3 years. Discard one month after opening.

Legal category POM.

Package quantities 4.5 g tube.

Further information Nil.

Product licence number 0003/0150.

*Trade Mark

Winthrop Laboratories
Sterling-Winthrop House
Uxbridge-upon-Thames
Uxbridge KT6 4PH

WINTHROP

ACTAL*

Presentation 1. Flat, white tablets with bevelled edges. 12.7 mm in diameter, marked Actal on both faces, containing 360 mg alxetol sodium.

2. A white suspension with a slight odour and a sweet taste. Each 5 ml contains 360 mg alxetol sodium.

Uses Actal is an antacid. It is recommended for the relief of hyperacidity, dyspepsia and pain due to peptic ulcer.

Dosage and administration For oral administration only.

Adults: Tablets – 1 or 2 to be sucked. Suspension – one to two 5 ml spoonfuls. The dose may be repeated as required.

Contra-indications, warnings, etc There are no known contra-indications or adverse reactions and no cases of overdosage have been reported. If a large amount is taken it should be sufficient to empty the stomach by emesis.

Pharmaceutical precautions Store the tablets in a cool place.

Legal category Actal Tablets GSL
Actal Suspension P.

Package quantities Actal tablets are available in packs of 24, 48, 96 and 250.
Actal Suspension is supplied in white polyethylene bottles containing 300 ml.

Further information Each Actal tablet (or 5 ml of suspension) contains 14 mg sodium.

Product licence numbers

Actal Tablets 0071/5018

Actal Suspension 0071/0089

ALEVAIRE*

Presentation A clear, colourless solution which foams on shaking, containing tyloxapol 0.125% w/v. Alevaire has a slight characteristic odour.

Uses Alevaire is recommended for use as a mucolytic agent in the treatment of lung conditions accompanied by complicated by excessive or thickened bronchopulmonary secretions. It may also be used as a vehicle for aerosol medication. Alevaire containing one or more antibiotics may be used in a closed irrigation system for the treatment of pyogenic bone or joint infections.

Dosage and administration

As a mucolytic agent: In continuous therapy the dose of Alevaire delivered will depend on the nebuliser used and the oxygen/air flow rate. For example, using an oxygen/air atomiser from 144 to 360 ml is nebulised in 24-hour period with gas flows of 4–8 litres per minute.

In intermittent therapy, Alevaire is inhaled three or four times a day for periods of 20 minutes, resulting in the administration of from 6 ml to 20 ml of Alevaire in a 24-hour period. Infants and small children are best treated in an oxygen tent or incubator, the mist being led into the tent through one of the nursing apertures. Treatment should be maintained for one or two days or until improvement is apparent.

2. *As a vehicle for aerosol medication:* Because of its stability and carrying properties, Alevaire mist can be used to deliver certain medicaments to the lungs. The use of Alevaire enables the drugs to reach the fine subdivisions of the bronchioles and facilitates their distribution over a wide area.

3. *In pyogenic bone or joint infections:* A suitable irrigation solution may be prepared by mixing 200 ml Alevaire with 800 ml physiological saline in which one or more appropriate antibacterial agents are dissolved. This solution is run into the wound at the rate of 80 ml per hour (about 2 litres in 24 hours).

Contra-indications, warnings, etc There are no known contra-indications.

After prolonged therapy, slight inflammation of the eyelids may develop, but this clears rapidly when treatment is discontinued.

Pharmaceutical precautions Containers of Alevaire which have been opened are easily contaminated by mould or bacteria which grow readily in the solution. If only small amounts of Alevaire are required they should be removed from the original containers with aseptic precautions. Alternatively, any unused solution in containers should be discarded after 24 hours. Alevaire should not be used if it becomes cloudy or develops a sediment.

Any Alevaire Solution remaining in a nebuliser after use should be discarded and the nebuliser rinsed and cleaned. If nebulisers are left uncleaned the Alevaire evaporates leaving a gummy residue. Alevaire should not be allowed to come into contact with brass or copper because of possible damage to the metal surface.

As a general rule, the addition of supplementary drugs to bulk containers of Alevaire is not recommended, as it may prove wasteful and difficult to determine the amount of nebulised drug received by the patient. It is preferable to dissolve the medication in a small quantity of Alevaire for administration over a short period.

Legal category P.

Package quantities Alevaire is supplied in non-reclosable amber glass bottles containing 60 or 200 ml.

Further information Alevaire is best administered as a fine mist produced by a nebuliser activated by oxygen or a motor-driven air compressor capable of reducing particle size to 0.5–5 µm.

Product licence number 0071/5019.

BENORAL* TABLETS AND SUSPENSION

Presentation

1. Benoral Suspension is a white suspension, 10 ml of which contain 4 g benorylate.

2. Benoral Tablets are white, capsule-shaped tablets marked benoral on one side only.

Each tablet is 17.5 mm long and 8 mm wide and contains 750 mg benorylate.

3. Benoral Granules: P.F.P. laminate sachets filled with a white, free-flowing powder with a sweet taste, which disperses readily in water. The contents of each sachet are equivalent to 2 g benorylate.

Uses Benorylate is an anti-inflammatory analgesic and antipyretic. Benoral is recommended for the treatment of rheumatoid arthritis, osteoarthritis and painful musculoskeletal conditions. It may also be used to relieve mild to moderate pain of non-rheumatic origin such as dysmenorrhoea and as an antipyretic in febrile conditions.

Dosage and administration Benoral is for oral administration only.

Benoral tablets: Adults: Two 750 mg tablets (1.5 g benorylate) three times a day is usually adequate to relieve pain and stiffness in osteoarthritis, quiescent rheumatoid arthritis and soft tissue rheumatism.

Benoral suspension: Adults: 10 ml of suspension (4 g benorylate) twice daily is normally required to treat active rheumatoid arthritis.

Patients with osteoarthritis, quiescent rheumatoid arthritis or soft tissue (non-articular) rheumatism who prefer the liquid preparation may be given 5 ml Benoral Suspension (2 g benorylate) twice daily.

Children: 6–12 years: 500 mg not more than four times daily.

2–6 years: 500 mg not more than three times daily.

1–2 years: 250 mg not more than four times daily.

3 months–1 year: 25 mg/kg body weight not more than four times daily.

Benoral should not be given to children under the age of three months.

In children with Still's disease, an initial dose of 200 mg/kg body weight daily has been used with adjustment after 7 days to a level sufficient to maintain blood salicylate at an anti-inflammatory level (25–30 mg/100 ml).

Benoral Granules: The contents of the prescribed number of sachets should be stirred into half a glass of water (or milk, if preferred) and drunk immediately.

Adults: For acute rheumatic conditions up to 4 sachets daily in divided doses may be required but 3 sachets are often adequate. For milder rheumatic conditions and for the relief of non-rheumatic pain, one sachet twice daily is recommended.

Not suitable for children: use Benoral Suspension.

Contra-indications, warnings, etc

Contra-indications: Benoral should not be given to patients with active peptic ulcer, or to those known to be hypersensitive to aspirin (including those with haemophilia and similar coagulation disorders).

Precautions: Patients who are also taking anticoagulants should have their prothrombin time checked.

Patients taking Benoral should be advised against taking analgesics containing aspirin or paracetamol. The safety of benorylate has not been established in pregnancy, but there is clinical and epidemiological evidence that salicylate and paracetamol (which occur as meta-

bolic products of benorylate) are safe in human pregnancy.

Overdosage: Symptoms are likely to resemble those caused by salicylate overdosage. Treatment should be based on the levels of salicylate and paracetamol found in the blood.

Side-effects: Overall tolerance is excellent. Adverse effects may include gastric intolerance (nausea, constipation or diarrhoea, indigestion or heartburn) and drowsiness and rashes have also been reported. The possibility that gastro-intestinal haemorrhage may be induced by Benoral cannot be excluded though there is no definite evidence that Benoral was responsible for the gastro-intestinal haemorrhage in the few cases reported. The high salicylate levels obtained with Benoral may give rise to dizziness, tinnitus and deafness. If this happens, the dose should be reduced.

Pharmaceutical precautions No special storage requirements. Use Syrup BP to dilute the suspension.

Legal category P.

Package quantities *Benoral Suspension:* bottles of 150 or 300 ml.

Benoral Tablets: bottles of 100 or 500.

Benoral Granules: Cartons of 60 sachets.

Further information Benoral has analgesic and anti-inflammatory properties comparable to those of other antiarthritis compounds. Its antipyretic effect is similar to that of aspirin or paracetamol but more prolonged than either. Gastro-intestinal tolerance is superior to that of comparable doses of aspirin or mixtures of aspirin and paracetamol.

Product licence numbers

Benoral Suspension 0071/5022

Benoral Tablets 0071/5901

Benoral Granules 0071/0149

BIOGASTRONE*

Presentation White, flat, round, bevelled-edged tablets 9.6 mm in diameter, marked BG and scored on one side and unmarked on the other. Each tablet contains Carbenoxolone Sodium BP 50 mg.

Uses For the treatment of gastric ulcers.

Dosage and administration For oral administration only. Adults should take 2 tablets three times daily after meals for the first week. Thereafter, 1 tablet should be taken three times a day until the ulcer has healed. For 6 to 8 weeks' treatment is usually needed but up to 12 weeks may be needed in resistant cases.

Contra-indications, warnings, etc

Contra-indications: Biogastone should not be prescribed for patients suffering from severe cardiac, renal and hepatic failure. Nor should it be prescribed for patients on digitalis glycosides unless serum electrolyte levels are monitored at weekly intervals and measure taken to avoid the development of hypokalaemia.

Precautions: Special care should be exercised with patients pre-disposed to sodium and water retention, potassium loss and hypertension (e.g. the elderly and those with cardiac, renal and hepatic disease) since carbenoxolone can induce similar changes.

Potassium supplements should be considered for those at risk from developing hypokalaemia.

Regular monitoring of weight and blood pressure which should indicate the development of such effects is advisable for all patients. A thiazide diuretic should be administered if oedema or hypertension occurs (spironolactone or amiloride should not be used because they interfere with the therapeutic action of carbenoxolone). Potassium loss should be corrected by the administration of potassium supplements.

No teratogenic effects have been reported with carbenoxolone sodium but careful consideration should be given before prescribing Biogastrone for women who may become pregnant.

Overdosage: If the tablets have been recently ingested, the stomach should be emptied by gastric lavage. Serum electrolytes should be monitored and any deficiency in potassium should be corrected, using the intravenous route if necessary, or slow-release or effervescent potassium chloride tablets. Water retention and sodium balance should be corrected by means of a diuretic (spironolactone or amiloride would appear to be a logical choice).

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Bottles of 100 tablets.

Further information Carbenoxolone has been shown to exert a healing effect on gastric ulcers, possibly by promoting mucus synthesis and by prolonging the life-span of gastric epithelium.

Made under licence from Biorex Laboratories Ltd, London. Brit. Pat. No. 1124976.

Product licence number 0071/5902.

BIORAL GEL*

Presentation A buff-coloured gel containing 2% carbenoxolone Sodium BP.

Uses For the treatment of mouth ulcers.

Dosage and administration Adults and children. Apply thickly to the lesion after meals and at bedtime. The gel should be allowed to remain on the ulcer as long as possible.

Contra-indications, warnings, etc There are no known contra-indications and no side-effects have been reported.

If the lesion is infected, additional appropriate therapy should be used. If the ulcer fails to heal within three weeks, treatment and diagnosis should be reviewed.

Pharmaceutical precautions Tubes should be kept well closed to avoid deterioration.

Legal category P.

Package quantities Tubes containing 5 g.

Further information Bioral Gel contains carbenoxolone sodium in a specially formulated base which adheres to the moist oral mucosa and ensures prolonged contact with the ulcer.

Made under licence from Biorex Laboratories Ltd, London. Brit. Pat. No. 1124976.

Product licence number 0071/5904.

CALCIUM RESONIUM*

Presentation Calcium Resonium is ground and flavoured calcium polystyrene sulphonate and is a yellow to golden brown fine powder with a pleasant vanilla odour and sweet taste. It contains about 8% w/w of calcium.

Uses Calcium Resonium is an ion-exchange resin. It is recommended for the treatment of hyperkalaemia associated with anuria or severe oliguria. It is also used to treat hyperkalaemia in patients requiring dialysis and in patients on regular haemodialysis or on prolonged peritoneal dialysis.

Dosage and administration Calcium Resonium is for oral or rectal administration only. The dosage recommendations detailed below are a guide only; the precise requirements should be decided on the basis of regular serum electrolyte determinations.

Adults:

1. **Oral:** Usual dose 15 g three or four times a day. The resin is given by mouth in a little water, or it may be made into a paste with some sweetened vehicle.

2. **Rectal:** In cases where vomiting may make oral administration difficult the resin may be given rectally as a suspension of 30 g resin in 100 ml 2% methylcellulose (medium viscosity) and 100 ml water, as a daily retention enema. In the initial stages administration by this route as well as orally may help to achieve a more rapid lowering of the serum potassium level.

The enema should if possible be retained for at least nine hours. If both routes are used initially it is probably unnecessary to continue rectal administration once the oral resin has reached the rectum.

Children: 1 g/kg body weight daily in divided doses in acute hyperkalaemia. Dosage may be reduced to 0.5 g/kg body weight daily in divided doses for maintenance therapy.

The resin is given orally, preferably with a drink (not a fruit squash) or a little jam or honey. When refused by mouth it should be given rectally using a dose at least as great as that which would have been given orally.

Contra-indications, warnings, etc

Contra-indications: Calcium Resonium should not be used to treat patients with hyperparathyroidism, multiple myeloma, sarcoidosis or metastatic carcinoma who may present with renal failure and hypercalcaemia.

Precautions: The possibility of severe potassium depletion should be considered, and adequate biochemical control is essential during treatment.

Administration of the resin should be stopped when the serum potassium falls to 5 mmol/litre. Serum calcium levels should be estimated at weekly intervals to detect the early development of hypercalcaemia, and the dose of resin adjusted to levels at which hypercalcaemia and hypokalaemia are prevented.

Overdosage: In the event of overdosage the resin should be removed from the alimentary tract by the use of laxatives or enemas, and appropriate measures should be taken to restore serum potassium levels to normal, and to reduce blood calcium levels if these are raised.

Side-effects: Hypercalcaemia has been reported in well-dialysed patients receiving calcium resin, and in the occasional patient with chronic renal failure. Many patients in chronic renal failure have low serum calcium and high serum phosphate, but some, who cannot be screened out beforehand, show a sudden rise in serum

calcium to high levels after therapy. The risk emphasises the need for adequate biochemical control.

Pharmaceutical precautions It is suggested that Calcium Resonium should not be administered in fruit squashes since these have a high potassium content.

Legal category P.

Package quantities Polystyrene containers of 300 g each containing a plastic 15 g spoon.

Further information Nil.

Product licence number 0071/5025.

DANOL*

Presentation

1. *Danol*: white No. 1 hard gelatin capsules printed in black ink with an identification mark and D200 and filled with a white or almost white powder containing 200 mg danazol.

2. *Danol-½ (Half Strength)*: white No. 3 hard gelatin capsules printed in black ink with an identification mark and D100 and filled with a white or almost white powder containing 100 mg danazol.

Uses Danol is recommended for the treatment of endometriosis and associated infertility, benign breast disease (e.g. fibrocystic mastitis) and menorrhagia. Danol has also been used to treat virginal breast hypertrophy, primary constitutional precocious puberty, gynaecomastia and other similar endocrine disorders where regulation of the release of pituitary gonadotrophins LH and FSH would be of therapeutic value.

Dosage and administration Danol is for oral administration only. Dosage depends on the condition being treated and the patient's response and, for adults, is usually within the range of 200–800 mg daily in two to four divided doses. The effect of Danol is a function of dosage and time and therefore in some patients, once a satisfactory response has been obtained, it may be possible to maintain improvement with a reduced dose. It is recommended that Danol therapy in adult females should start on the first day of the menstrual cycle with an adjustment of dosage being made subsequently to achieve amenorrhoea when desired. Further adjustments may be made in succeeding months consistent with the patient's response.

1. *Adults*: In endometriosis it is recommended that a starting dose of 400 mg daily be used, reducing or increasing as necessary. Treatment should be continued for six months or until the condition resolves.

In benign breast disorders, a starting dose of 300 mg daily in divided doses is recommended.

In menorrhagia, daily doses of 100–400 mg have been found effective but 200 mg daily is usually sufficient to reduce menstrual blood loss to acceptable levels.

2. *Children*: The recommended dose in precocious puberty is 100–400 mg daily, depending on the patient's age, weight and clinical response.

Contra-indications, warnings, etc

Contra-indications: Although no teratogenic effects have been observed in animal studies, it is recommended that Danol should not be given to patients who are pregnant. In patients with amenorrhoea before treatment, tests should be considered to establish that they are not pregnant. Administration should be stopped if a patient is found to be pregnant after starting a course of

treatment. Continuing treatment may result in an androgenic effect on the foetus.

Precautions: Contraception: Although Danol can inhibit ovulation, it must not be relied upon for contraceptive and non-hormonal methods should be advised during the course of treatment. This is because the concurrent administration of oestrogens and/or progestogens, including oral contraceptives may modify the action of Danol.

Because Danol may cause some degree of fluid retention, patients with conditions which may be influenced by this factor, such as cardiac or renal dysfunction, epilepsy or migraine, require careful observation.

Danol does not appear to have any adverse effect on the liver, nevertheless, since the compound is metabolised in the liver, care is needed in patients with hepatic dysfunction.

Care is needed in patients with diabetes mellitus because Danol may increase insulin resistance and thus aggravate the condition.

Danol may potentiate the action of anticoagulants.

Overdosage: In animal tests, doses of 16,000 mg/l body weight produced no fatalities, and it is unlikely that any immediate serious reactions would be seen from a single excessive dose in man.

In the case of acute overdosage, the drug should be removed by emesis or stomach pump (if ingestion recent) and the patient should be kept under observation in case of any delayed reactions.

Side Effects: Danol administration has had little overall effect on libido and no episodes of deep-vein thrombosis; nor any thrombo-embolic complications have been attributed to the drug.

Acne, oily-skin, fluid retention, mild hirsutism and rarely, clitoral hypertrophy, all of which can be attributed to the mild androgenic activity of Danol, have been reported on occasions, particularly in patients where such tendencies were already present. Flushing and reduction in breast size have also been noted. If signs of virilisation (e.g. voice changes) develop, Danol should be discontinued.

Other adverse reactions which have been reported include rashes, nervousness and nausea, headache, dizziness, vertigo, emotional lability, backache, skeletal muscle spasm and hair loss.

An increase in overall weight in some patients has been recorded during Danol treatment. This was considered to be associated with its mild anabolic activity. Increases greater than 4 or 5 kg (10 lbs), however, were not common and tended to be associated with high doses and longer periods of treatment. Control of diet may be beneficial in some susceptible patients.

In long-term high-dosage toxicity studies in the rhesus monkey, although no change was seen in the activity of the drug-metabolising enzymes, azoreductase and nitroanisole O-demethylase, a decrease was observed in aminopyrine N-demethylase and aniline hydroxylase.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Danol capsules are supplied in bottles of 50 and 100.

Danol-½ (Half Strength) capsules are supplied in bottles of 50 and 100.

Further information The effect of Danol on the hypothalamic-pituitary-gonadal axis is reversible when treatment is stopped. In those patients who have

received after treatment, there is no evidence to suggest that the compound has any effect on the course or outcome of pregnancy. There is no clinical or oratory evidence that Danol affects other pituitary-thyroid axes. It should be noted, however, that while T_4 levels are unaffected by Danol, some patients who clinically euthyroid may show increased T_3 uptake, increased T_4 levels, and a decrease in thyroxine binding protein.

Product licence numbers

100 mg	0071/0095
50 mg (Half Strength)	0071/0094

DUOGASTRONE*

Presentation Colourless, transparent, unmarked position-release capsules filled with a white powder. Each contains 50 mg Carbenoxolone Sodium BP.

Uses For the treatment of duodenal ulcers.

Dosage and administration *Adults:* One capsule to be swallowed whole and unbroken with liquid, four times daily, 15–30 minutes before meals. Patients taking antacids should continue to do so until symptoms appear but anticholinergic drugs should be discontinued. Despite early relief of symptoms, treatment should continue for at least six weeks and should usually be continued to 12 weeks to ensure maximum healing effect.

Contra-indications, warnings, etc

Contra-indications: Duogastrone should not be prescribed for patients suffering from severe cardiac, renal or hepatic failure. Nor should it be given to patients on digitalis glycosides unless serum electrolyte levels are monitored at weekly intervals, and measures taken to avoid the development of hypokalaemia.

Precautions: Special care should be exercised with patients predisposed to sodium and water retention, potassium loss and hypertension (e.g. the elderly and those with cardiac, renal or hepatic disease) since carbenoxolone can induce similar changes. Potassium supplements should be considered for those at risk from developing hypokalaemia.

Regular monitoring of weight and blood pressure which should indicate the development of such effects is advisable for all patients. A thiazide diuretic should be administered if oedema or hypertension occurs (spironolactone or amiloride should not be used because they interfere with the therapeutic action of carbenoxolone). Potassium loss should be corrected by the administration of potassium supplements.

No teratogenic effects have been reported with carbenoxolone sodium but careful consideration should be given before prescribing Duogastrone for women who may become pregnant.

Overdosage: If the capsules have been recently ingested, the stomach should be emptied by gastric lavage. Serum electrolytes should be monitored and any deficiency in potassium should be corrected, using the intravenous route if necessary, or slow-release or effervescent tablets of potassium chloride. Water retention and sodium imbalance should be corrected by means of a diuretic. Spironolactone or amiloride would appear to be a logical choice.

Pharmaceutical precautions Care should be taken not to damage the capsules. Store in a cool, dry place.

Legal category POM.

Package quantities Containers of 28 capsules.

Further information Duogastrone is a unique 'position-release' capsule designed to deliver carbenoxolone sodium into the duodenum. The capsule contents are released only when it is ruptured by the pressure of the antral or pyloric contractions. Carbenoxolone sodium exerts a local healing effect on the ulcer possibly by improving mucus synthesis and by prolonging the life span of epithelium cells of the duodenum.

Made under licence from Biorex Laboratories Ltd, London. Brit Pat. No. 1093286.

Product licence number 0071/5903.

EUMYDRIN*

Presentation Eumydrin is a clear, colourless solution containing 0.6% w/v Atropine Methonitrate BP in ethyl alcohol.

Uses Eumydrin is recommended for the treatment of pylorospasm in infants and congenital hypertrophic pyloric stenosis. Eumydrin drops are also used in the symptomatic alleviation of the paroxysms of whooping cough, and certain types of dry spasmodic cough.

Dosage and administration Eumydrin drops are for oral administration only. To ensure correct dosage, Eumydrin should be dispensed from the dropper provided in each pack. Each drop then contains approximately 0.2 mg atropine methonitrate.

Adults: The usual dosage is 5–15 drops (1–3 mg).

Children: In the treatment of pyloric stenosis it is important that dehydration and alkalosis should be treated before Eumydrin is given. Usually 1–2 drops are given 20 minutes before each feed, and this dose may be increased to 3 or 4 drops after several days. Feeds are usually given every two hours in gradually increasing amounts. Treatment is usually continued for nine weeks or so, the patient usually being discharged from hospital after two weeks. Subsequently the dose of Eumydrin is gradually decreased until administration ceases.

In the treatment of whooping cough the dose depends on the age of the child and the severity of the attack. The following scheme serves as a guide, the doses being repeated every four hours:

6–10 years and over	6–12 drops
2–6 years	4–8 drops
6 months to 2 years	3–6 drops
Infants up to 6 months	2–4 drops

The lower dose should be used first and increased to the higher one if necessary. The drops may be given in water or fruit juice, or they may be put on a lump of sugar and allowed to evaporate. When vomiting is troublesome or a rapid action is needed, the drops may be placed directly on the tongue.

If side-effects such as dryness of the mouth, dilation of the pupils or 'lobster' skin occur, the dose should be reduced.

Contra-indications, warnings, etc

Contra-indications: Eumydrin should not be given to patients known to be hypersensitive to anticholinergics or to those with paralytic ileus, prostatic enlargement, closed angle glaucoma or those with a shallow anterior chamber.

Precautions: Because of the possibility of hyperpyrexia in abnormally sensitive patients, care is needed in the use of Eumydrin or any other atropine derivatives where there is a preexisting cause of fever, such as upper

respiratory infection. It should be noted that the solvent in Eumydrin drops is 90% alcohol, they must not therefore be used for the eyes.

Eumydrin should be used with caution in conditions characterised by tachycardia. Concurrent administration of certain drugs with anticholinergic properties, such as amantidine, some antihistamines, butyrophenones, phenothiazines, and tricyclic antidepressants may enhance the action of Eumydrin.

Overdosage: Signs and symptoms of overdosage are the same as for atropine. Symptomatic treatment consists of sponging and cold packs for fever, paraldehyde intramuscularly for excitement or convulsions, and oxygen and artificial respiration for the depressed state. Neostigmine, physostigmine or pilocarpine may be used as antidotes.

Side-effects: These resemble those seen with atropine (e.g. dry mouth, dysphagia, thirst, dry skin, dilated pupils, fever, increased pulse and respiration rate, etc), though atropine methonitrate has a weaker stimulant effect on the central nervous system. It is well tolerated by infants and considerable overdosage is necessary before toxic symptoms appear.

Pharmaceutical precautions Because of the volatile nature of the solvent Eumydrin should be stored in a cool place and the bottles should be tightly closed. If evaporation occurs during storage the solution should not be used because of the risk of overdosage.

Legal category POM.

Package quantities Amber glass bottles containing 15 ml complete with dropper.

Further information Nil.

Product licence number 0071/5029.

EVIDORM®

Presentation Evidorm Tablets are near-white bi-convex tablets 11 mm in diameter, marked E on one face and scored on the other. Each tablet contains 250 mg hexobarbitone and 100 mg Cyclobarbitone Calcium BP.

Uses Evidorm Tablets are recommended for the treatment of severe, intractable insomnia.

Dosage and administration Evidorm Tablets are for oral administration only.

Adults: 1 tablet on retiring; 2 tablets may be needed occasionally.

Contra-indications, warnings, etc

Contra-indications: Barbiturate hypnotics should not be used in children, young adults, the elderly or in patients who are debilitated, or in those who have a history of alcohol or drug abuse. They are also contra-indicated in the presence of uncontrolled pain, pregnancy or breast feeding and porphyria.

Precautions: In patients with renal or hepatic failure, the dose should be reduced. Because barbiturates can increase the activity of hepatic enzymes involved in drug metabolism, the availability and blood concentration of concurrently administered drugs may be altered. Among the compounds known to be affected are coumarin-type anticoagulants, systemic steroids (including oral contraceptives), phenytoin, griseofulvin, rifampicin, phenothiazines and tricyclic antidepressants.

Overdosage: Where patients are seen within four hours

of taking an overdose, gastric aspiration or lavage may be beneficial in adults, while children who are conscious may be given an emetic, e.g. Syrup of Ipecacuanha.

The prime objective in treating barbiturate overdosage is to maintain vital functions (respiration, cardiovascular and renal function and electrolyte balance) while the majority of the drug is metabolised by hepatic enzymes. At the same time some of the drug is excreted unchanged by the kidneys. Given normal renal function, this latter process may be enhanced by alkaline diuresis, maintaining the urinary pH at about 8 by appropriate intravenous infusion. In severe cases, haemodialysis may help, but extracorporeal haemoperfusion is probably more effective.

Side Effects: Drowsiness, sedation, unsteadiness, vertigo and inco-ordination may occur. During the first week of administration, performance and alertness may be impaired; patients should be warned not to drive or operate machinery if affected. These effects may be potentiated by alcohol.

Other adverse reactions may include a 'hang-over' effect, paradoxical excitement, confusion, memory defects and skin rashes in patients who may be sensitive to this type of drug.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Evidorm is supplied in bottles of 50 tablets.

Further information Barbiturates have a high addiction potential. Long-term use or use of high doses for short periods may lead to tolerance and subsequently physical and psychological dependence. Symptoms of dependence include confusion, defective judgement and loss of emotional control. Withdrawal symptoms occur after long-term normal use (and particularly after abuse) if barbiturate treatment is stopped abruptly. They include nightmares, irritability and insomnia and, in severe cases, tremors, delirium, convulsions and death. Withdrawal symptoms have been reported in neonates after barbiturate treatment during pregnancy and labour.

Product licence number 0071/5030.

FERGON®

Presentation Fergon Tablets are smoothly polished red, sugar-coated tablets with no markings, each containing 300 mg Ferrous Gluconate BP.

Uses Fergon Tablets are recommended for the treatment of hypochromic anaemia caused by deficient iron intake, excessive iron loss as in menorrhagia, or chronic bleeding from the gastro-intestinal tract. They are also used as a supplement during pregnancy, in idiopathic hypochromic anaemia and in the treatment of iron deficiency in childhood.

Dosage and administration Fergon is for oral administration. It is best administered about one hour before meals.

Adults Prophylactic: 2 tablets (600 mg, daily).

Therapeutic: 4-6 tablets (1.2-1.8 g) daily in divided doses.

Children: Children aged 6-12 years may be given 1-2 tablets daily for therapeutic or prophylactic purposes.

Contra-indications, warnings, etc There are no

recorded contra-indications to Fergon but it should be used with caution in patients with haemochromatosis or aemolytic anaemia.

Patients should be warned to keep Fergon Tablets out of the reach of young children. The absorption of iron salts is decreased in the presence of antacids. They will also diminish the absorption of concurrently administered tetracyclines.

Overdosage: It is well known that overdosage of ferrous salts is particularly dangerous to small children.

The following treatment is suggested. Gastric lavage with 5% sodium bicarbonate and saline cathartics (e.g. sodium sulphate 30 g for adults). Milk and eggs with 5 gismuth carbonate every hour as demulcents. Blood or plasma transfusion for shock, oxygen for respiratory embarrassment. Chelating agents such as disodium alium edetate may be tried (500 mg in 500 ml by continuous i.v. infusion). Dimercaprol should not be used since it forms a toxic complex with iron. Desferrioxime is a specific iron chelating agent.

Side-effects: are mainly gastro-intestinal. They appear to occur less frequently than with ferrous sulphate, and patients are therefore less likely to default during treatment.

Pharmaceutical precautions Store in well-closed containers. Protect from light.

Legal category P.

Package quantities Fergon is supplied in bottles of 10 or 100 tablets.

Further information Nil.

Product licence number 0071/5032.

FORTAGESIC®

Presentation White tablets 12.7 mm diameter, marked with an ankh on one side and Fortagesic on the other. Each tablet contains Pentazocine BP 15 mg (as the hydrochloride) and Paracetamol BP 500 mg.

Uses Fortagesic is a compound analgesic for the relief of moderate pain associated with musculo-skeletal disorders or injuries, such as bursitis, sprains, strains, bronchitis, sciatica and osteoarthritis, and for rheumatoid arthritis in patients sensitive to aspirin.

Dosage and administration Fortagesic is for oral administration only.

Adults: 2 tablets up to four times daily.

Children: 7-12 years: 1 tablet not more frequently than every four hours. Not more than 4 doses to be taken in any 24-hour period. Not recommended for children under 7 years of age.

Contra-indications, warnings, etc

Precautions: Fortagesic should not be administered to patients with established respiratory depression, raised intracranial pressure, head injuries or pathological brain conditions where clouding of the sensorium is undesirable.

Because pentazocine is a narcotic antagonist, Fortagesic may provoke withdrawal symptoms if given to narcotic addicts and it should be given with caution to patients who have recently been treated with large doses of narcotics.

Fortagesic may produce sedation so ambulant patients should be warned not to operate machinery or drive if

affected: alcohol may reinforce the sedative effect. There is epidemiological evidence for the safety of paracetamol in human pregnancy. No such evidence exists for pentazocine but it has been widely used for many years without apparent ill consequences. When it is prescribed for chronic use, the physician should take precautions to avoid unnecessary increase in dose of Fortagesic by the patient. Fortagesic should be used with caution in patients who are receiving monoamine oxidase inhibitors, and in those with severe renal, hepatic or respiratory impairment.

Overdosage: In the absence of any experience of overdosage with Fortagesic it is reasonable to assume that signs and symptoms would resemble those which may occur after excessive amounts of the individual ingredients.

Means of maintaining proper oxygenation should be available and naloxone should be used to reverse any CNS depression.

Patients who have taken an overdose of paracetamol may appear well for the first three days, then succumb with liver damage. The hepatic changes produced by overdosage of paracetamol appear to result from the accumulation of a highly active intermediate metabolite in the hepatocytes. N-acetylcysteine intravenously or l-methionine orally protects the liver if administered within 10 hours of ingesting an overdose.

Side-effects: are more likely to be due to pentazocine than to paracetamol, for adverse reactions to this latter compound are uncommon and it is without any irritant effect on the gastro-intestinal tract. The reactions to the oral administration of pentazocine which have sometimes occurred include dizziness, nausea, vomiting, headache and sedation. These effects have been self-limiting and tend to decrease after the first few doses. Less frequent reactions have included sweating, psychotomimetic effects and flushing.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Fortagesic is supplied in bottles of 100 and 500 tablets.

Further information Fortagesic is a logical combination of two analgesics, one (paracetamol) acting peripherally, the other (pentazocine) exerting a central action. They are presented in a ratio which has been found effective for the relief of moderate pain.

Product licence number 0071/0022.

FORTRAL®

Presentation

1. A sterile, isotonic aqueous solution for intramuscular, intravenous or subcutaneous injection containing Pentazocine BP 30 mg/ml as the lactate in 1 ml or 2 ml ampoules.

2. No. 4 hard gelatine, grey/yellow capsules marked Fortral 50. Each capsule contains Pentazocine Hydrochloride BP 50 mg (equivalent to 44.3 mg base).

3. White, torpedo-shaped suppositories, average weight 1.86 g, for rectal administration. Each suppository contains Pentazocine BP 50 mg as the lactate.

4. White, bi-convex film-coated tablets, 9.5 mm diameter, marked Fortral on one face and with an ankh on the other. Each tablet contains Pentazocine Hydrochloride BP 25 mg (equivalent to 22.15 mg base).

Uses Fortral is a strong analgesic for the relief of moderate to severe pain.

Dosage and administration

1. Fortral Ampoules: Adults: Fortral injections may be administered subcutaneously, intramuscularly or intravenously. For severe pain, 45–60 mg. For moderate pain, 30 mg. The dose should be adjusted according to response and repeated as necessary every three to four hours.

Children: In the case of patients between the ages of 1 year and 12 years, the *maximum* single dose of parenteral Fortral should be calculated on the basis of 1 mg/kg body weight by subcutaneous or intramuscular injection or 0.5 mg/kg body weight intravenously.

As with most parenteral drugs, when frequent daily injections are needed over long periods, intramuscular administration is preferable to subcutaneous. It is recommended that intramuscular sites of injection be rotated, e.g. deltoid areas, upper outer quadrants of the buttocks and mid-lateral aspects of the thighs.

2. Fortral Capsules: Adults: The usual recommended dosage is one to two 50 mg capsules every three to four hours after meals according to the response of the patient. Dosage is best tailored to the individual patient and to the degree of pain.

Children: For children under 12 years of age, it is recommended that other dosage forms of Fortral, tablets or injection, be used as appropriate.

3. Fortral Suppositories: Adults: 1 suppository at any one time. It will not normally be necessary to exceed 4 suppositories daily.

Children: Fortral Suppositories are not suitable for administration to children under 12 years of age.

4. Fortral Tablets: Adults: The usual starting dose is two 25 mg tablets every four hours after meals, but dosage is best tailored to the individual patient and to the degree of pain within the range of 25–100 mg every three to four hours.

Children: 6–12 years: One 25 mg tablet every three to four hours as required.

1–6 years: The recommended dosage is such that Fortral injection is considered to be a more convenient dosage form.

Under 1 year: There are no dosage recommendations for children less than 1 year old.

Contra-indications, warnings, etc

Precautions: Fortral should not be administered to patients with established respiratory depression, raised intracranial pressure, head injuries or pathological brain conditions, where clouding of the sensorium is undesirable.

Because pentazocine is a narcotic antagonist, it may provoke withdrawal symptoms if given to narcotic addicts.

Fortral should be given with caution to patients with severely impaired renal or hepatic function and to those previously on large doses of narcotics. Fortral may produce sedation, so ambulant patients should be warned not to operate machinery or drive if affected; alcohol may reinforce the sedative effect. There is no epidemiological evidence for the safety of pentazocine in human pregnancy but it has been widely used for many years without apparent ill consequences. When Fortral is prescribed for chronic use, the physician should take precautions to avoid any unnecessary increase in

dose by the patient. Until further information is available Fortral, like most other strong analgesics, should be used with caution in patients who are receiving monoamine oxidase inhibitors.

Overdosage: Means of maintaining proper oxygenation should be available, and naloxone should be used to reverse any CNS depression.

Side-effects: No serious toxic reactions have been observed where Fortral has been given in normal therapeutic doses and side-effects are generally of a minor nature. Sedation, the most common effect, is less than that associated with morphine. Nausea, vertigo, vomiting, diaphoresis, skin flushes and visual disturbances have also been reported. Respiratory depression, though not normally of clinical significance, can occur.

The psychotomimetic effects observed with nalorphine and other narcotic antagonists occur sometimes with Fortral. Local tissue damage at injection sites has been reported, particularly after subcutaneous administration.

Dependence liability: Abrupt discontinuation of Fortral in patients receiving large parenteral doses over a prolonged period has occasionally resulted in mild withdrawal symptoms. There have also been rare reports of a similar effect in the new-born after prolonged maternal use of Fortral during pregnancy. This abstinence syndrome of Fortral is not typical of opiate dependence. Symptoms include mild abdominal cramps, nausea, vomiting, nervousness or restlessness, dizziness, fever and chills, but are mild compared with opiate withdrawal symptoms. Withdrawal of Fortral from such patients has raised few problems, treatment with tranquillisers only being sometimes required. It should be emphasised that the majority of patients reported to have become dependent on Fortral had previously been dependent on opiates or had misused other drugs.

Pharmaceutical precautions Fortral Suppositories should be stored in a cool place and the ampoules should be protected from light. Fortral is chemically compatible with atropine sulphate, hyoscine hydrobromide and promethazine hydrochloride. Precipitation will occur if Fortral injection is mixed in the same syringe with soluble barbiturates, diazepam or with chlordiazepoxide. Fortral injection appears to be compatible for up to seven days with most commonly used infusion solutions. The exceptions are those which contain sodium bicarbonate, where the high pH causes immediate precipitation of pentazocine base.

Legal category POM.

Package quantities

1. Ampoules in boxes of ten 1 ml or 2 ml.
2. Capsules in bottles of 100 or 500.
3. Suppositories in cellulose acetate strips. Boxes of 20.
4. Tablets in bottles of 100 or 500.

Further information Fortral is a strong analgesic with weak narcotic antagonist properties. In action it is comparable to morphine and other narcotics. It is not subject to the Misuse of Drugs Act.

Product licence numbers

Fortral Ampoules	0071/5033
Fortral Capsules	0071/5034
Fortral Suppositories	0071/0064
Fortral Tablets	0071/5035

FRANOL*

Presentation Franol Tablets are flat, white tablets with bevelled edges, 8.7 mm in diameter, marked F on one side and plain on the other side. Each tablet contains 120 mg Theophylline BP, 8 mg Phenobarbitone BP and 1 mg Ephedrine Hydrochloride BP.

Uses Franol Tablets are recommended for the treatment of bronchial asthma and bronchitis.

Dosage and administration Franol Tablets are for oral administration only.

Adults:

1. *Bronchial asthma:* Dosage varies with individual requirements and should be adjusted accordingly. The usual dosage is 3 tablets a day (morning, midday and evening). For the patient who suffers nocturnal attacks, an extra tablet taken at bedtime is recommended.

In order to avoid recurrences, it is important that treatment should be continued for a considerable time after attacks have stopped.

2. *Bronchitis:* Usual dosage 3 tablets a day. This may be increased if necessary.

Children: The usual dose is one-third to one-half the adult dose, though full doses may be used should these be needed. The dose will depend on the severity of the condition, on individual tolerance and on the response obtained.

Contra-indications, warnings, etc Franol should not be given to patients with acute intermittent porphyria or to those who are hypersensitive or exhibit idiosyncrasy to barbiturates.

It should not be given to those who are taking MAO inhibitors or have received them during the previous 14 days. Franol should not normally be given during pregnancy or lactation and it should be used with caution in patients with cardiovascular disease, severe hypertension, hyperthyroidism, prostatic hypertrophy or glaucoma.

Overdosage: The symptoms of overdosage are likely to be those attributable to ephedrine and include excessive irritability, fever, nausea and vomiting, cyanosis, tachycardia, dilated pupils, opisthotonus, spasm, convulsion and respiratory embarrassment. If recently ingested and vomiting (due to the theophylline) has not occurred, the stomach should be emptied. Subsequent treatment should be symptomatic.

Side-effects: These are rare. The phenobarbitone in the formula will usually overcome any stimulation due to the ephedrine. Any minor gastric disturbances can be avoided by taking the tablets with meals.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Franol Tablets are supplied in bottles of 100, 500 and 1,000.

Further information Nil.

Product licence number 0071/5036.

FRANOL* EXPECT.

Presentation Franol Expect. is a clear, deep red, viscous solution with an odour of aniseed. Each 10 ml dose contains 120 mg Theophylline (equivalent to 130 mg Theophylline Hydrate BP), BP, 8 mg Phenobar-

bitone BP, 9.5 mg Ephedrine BP and 50 mg guaiphenesin.

Uses Franol Expect. is recommended for the treatment of chronic bronchitis, bronchial asthma associated with productive bronchitis, and coughs associated with tracheobronchitis and influenza.

Dosage and administration Franol Expect. is for oral administration only. Dosage depends on individual needs and tolerance.

Adults: 10 ml (2 × 5 ml spoonfuls) three times a day, with an additional dose before retiring, if required.

Children: The usual dose is one-third to one-half the adult dose, though older children will tolerate full doses, should these be needed.

Contra-indications, warnings, etc Franol Expect. should not be given to patients with acute intermittent porphyria or to those who are hypersensitive or exhibit idiosyncrasy to barbiturates.

It should not be given to those who are taking MAO inhibitors or have received them during the previous 14 days. Franol should not normally be given during pregnancy or lactation and it should be used with caution in patients with cardiovascular disease, severe hypertension, hyperthyroidism, prostatic hypertrophy or glaucoma.

Overdosage: The symptoms of overdosage are likely to be those attributable to ephedrine and include excessive irritability, fever, nausea and vomiting, cyanosis, tachycardia, dilated pupils, opisthotonus, spasm, convulsions and respiratory embarrassment. If recently ingested and vomiting (due to the theophylline) has not occurred, the stomach should be emptied. Subsequent treatment should be symptomatic.

Side-effects: These are rare. The phenobarbitone in the formula will usually overcome any stimulation due to the ephedrine. Minor gastric disturbances can be overcome by taking the dose with meals.

Pharmaceutical precautions When doses of less than 5 ml are ordered Franol Expect. may be diluted with Syrup BP. A 50:50 dilution is stable for at least two to three weeks.

Legal category POM.

Package quantities Franol Expect. is supplied in bottles containing 150 ml or 1 litre.

Further information Nil.

Product licence number 0071/5038.

FRANOL* PLUS

Presentation Franol Plus Tablets are flat, white tablets with bevelled edges, 8.7 mm in diameter, marked F+ on one side and W on the other. Each tablet contains 120 mg Theophylline BP, 8 mg Phenobarbitone BP, 15 mg ephedrine sulphate and 10 mg phenylephrine hydrochloride.

Uses Franol Plus Tablets are recommended for the treatment of asthma and bronchitis, especially where exacerbated by allergy and hay fever.

Dosage and administration **Adults:**

1. *Bronchial asthma:* Dosage varies with individual requirements and should be adjusted accordingly. The usual dosage is 3 tablets a day (morning, midday and

evening). For the patient who suffers from nocturnal attacks, an extra tablet taken at bedtime is recommended.

In order to avoid recurrences, it is important that treatment should be continued for a considerable time after attacks have stopped.

2. *Bronchitis*: Usual dosage 3 tablets a day. This may be increased if necessary.

3. *Hay fever*: 1 tablet three times a day.

Children: The usual dose is one-third to one-half the adult dose, though full doses may be used should these be needed. The dose will depend on the severity of the condition, on individual tolerance and on the response obtained.

Contra-indications, warnings, etc Franol should not be given to patients with acute intermittent porphyria or to those who are hypersensitive or exhibit idiosyncrasy to barbiturates.

It should not be given to those who are taking MAO inhibitors or have received them during the previous 14 days. Franol should not normally be given during pregnancy or lactation and it should be used with caution in patients with cardiovascular disease, severe hypertension, hyperthyroidism, prostatic hypertrophy or glaucoma.

Overdosage: The symptoms of overdosage are likely to be those attributable to ephedrine and include excessive irritability, fever, nausea and vomiting, cyanosis, tachycardia, dilated pupils, opisthotonus, spasm, convulsions and respiratory embarrassment. If recently ingested and vomiting (due to the theophylline) has not occurred, the stomach should be emptied. Subsequent treatment should be symptomatic.

Side-effects: These are rare, any minor gastric disturbances can be avoided by taking the tablets with meals. The principal side-effects of theophylline when used alone is sedation, but in Franol Plus, this effect is counteracted by the increased dose of ephedrine.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Franol Plus is supplied in bottles of 50 and 250 tablets.

Further information Franol Plus consists of the Franol formulation with the addition of the antihistamine theophylline hydrochloride and an increased dose of ephedrine.

Product licence number 0071/5037.

GLURENORM*

Presentation Flat, white, bevelled-edged tablets, 9 mm in diameter, scored on one side and with G on the other, each containing 30 mg gliquidone.

Uses For the treatment of maturity-onset diabetes, including those with impaired renal function, who do not respond adequately to dietary control.

Dosage and administration Glurenorm should be taken up to half an hour before a meal. The daily dose should be adjusted according to the patient's metabolic state, and the frequency of administration may be varied to obtain the best possible control of the diabetes throughout the day. Most patients respond to a total daily dose of 45–60 mg given in two or three divided doses, of which the largest dose is usually taken in the

morning with breakfast. The recommended maximum single dose is 60 mg (2 tablets) and the maximum daily dose 180 mg (6 tablets).

During stabilisation, dosage adjustment should be based on frequent blood and urinary sugar determinations.

Stabilisation of previously untreated cases: Optimum control is usually obtained with divided doses spaced by reference to diet, normal daily activities of the patient and the daily blood-sugar profile. Normally, treatment should begin with 15 mg (half a tablet) before breakfast and this should be gradually increased by 15 mg increments. It should be noted that increasing the single dose beyond 60 mg or the daily dose beyond 120 mg produces little additional improvement in the blood-sugar levels of most patients.

Change-over in patients previously treated with other oral anti-diabetic agents: Patients can be changed over from other sulphonylureas to Glurenorm without interruption. It is usual to start with 30 mg Glurenorm increasing as necessary by increments of 15 mg. An estimate of the likely dose for each patient can be made from their original regimens because, in terms of potency 30 mg Glurenorm corresponds approximately to 1,000 mg tolbutamide, 5 mg glibenclamide, 1,000 mg glymidine, 250 mg tolazamide, 250 mg chlorpropamide or 500 mg acetohexamide. Note that chlorpropamide has a much longer half-life than Glurenorm.

Change-over in maturity-onset diabetics previously treated with insulin: In patients treated with up to 30 i.u. of insulin daily, change-over to Glurenorm may be attempted with an initial dose of 30 mg accompanied by a simultaneous gradual reduction of the amount of insulin, provided the pancreas still contains some functioning β cells. Patients who change from insulin to Glurenorm should be strictly supervised and response assessed by frequent and regular blood-sugar determinations.

It may be possible to reduce the insulin requirements of patients who require more than 30 i.u. daily by the concurrent administration of Glurenorm. Blood-sugar should be monitored frequently during the change-over period.

Combined treatment: The administration of a biguanide with Glurenorm to patients who cannot be adequately controlled by Glurenorm alone will often achieve satisfactory stabilisation of blood-sugar levels.

Contra-indications, warnings, etc Glurenorm should not be used to replace insulin in insulin-dependent (juvenile) diabetics.

Patients subject to the stress of surgery or acute infections should be temporarily transferred to insulin. It will also be easier to control blood-sugar with insulin during pregnancy and in patients with severe hepatic or renal failure.

Patients who miss a meal (particularly the elderly or debilitated) should be warned not to take their dose of Glurenorm, in order to reduce the risk of a hypoglycaemic reaction.

The effect of Glurenorm may be increased by physical exertion, alcohol, salicylates, sulphonamides, phenylbutazone, ethionamide, coumarin anticoagulants, chloramphenicol, tetracyclines, cyclophosphamide, MAO inhibitors and β -adrenergic blocking agents.

It may be necessary to increase the dose of Glurenorm when any of the following are administered concurrently: oral contraceptives, chlorpromazine, sympathomimetic

agents, corticosteroids, thyroid hormones and nicotinic acid preparations.

The effect of barbiturates, vasopressin and oral anti-coagulants are potentiated by the administration of Glurenorm.

Side-effects: Glurenorm is well tolerated. There have been some reports of minor skin allergies, gastric upsets and other non-specific side-effects. Reversible leucopenia has been reported on one occasion and reversible thrombocytopenia twice, but a causal connection with Glurenorm was not established.

Hypoglycaemic reactions are infrequent, but should they occur, they may be treated with oral carbohydrate, or with intravenous dextrose if the oral route is impractical. Glucagon (1 mg subcutaneously) could also be given.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Bottles of 100 tablets.

Further information Glurenorm is a sulphonylurea hypoglycaemic agent which is rapidly absorbed, its action starts within one hour and its optimum effect lasts two to three hours. It is almost completely metabolised in the liver by hydroxylation and demethylation. Only 5% of the pharmacologically inactive metabolites is excreted by the kidneys, the remainder is eliminated in the faeces via the bile. There is thus little risk of hypoglycaemia due to drug accumulation in patients with impaired renal function.

Product licence number 0071/0155.

HAYPHRYN* NASAL SPRAY

Presentation Hayphryn Nasal Spray is a clear, colourless solution containing 0.5% w/v Phenylephrine Hydrochloride BP and 0.1% w/v phenyldiamine hydrochloride in a plastic spray bottle presentation. The solution has a faint odour and foams when shaken.

Uses Hayphryn Nasal Spray is recommended for the relief of nasal congestion in such conditions as the common cold, sinusitis and vasomotor rhinitis, particularly when an allergic factor is present as, for example, in hay fever and allergic rhinitis.

Dosage and administration For nasal administration only.

Adults: The tip of the atomiser should be inserted into each nostril in turn and the container squeezed twice, sharply, as the patient breathes in. The application may be repeated in three to four hours if necessary.

Children: For children the product may be administered as for adults, except that the container is squeezed once only into each nostril.

Contra-indications, warnings, etc Because it contains a sympathomimetic amine. Hayphryn Nasal Spray should not be used by patients taking monoamine oxidase inhibitors and it should be used with caution by patients taking β -adrenergic blocking agents. Hayphryn Nasal Spray should not be used for longer than three weeks, and should not be used for chronic nasal congestion.

Excessive or too prolonged use of Hayphryn Nasal Spray may lead to secondary congestion. Oral overdosage is unlikely to be a problem since the quantities of

active ingredients in each spray are insufficient to cause any serious reaction.

Adverse effects are uncommon when the spray is used as recommended.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Plastic spray bottles containing 15 ml.

Further information Nil.

Product licence number 0071/5041.

HEXOPAL* TABLETS AND SUSPENSION

Presentation 1. Hexopal Suspension is a smooth white fluid with a sweet odour and taste, which contains Inositol Nicotinate BP 1,000 mg in each 5 ml.

2. Hexopal Tablets are white or almost white, flat tablets with bevelled edges, 12.7 mm in diameter, marked with a symbol on one side and scored on the other. Each tablet contains 500 mg Inositol Nicotinate BP.

Uses Hexopal is recommended for the symptomatic treatment of conditions arising from arterial insufficiency, such as intermittent claudication, and in peripheral and cerebral arteriosclerosis.

It is also recommended for the treatment of vasospastic conditions including chilblains, primary and secondary Raynaud's phenomenon, night cramps, restless legs, acrocyanosis and erythrocyanosis, and other conditions where a peripheral vasodilator is required.

Dosage and administration For oral administration only.

Adults: In the symptomatic treatment of conditions arising from arterial insufficiency, such as intermittent claudication, and in peripheral and cerebral arteriosclerosis, the usual starting dose is 1 g three times a day (i.e. 5 ml of Hexopal Suspension or 2 Hexopal Tablets three times a day), but this may be increased to 4 g daily if necessary. For patients with vasospastic conditions, including chilblains, primary and secondary Raynaud's phenomenon, night cramps, restless legs, acrocyanosis and erythrocyanosis, an initial dosage of 3 tablets daily is recommended, but dosage depends on response to treatment and may be increased to 3 or 4 g daily if necessary.

Contra-indications, warnings, etc There are no known contra-indications or precautions associated with the use of Hexopal, and side-effects are uncommon.

Hexopal appears to be virtually non-toxic to animals even in doses up to 100 times the normal therapeutic level. Despite extensive clinical experience in Britain since 1959, no case of poisoning or overdosage with Hexopal has been reported. In an emergency it is suggested that the stomach should be emptied by gastric lavage and symptomatic treatment given.

Pharmaceutical precautions When doses of less than 5 ml are ordered. Hexopal suspension may be diluted with Syrup BP so that the standard 5 ml spoonful may be given.

Legal category Hexopal Tablets GSL
Hexopal Suspension P.

Package quantities *Hexopal Tablets:* Bottles of 100 or 500

Hexopal Suspension: Bottles of 300 ml.

Further information In addition to a vasodilator effect thought to be due to the slow release of nicotinic acid, Hexopal appears to reduce blood viscosity. It also has a beneficial effect on the fibrinolytic system and on raised blood lipid levels.

Product licence numbers

Hexopal Tablets 0071/5043
Hexopal Suspension 0071/0090

HEXOPAL* FORTE

Presentation White or almost white, oval, bi-convex tablets marked HEX 750 on one side and scored on the other. Each tablet contains 750 mg Inositol Nicotinate BP.

Uses Hexopal Forte is for the symptomatic treatment of conditions arising from arterial insufficiency, such as intermittent claudication and in peripheral arteriosclerosis.

It is also recommended for the treatment of vasospastic conditions including chilblains, primary and secondary Raynaud's phenomenon, night cramps, 'restless legs', acrocyanosis and erythrocyanosis and other conditions where a peripheral vasodilator is required.

Dosage and administration *Adults:* In the symptomatic treatment of conditions such as secondary Raynaud's phenomenon, intermittent claudication and other forms of peripheral ischaemia due to arteriopathy, the usual starting dose is 3 g daily in divided doses. For arteriospastic conditions such as chilblains, acrocyanosis, erythrocyanosis, night cramps and 'restless legs', treatment may be started with a daily dose of 1.5 g, increasing to 3 g daily if necessary.

Contra-indications, warnings, etc There are no known contra-indications or precautions associated with the use of Hexopal, and side effects are uncommon. Hexopal appears to be virtually non-toxic to animals even in doses up to 100 times the normal therapeutic level. Despite extensive clinical experience in Britain since 1959, no cases of poisoning or overdosage with Hexopal have been reported. In an emergency, it is suggested that the stomach should be emptied by gastric lavage and symptomatic treatment given.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Hexopal Forte is supplied in bottles of 100 tablets.

Further information In addition to a vasodilator effect thought to be due to the slow release of nicotinic acid, Hexopal appears to reduce blood viscosity. It also has a beneficial effect on the fibrinolytic system and on raised blood lipid levels.

Product licence number 0071/0164.

KANNASYN*

Presentation Kannasyn Powder is a white, or almost white, crystalline powder. The powder is filled into vials containing Kanamycin Acid Sulphate BP equivalent to 1 g kanamycin base.

Kannasyn Solution is a sterile aqueous solution containing Kanamycin Sulphate equivalent to 250 mg/ml kanamycin base in clear glass vials. The vials

are of 4 ml nominal fill to provide doses of 1.0 g kanamycin base as the sulphate.

Uses Kannasyn is recommended for the treatment of infections due to Gram-negative organisms resistant to other antibiotics. It may also be used in the treatment of certain staphylococcal infections due to multiple-resistant strains, and in gonorrhoea.

Dosage and administration

1. **Intramuscular injection:** *Adults:* In acute infections: 1 g daily in two to four equally divided doses. Therapy should be limited to either a total dosage of 10 g or six days' treatment, whichever represents the greater quantity of antibiotic.

In chronic infections: 3 g weekly (1 g on alternate days) or 1 g twice a day, twice weekly (4 g weekly). The total amount administered should not exceed 50 g.

Children: In acute infections: 15 mg/kg body weight daily in 2-4 equally divided doses.

In chronic infections: there are no specific dosage recommendations.

2. **Intravenous use:** This route is recommended only for gravely ill patients with overwhelming infections or with impending vascular collapse. Kannasyn may be given as a solution containing 2.5 mg/ml by slow intravenous infusion at the rate of 3-4 ml per minute. The dosage for both adults and children is 15-30 mg/kg body weight daily in 2 or 3 divided doses.

3. **Intrathecal administration:** *Adults:* 100 mg in 10 ml saline once per day.

Children: Under 1 year: 25 mg in 10 ml saline once per day.

Over 1 year: 50 mg in 10 ml saline once per day.

It should be noted, however, that 7.5 mg/kg intramuscularly has produced CSF concentrations of 9 mcg/ml in infants with bacterial meningitis. This is about double the CSF concentration produced in normal infants and exceeds the MIC of many pathogens.

Contra-indications, warnings, etc Local intolerance to intramuscular injection has sometimes been reported, but it is transient and does not require interruption of therapy. Echinomoses have also been observed at the site of injection in a few patients. It has been suggested that high concentrations of kanamycin have anticoagulant properties, and this may explain these local haematomas at the injection site. It should, however, be noted that anticoagulant levels of kanamycin are not obtained in the blood with therapeutic doses. Sensitivity rashes appear to be uncommon. Intravenous injections are well tolerated and pain is not a problem. Thrombophlebitis has only been reported once in a patient who was receiving 50 million units of penicillin with the kanamycin.

As with other aminoglycoside antibiotics, apnoea and respiratory depression has been reported following the intraperitoneal use of kanamycin because of a curare-like effect. In addition, motor and sensory neuropathy has occurred following local application of kanamycin during spinal surgery, it has also produced slight weakening in muscle strength in a patient with myasthenia gravis. Because of these effects, it has been suggested that kanamycin should not be given intraperitoneally during surgery to patients who have received neuromuscular blocking agents.

Calcium gluconate has been suggested to counteract this curare-like action of kanamycin, but neostigmine appears to be more effective.

It has been shown that calcium can inhibit the antibacterial activity of kanamycin against certain organisms and for this reason the routine prophylactic use of calcium solutions with intraperitoneal kanamycin should be discouraged. In common with certain other antibiotics, kanamycin can affect the hearing when used in large doses or for long periods. This auditory damage, which may be permanent, is usually but not always preceded by tinnitus. Should this appear, the dose of kanamycin should be reduced or it should be discontinued. This antibiotic should always be administered with caution and preferably only in severe or resistant infections caused by organisms known to be sensitive to the compound, and blood levels should not be allowed to rise above 30 mcg/ml.

Hyaline and granular casts are sometimes observed in urine samples collected in the first 16 hours after administration in patients who have been given high doses of kanamycin. In these cases no permanent impairment of renal function occurs and the casts disappear within a few days of stopping treatment. Although nephrotoxic effects have been reported in some studies serious renal toxicity is not a frequent problem with the doses now used. It should be noted that prior treatment with streptomycin or viomycin may increase the likelihood of a nephrotoxic reaction with kanamycin.

In cases of impaired renal function, the kidney may be unable to eliminate kanamycin effectively and as a result the serum level will rise quickly. In these conditions reduced doses are necessary to avoid toxic effects. It has been reported that kanamycin is retained in the serum of patients with renal disease for a considerable time. If it is necessary to give the antibiotic to anuric patients, they should not receive increments more frequently than every three to four days and these increments should be one-half the loading dose used. The safest procedure, however, is to control the dosage by blood-level studies to prevent a rise above 30 mcg per ml.

The use of potent diuretics such as ethacrynic acid or frusemide with kanamycin should be avoided because they are known to potentiate the toxic action of aminoglycoside antibiotics.

Kanamycin is poorly absorbed from the gastro-intestinal tract and oral administration does not normally give rise to systemic side-effects.

Pharmaceutical precautions Kannasyn should be protected from light. The powder may be stored at room temperature but should be used within three years of assay. When dissolved in water, the solution will keep for two to three weeks at room temperature and for three weeks to one month if refrigerated. Solutions left at room temperature may discolour slightly, but there is no loss of activity for 24 days. This colour change may be prevented or retarded by adjusting the pH to 5.5. A bacteriostat such as a 0.5% phenol or 0.1% chlorocresol may be added.

Kannasyn Solution (4 ml vials) may also be stored at room temperature but should be used within two years of assay. There is no loss of potency when it is subjected to a temperature of 100°C for one hour. Dilutions of Kannasyn Solution may be made with normal saline or 5% dextrose and these remain stable for two to three months at room temperature. It should be noted, however, that such dilution may reduce the amount of bacteriostats to ineffective levels, and the reduction in concentration of sodium metabisulphite could lead to the solution developing a yellowish tint.

Infusion solutions containing kanamycin have been reported to be incompatible with the following substances: amphotericin, barbiturates, cephalothin sodium, chlorpromazine, electrolytes (Ca^{++} Mg^{++} , citrate or phosphate ions), heparin, hydrocortisone, methicillin sodium, methohexitone, nitrofurantoin, phenytoin, prochlorperazine, sulphafurazole.

Legal category POM.

Package quantities *Kannasyn Powder*: Boxes of 5 vials.

Kannasyn Solution: Boxes of 5 vials each containing 4 ml.

Further information Nil.

Product licence numbers

Kannasyn Powder 0071/5052

Kannasyn Solution 0071/5053

LENIUM®

Presentation Lenium is an orange-yellow cream which, on mixing with water, gives a copious soft foam and leaves a fine red to orange colour precipitate. It has a characteristic lavender odour, and contains 2.5% w/w Selenium Sulphide BP.

Uses Lenium is recommended for the control of pityriasis capitis and seborrhoeic dermatitis of the scalp and dandruff.

Dosage and administration Lenium is for topical use only for adults or children. The amount of Lenium required varies from person to person; sufficient should be used to allow the lather to penetrate to the scalp.

Lenium should be applied twice a week for two weeks, once a week for a further two weeks, then as required to maintain control of dandruff (every three to six weeks). After initial treatment it is neither necessary nor desirable to use Lenium weekly to maintain control.

Selenium sulphide has a low index of sensitivity and a low toxicity when applied to the intact skin. When used in accordance with the instructions it should not discolour grey or light hair and it can be used on hair which has been waved or tinted.

Contra-indications, warnings, etc The successful control of dandruff with Lenium may cause an increase in the secretion of the natural oil of the scalp. If this becomes excessive an ordinary shampoo should be used between Lenium treatments.

Precautions: Wash the hands thoroughly after use. Keep out of reach of children. Do not apply to broken or denuded skin. Selenium sulphide may discolour some metals. Do not apply at the time hot or cold permanent waves are being given. Do not allow to enter the eyes. More than 48 hours should elapse between the use of Lenium and the application of hair-tinting agents.

Accidental ingestion: Although insoluble selenium sulphide is less toxic than soluble selenium compounds it may produce signs of acute toxicity if swallowed. Apart from symptomatic measures treatment consists of gastric lavage and saline cathartics. Ascorbic acid orally may increase the rate of excretion in the urine. BAL should not be used as an antidote since it may aggravate symptoms.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Lenium is available in 9 g sachets and flexible plastic tubes containing 42 g or 100 g.

Further information Nil.

Product licence number 0071/5055.

LEVOPHED® LEVOPHED® SPECIAL

Presentation Levophed is a clear, colourless or almost colourless solution containing 2 mg/ml Noradrenaline Acid Tartrate BP (equivalent to 1 mg/ml noradrenaline base).

Levophed Special is a clear, colourless or almost colourless, sterile solution containing 0.2 mg/ml Noradrenaline Acid Tartrate BP (equivalent to 0.1 mg/ml of noradrenaline base).

Uses Levophed is recommended for use as an emergency measure to restore the blood pressure to normal in cases of acute hypotension.

Dosage and administration Levophed Solution should be diluted and administered as an intravenous infusion, preferably through a fine polythene catheter inserted into an arm or leg vein where blood flow is rapid. It is recommended that Levophed be administered in 5% dextrose or dextrose-saline solution.

Adults: A suitable initial concentration is obtained by adding 4 ml Levophed to a litre of infusion fluid to give a drug concentration of 4 mcg per ml. There is a direct relationship between the drip rate and the blood pressure. After observing the response to an initial dose of 2 ml or 3 ml per minute, the rate of flow should be adjusted to establish and maintain a low normal blood pressure (100–120 mm Hg systolic), or somewhat higher in previously hypertensive patients. In patients with severe haemorrhagic or hypovolaemic shock, when blood or fluid replacement has not been completed, it is preferable to maintain the pressure at a lower level sufficient to maintain the circulation to vital organs. The average maintenance dose ranges from 0.5 ml to 1 ml per minute, but there is great individual variation in the dose required to attain and maintain normotension. Infusion should be continued until adequate blood pressure is maintained without the help of Levophed. The concentration of the solution employed depends on the clinical needs. If larger volumes of fluid are required at a flow rate which would involve an excessive dose of pressor agent, the solution may be used more diluted than the 4 mcg/ml suggested. Conversely, where fluid volume should be restricted as in congestive heart failure, higher concentrations may be used.

Levophed Special: In cases of cardiac standstill the rapid intravenous or intracardiac injection of 0.50–0.75 ml of undiluted Levophed Special may restore a recordable blood pressure for one to four minutes. After intravenous injection the solution should be massaged towards the heart.

A similar dose may be repeated when the blood pressure starts to fall again or blood pressure can be maintained with normal Levophed drip. If there is no response to Levophed Special Solution administration intravenously, cardiac massage should be started with the injection of 0.50–0.75 ml Levophed Special into the ascending aorta or into the left auricle. Injection into the ventricle should be avoided because of the possible risk of inducing fibrillation. If the myocardium is fibrillating, a dose of Levophed Special may be injected after normal

rhythm has been restored by massage or by electrical defibrillation.

Contra-indications, warnings, etc Check blood pressure frequently during administration to avoid hypotension. Extravasation of the solution may cause local tissue necrosis. It has been suggested that phentolamine may be added directly to the infusion flask to act as an antidote against sloughing without affecting the vaso-pressor activity of the Levophed.

The use of pressor amines during halothane anaesthesia may cause serious cardiac arrhythmias. Because of the possibility of increasing the risk of ventricular fibrillation, Levophed should be used with caution in patients receiving cyclopropane or any other cardiac sensitising agent.

Pharmaceutical precautions Protect from light. The solution should not be used if it is brown in colour. Levophed is best administered in 5% dextrose or dextrose saline solution because the dextrose protects against significant loss of potency due to oxidation. Deterioration occurs more rapidly in normal saline, but plasma, blood and blood substitutes can be used as diluents, though Levophed is less stable in these than in dextrose solution. If Levophed is administered in blood, ascorbic acid (10^{-6}) should be added to reduce the rate of oxidation.

Infusion solutions containing noradrenaline acid tartrate have been reported to be incompatible with the following substances: alkalis and oxidising agents, barbiturates, chlorpheniramine, chlorothiazide, nitrofurantoin, novobiocin, phenytoin, sodium bicarbonate, sodium iodide, streptomycin.

Legal category POM.

Package quantities *Levophed:* Boxes of six 2 ml or 4 ml ampoules.

Levophed Special: Boxes of five 2 ml ampoules.

Further information Nil.

Product licence numbers

Levophed 0071/5056

Levophed Special 0071/5057

LINGRAINE®

Presentation Lingraine Tablets are bright green, bi-convex tablets, 6.4 mm in diameter, with no markings. Each tablet contains 2.0 mg Ergotamine Tartrate BP.

Uses Lingraine Tablets are recommended for the relief of migraine and other vascular headaches.

Dosage and administration Lingraine Tablets are for sublingual administration only.

Adults: 1 tablet to be taken at the first sign of an attack of migraine. If necessary another tablet may be taken half an hour to an hour later. No more than 3 tablets should be taken in 24 hours and not more than 8 tablets in any one week.

Contra-indications, warnings, etc Because ergotamine brings about constriction of peripheral blood vessels it should not be used in the presence of severe arteriosclerosis, coronary artery disease, thrombophlebitis, Raynaud's syndrome or Buerger's disease. Lingraine should not be used where there is liver or kidney dysfunction, and since (like other ergot alkaloids) it causes contraction of uterine muscle it should not be used during pregnancy.

dosage: Like all the natural amino-acid alkaloids of opium, ergotamine is a highly toxic substance which may cause chronic or acute poisoning, although the latter is infrequent. The oral administration of 26 mg over several days has proved fatal, and there have also been deaths from as little as 0.5 mg to 1.5 mg in a single action.

The principal signs of overdosage are convulsions and severe peripheral vasoconstriction, leading to gangrene of the extremities.

The main symptoms consist of vomiting, diarrhoea, quenchable thirst, tingling, itching and coldness of the skin, a rapid and weak pulse, confusion and consciousness. Amyl nitrate inhalations (0.2–0.3 ml) are suggested to maintain vasodilation. Gangrene of the extremities calls for surgical measures.

side-effects: These are a relatively minor problem if the use is carefully regulated. Nausea and vomiting are most frequently reported; other side-effects encountered include abdominal pain, leg cramps, vertigo, diarrhoea and, occasionally, increased headache.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Lingrain Tablets are available in 20 P. laminate strips in boxes of 12 tablets.

Further information Nil.

Product licence number 0071/5058.

LOBAK*

Presentation Lobak Tablets are white, flat tablets with bevelled edges, 12.7 mm in diameter, marked Lobak on one side and scored on the other. Each tablet contains 100 mg Paracetamol BP and 100 mg chlormezanone.

Uses For the treatment of painful conditions where the combination of an analgesic and a mild tranquilliser/muscle relaxant would be of value. Such conditions include the short-term symptomatic treatment of acute musculoskeletal disorders associated with painful muscle spasm.

Dosage and administration For oral administration only.

Adults: The usual dose is 1 or 2 tablets three times daily. The dosage should be adjusted to the patient's response, but should not exceed 8 tablets daily.

Elderly: Half the normal adult dose or less may be sufficient for a therapeutic response in the elderly. Not recommended for children.

Contra-indications, warnings, etc *Precautions and drug interactions:* Chlormezanone at high doses may modify the patient's reactions (performance at skilled tasks, alertness, etc.) to a varying extent, depending upon individual susceptibility. Therefore patients should be advised not to drive or operate machinery during treatment, if affected. If Lobak is administered with CNS depressants, it is possible that their sedative effect may be intensified. As with other drugs acting on the central nervous system, patients should avoid alcohol while receiving Lobak since the response cannot be predicted.

Lobak should be given with caution to patients with hepatic or renal insufficiency.

There is insufficient evidence of safety of chlormezanone in human pregnancy nor is there evidence from

animal work that it is free from hazard. Do not use Lobak during pregnancy especially the first trimester, unless there are compelling reasons.

Overdosage: should be treated by gastric lavage (if the product has been recently ingested). The signs and symptoms following chlormezanone overdosage will probably resemble those seen with other central depressant drugs, for example, somnolence, prostration, muscular incoordination and memory disturbance. In severe cases hypotension, respiratory depression and loss of consciousness may occur. Symptomatic treatment is suggested for chlormezanone overdosage.

Patients who have taken an overdose of paracetamol may appear well for the first three days then succumb with liver damage. The hepatic changes produced by overdose of paracetamol result from the accumulation of a highly reactive intermediate metabolite in the hepatocytes. N-acetylcysteine intravenously or 1-methionine orally protect the liver if administered within 10 hours of ingesting an overdose.

Side-effects: Drowsiness and dizziness have been the commonest side effects, particularly at higher doses. Other reported side effects include nausea, lightheadedness, headache, lethargy, skin rashes and dryness of the mouth. Cholestatic jaundice has occurred.

The dependence potential of chlormezanone is not known.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Lobak is supplied in bottles of 50 or 500.

Further information Chlormezanone acts by blocking polysynaptic reflex pathways both in the subcortical centres and in the spinal cord. It has no direct action on skeletal muscle, nor does it affect myoneurial junctions or peripheral nerves. At non-toxic levels, it has no action on the autonomic nervous system, nor any direct action on smooth muscle.

Product licence number 0071/5059.

LUMINAL*

Presentation Luminal Tablets are white, bi-convex tablets, 6.0 mm in diameter, marked III on one side and either LUM 15, LUM 30 or LUM 60 on the other. Each tablet contains 15 mg, 30 mg or 60 mg Phenobarbitone BP respectively.

Uses Luminal Tablets are recommended primarily for use as a general sedative, particularly in epilepsy and all other conditions requiring long-term sedation. They may also be used as a hypnotic.

Dosage and administration For oral administration only.

Adults: As a general sedative the dosage ranges from 15 mg to 30 mg two or three times daily and 100–300 mg may be employed as a hypnotic. The dose should not exceed 600 mg in 24 hours, and the effect of such large doses should be carefully watched.

Children: 1–12 years: 30–60 mg daily.

Up to 1 year: 15–30 mg daily.

Contra-indications, warnings, etc

Contra-indications: Acute intermittent porphyria and

patients who are hypersensitive or who exhibit idiosyncrasy to barbiturates.

Precautions: Phenobarbitone in daily doses is cumulative and its effects will eventually extend into the day if used on many successive nights. It is therefore more suitable for continuous sedation than for regular hypnosis. Continuous use of excessive amounts may result in ataxia, stupor and delirium, and the possibility of tolerance and drug dependence of the barbiturate-alcohol type should always be borne in mind. In these circumstances, abrupt cessation of treatment may give rise to withdrawal symptoms.

Some patients exhibit idiosyncrasy to barbiturates, and such individuals' response to these compounds is likely to be restlessness and excitement even in the absence of pain.

Barbiturates should be used with caution in debilitated or senile patients. Large doses should not be given to patients with renal impairment or with diseases of the liver. In severe pulmonary insufficiency even hypnotic doses of barbiturates will depress the respiration. Barbiturates may potentiate the central depressant effect of alcohol and affect the action of a number of other drugs, by hepatic enzyme induction including coumarin type anticoagulants, systemic steroids (including oral contraceptives), phenytoin, griseofulvin, rifampicin, phenothiazines and tricyclic antidepressants.

Overdosage: Where patients are seen within four hours of taking an overdose, gastric aspiration or lavage may be beneficial in adults, while children who are conscious may be given an emetic, e.g. Syrup of Ipecacuanha.

The prime objective in treating phenobarbitone overdose is to maintain vital functions (respiration, cardiovascular and renal function, and electrolyte balance) while the majority of the drug is metabolised by hepatic enzymes. At the same time some of the drug is excreted unchanged by the kidneys. Given normal renal function, this latter process may be enhanced by alkaline diuresis, maintaining the urinary pH at about 8 by appropriate intravenous infusion. In severe cases, haemodialysis may help, but extracorporeal haemoperfusion is probably more effective.

Side-effects: These are usually manifestations of the drug's depressant effect on the CNS but rashes can also occur.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities *Luminal Tablets 15 mg:* Bottles of 100.

Luminal Tablets 30 mg: Bottles of 100 or 500.

Luminal Tablets 60 mg: Bottles of 250.

Further information Nil.

Product licence numbers

Luminal 15 mg 0071/5060

Luminal 30 mg 0071/5061

Luminal 60 mg 0071/5062

MICTRAL*

Presentation A mixture of granules containing particles varying in colour from white to yellow. When added to water, they disperse with slight effervescence, yielding a butterscotch-flavour suspension. Each 7 g of granules contains Nalidixic Acid BP 660 mg, Sodium Citrate BP

3.75 g, Anhydrous Citric Acid BP 250 mg and Sod Bicarbonate BP 250 mg.

Uses For the treatment of cystitis and lower urinary tract infections caused by pathogens sensitive to nalidixic acid.

Dosage and administration For oral administration only.

Adults: The contents of one sachet should be dissolved in a tumblerful of water and taken three times a day. A day course is normally sufficient. Not recommended for children.

Contra-indications, warnings, etc Nalidixic acid should not be given to patients with a history of convulsive disorders. It should be used with caution in patients with liver disease. Patients should avoid excessive exposure to sunlight. Although there is no evidence that nalidixic acid has any harmful effect during pregnancy, careful consideration should, as with all drugs, be given to the use of Mictal granules during the first trimester. Small amounts of nalidixic acid may be excreted in human milk. When nalidixic acid is given to patients on anticoagulant therapy, it may be necessary to reduce the anticoagulant dosage. Mictal may precipitate a haemolytic reaction in G-6-PD-deficient individuals. Each sachet contains the equivalent of 950 mg sodium.

Active proliferation of the organisms is a necessary condition for the antibacterial action of nalidixic acid. The action of Mictal may therefore be inhibited by the presence of other antibacterial substances.

When testing for glycosuria in patients receiving Mictal, 'Clinistix' or 'Tes-Tape' should be used since other reagents may give a false-positive result.

Nalidixic acid, in therapeutic doses, can interfere with the estimation of urinary 17-ketosteroids and may cause high results in the assay of urinary vanilmandelic acid (Pisano method).

Overdosage: Because of the nature of the product, serious overdosage is unlikely. An excessive amount of granules is likely to cause vomiting.

Side Effects: Gastro-intestinal effects (constipation, diarrhoea, anorexia, nausea or vomiting) and subjective visual disturbances have been reported with nalidixic acid. They have resolved on reducing the dose or discontinuing treatment. If skin rashes occur, administration of Mictal should be stopped.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Cartons containing nine sachets.

Further information Sodium citrate raises the urinary pH. In these conditions, it has been shown that the amount of free nalidixic acid and of its active metabolite which appears in the urine is more than doubled as a result of a corresponding reduction in inactive glucuronides.

Product licence number 0071/0126.

MYCARDOL*

Presentation Mycardol Tablets are white, flat tablets with bevelled edges, 7.9 mm in diameter, marked M

e side and scored on the other. Each tablet contains mg pentaerythritol tetranitrate.

Uses Mycardol Tablets are recommended for the symptomatic treatment of angina pectoris. They are not recommended as a single measure for the treatment of ginal attacks, but rather as an adjunct to glyceryl trinitrate.

Dosage and administration For oral administration ly.

Adults: The usual dosage is 2 tablets three times a day, though some may need 2 tablets four times daily. If there nocturnal pain, the last dose should be taken before going to bed. The tablets should be taken before meals.

Children: There are no dosage recommendations for children.

Contra-indications, warnings, etc Mycardol should not be used immediately following a coronary thrombosis. It should be used with caution in cases of angina pectoris.

Overdosage: There have been no reports of Mycardol overdosage.

The possible effects of pentaerythritol tetranitrate toxicity are reported as being: cyanosis, methaemoglobinemia, severe headache, fall in blood pressure, muscular weakness, dizziness, palpitation, vomiting and diarrhoea. Chronic overdosage may result in confusion and collapse, particularly in sensitive patients.

In the event of severe headache due to overdosage, caffeine, neostigmine or amphetamine are indicated.

Methylene blue is usually recommended for the correction of methaemoglobinemia: it is also indicated in the event of cyanosis (up to 50 ml of 1% solution i.v.). Treatment of other serious toxic effects will consist of gastric lavage and saline cathartics (e.g. sodium sulphate, 30 g in 250 ml). Blood pressure should be restored by external means (prone position with feet raised) or by epinephrine, 15 mg i.m.

Side-effects: No serious side-effects have been encountered following normal dosage, even over long periods. Headache, lethargy and nausea can occur during the first few days of treatment. If palpitations or vomiting occur, treatment should be stopped.

Methaemoglobinemia is rarely seen with therapeutic dosage. Tolerance to Mycardol does not appear to develop.

Pharmaceutical precautions Store in a cool place and protect from light.

Legal category P.

Package quantities Mycardol Tablets are supplied in bottles of 100.

Further information Nil.

Product licence number 0071/5065.

NEOPHYRYN*

Presentation Neophryn Nasal Drops consist of a clear, colourless solution containing 0.25% w/v Phenylephrine Hydrochloride BP.

Neophryn Nasal Spray is a clear, colourless solution containing 0.5% w/v Phenylephrine Hydrochloride BP in a plastic spray bottle presentation. The solution has a faint aromatic odour and foams when shaken.

Uses Neophryn Nasal Drops and Neophryn Nasal

Spray are recommended for the relief of nasal congestion in such conditions as the common cold, sinusitis and vasomotor rhinitis.

Dosage and administration

1. **Neophryn Nasal Drops:** *Adults:* 2–3 drops in each nostril. In sinusitis, Neophryn Drops are well adapted to the Proetz displacement technique, but the alternative lateral head low method may equally well be used.

Children: 1–2 drops in each nostril.

2. **Neophryn Nasal Spray:** *Adults:* The tip of the atomiser should be inserted into each nostril in turn and the container squeezed twice, sharply, as the patient breathes in. The application may be repeated in three to four hours if necessary.

Contra-indications, warnings, etc Because Neophryn contains a sympathomimetic amine it should not be used by patients taking monoamine oxidase inhibitors and it should be used with caution by patients taking β -adrenergic blocking agents. Neophryn appears to be remarkably free from side-effects, but like all solutions for nasal application, it should be used for short periods only, because prolonged use may permanently damage the respiratory mucosa, and may even induce hypersensitivity. It is therefore suggested that Neophryn should not be used for longer than three weeks and that it should not be used for chronic nasal obstruction.

Toxicity resulting from local use is practically unknown because the local vasoconstrictor action of phenylephrine retards its absorption. In the alimentary tract, phenylephrine is hydrolysed and absorption is unpredictable. This, combined with the small amount in each pack, makes acute overdosage highly unlikely.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities *Neophryn Nasal Drops:* Bottles of 15 ml complete with dropper.

Neophryn Nasal Spray: Plastic spray bottles each containing 15 ml.

Further information Nil.

Product licence numbers

Neophryn Nasal Drops 0071/5069

Neophryn Nasal Spray 0071/5070

PANADEINE* CO.

Presentation Panadeine Co. Tablets are flat, white tablets with bevelled edges, 12.7 mm in diameter, marked Panadeine Co. on one side and scored on the other. Each tablet contains 500 mg Paracetamol BP and 8 mg Codeine Phosphate BP.

Uses Panadeine Co. Tablets are recommended for the treatment of most painful and febrile conditions such as headache, toothache, colds, influenza, dysmenorrhoea, arthritis and rheumatic pain.

Dosage and administration For oral administration only.

Adults: 2 tablets taken with a draught of water up to four times daily as required.

Children: 7–12 years: $\frac{1}{2}$ –1 tablet. This dose should not be repeated more frequently than every 4 hours and not more than 4 doses should be given in any 24-hour period.

Under 7 years: Panadeine Co. is not recommended.

Contra-indications, warnings, etc There is epidemiological evidence of the safety of paracetamol in human pregnancy. Codeine has been used for many years without apparent ill consequences and animal studies have not shown any hazard.

Overdosage: Nausea and vomiting are prominent symptoms of codeine toxicity and there is evidence of circulatory and respiratory depression. Suggested treatment is gastric lavage and catharsis, e.g. sodium sulphate 30 g. If CNS depression is severe, artificial respiration and oxygen may be necessary. Naloxone can be used to combat the depression.

Patients who have taken an overdose of paracetamol may appear well for the first three days, then succumb to liver damage. The hepatic changes produced by overdosage of paracetamol appear to result from the accumulation of a highly active intermediate metabolite in the hepatocytes. N-acetyl-cysteine intravenously, or l-methionine orally protects the liver if administered within 10 hours of ingesting an overdose.

Pharmaceutical precautions Panadeine Co. should be stored in well-closed containers protected from light and moisture.

Legal category P.

Package quantities Blister packs of 12, 24 and 48 tablets and bottles containing 100 or 1,000 tablets.

Further information Nil.

Product licence number 0071/5073.

PANADOL*

Presentation Panadol Tablets are flat, white tablets with bevelled edges, 12.7 mm in diameter, marked Panadol on both sides. Each tablet contains 500 mg Paracetamol BP.

Panadol Caplets. Capsule-shaped tablets, 17 mm long and 8 mm wide, marked Panadol on one face, each containing 500 mg Paracetamol B.P.

Panadol Soluble consists of white, bevelled-edged, unmarked, scored tablets which effervesce vigorously when placed in water. Each is 25.4 mm in diameter and contains 500 mg Paracetamol BP.

Panadol Elixir is a clear, yellow, viscous solution with a characteristic odour of passion fruit and containing 120 mg Paracetamol BP per 5 ml dose.

Uses Panadol is a mild analgesic and antipyretic. The tablets are recommended for the treatment of most painful and febrile conditions, for example, headache, toothache, colds, influenza, rheumatic pain and dysmenorrhoea.

Panadol Elixir is recommended for the treatment of painful and febrile conditions of childhood such as teething, headache, toothache, earache, general aches and pains, colds, influenza and reactions after immunisation and vaccination.

Dosage and administration For oral administration only. Panadol Soluble should be dissolved in a tumbler of water before taking. Panadol tablets, caplets and Panadol Soluble:

Adults: Two tablets up to 4 times a day, as required.

Children: 6–12 years: Half to one tablet. For younger children, use Panadol Elixir as follows:

3 months–1 year: Half to one 5 ml spoonful (preferably in milk).

1 year–6 years: One or two 5 ml spoonfuls.

6 years–12 years: Two to four 5 ml spoonfuls. Children should not be given doses of Panadol more frequently than every 4 hours and not more than 4 doses should be given in any 24-hour period.

Contra-indications, warnings, etc There is epidemiological evidence of the safety of paracetamol in human pregnancy. It should be noted that each Panadol Soluble tablet contains 421 mg ionic sodium and the fore caution is necessary in long-term use of them in patients with hypertension, cardiac or renal insufficiency, oedema of pregnancy or wherever salt-restricted intake is indicated.

Overdosage: It should be noted that patients who have taken an overdose of paracetamol may appear well for the first three days then succumb with liver damage. The hepatic changes produced by overdosage of paracetamol appear to result from the accumulation of a highly reactive intermediate metabolite in the hepatocytes. N-acetyl-cysteine intravenously, or l-methionine orally protects the liver if administered within 10 hours of ingesting the overdose.

Pharmaceutical precautions Where doses of less than 5 ml are ordered Panadol Elixir may be diluted with Syrup BP so that the standard 5 ml spoonful can be given. Such dilutions will remain stable for two to three weeks. Protect tablets from light and moisture.

Legal category 12s, 24s GSL, 48, 60s, 96s and 2,500 P. Panadol Elixir P.

Package quantities *Panadol Tablets:* Blister packs of 12, 24, 48 and 96 tablets and dispensing packs of 500 and 2,500.

Panadol Caplets are supplied in opaque blisters in cartons of 48.

Panadol Soluble tablets are packed in PFP laminated strips in cartons of 12, 24 and 60 tablets.

Panadol Elixir: Bottles containing 60 ml, 112 ml or 1 litre.

Further information Nil.

Product licence numbers

Panadol Tablets and Caplets	0071/5074
Panadol Elixir	0071/5075
Panadol Soluble Tablets	0071/0072

PANASORB*

Presentation Panasorb Tablets are flat, white tablets with bevelled edges, 12.7 mm in diameter, marked Panasorb on both faces. Each tablet contains 500 mg Paracetamol BP.

Uses Panasorb Tablets are recommended for the treatment of most painful and febrile conditions, for example, headache, toothache, colds, influenza, rheumatic pain and dysmenorrhoea.

Dosage and administration For oral administration only.

Adults: 2 tablets up to four times daily.

Children: Not suitable for children under 6 years old.

6–12 years: Half to one tablet.

These doses should not be repeated more frequently than every 4 hours, nor should more than 4 doses be given in any 24-hour period.

For younger children, it is recommended that Panadol (ir) be used.

Contra-indications, warnings, etc

There is epidemiological evidence of the safety of acetamol in pregnancy.

Dosage: It should be noted that patients who have had an overdose of paracetamol may appear well for the first three days, then succumb with liver damage. The metabolic changes produced by overdosage of paracetamol appear to result from the accumulation of a highly reactive intermediate metabolite in the hepatocytes. N-Acetyl-cysteine intravenously, or L-methionine orally protects the liver if administered within 10 hours of ingesting an overdose.

Pharmaceutical precautions Panasorb should be stored in well-closed containers protected from light and moisture.

Legal category 12s and 24s GSL, 250s and 1,000s P.

Package quantities Panasorb is available in blister packs of 12 or 24 tablets and in bottles of 250 and tins 1,000 tablets.

Further information Panasorb Tablets are formulated with a special sorbitol-containing base. Average blood levels of paracetamol with Panasorb are higher than those with crushed paracetamol tablets. Because of better absorption in poor paracetamol absorbers relief of symptoms may be more effective.

Product licence number 0071/5076.

PANODORM*

Presentation Panodorm Tablets are white, bi-convex tablets, 10.3 mm in diameter, marked with a triangle on one side and plain on the other side. Each tablet contains 10 mg Cyclobarbitone Calcium BP.

Uses Panodorm Tablets are recommended for the treatment of severe, intractable insomnia.

Dosage and administration For oral administration orally.

Dosage: $\frac{1}{2}$ –2 tablets before retiring.

Contra-indications, warnings, etc

Contra-indications: Barbiturate hypnotics should not be used in children, young adults, the elderly or in patients who are debilitated, or in those who have a history of alcohol or drug abuse. They are also contra-indicated in the presence of uncontrolled pain, pregnancy or breast feeding and porphyria.

Precautions: In patients with renal or hepatic failure, the dose should be reduced. Because barbiturates can decrease the activity of hepatic enzymes involved in drug metabolism, the availability and blood concentration of concurrently administered drugs may be altered. Among the compounds known to be affected are coumarin-type anticoagulants, systemic steroids (including oral contraceptives), phenytoin, griseofulvin, rifampicin, phenothiazines and tricyclic antidepressants.

Overdosage: Where patients are seen within four hours of taking an overdose, gastric aspiration or lavage may be beneficial in adults, while children who are conscious may be given an emetic, e.g. Syrup of Ipecacuanha. The prime objective in treating barbiturate overdosage is to maintain vital functions (respiration, cardiovascular

and renal function and electrolyte balance) while the majority of the drug is metabolised by hepatic enzymes. At the same time some of the drug is excreted unchanged by the kidneys. Given normal renal function, this latter process may be enhanced by alkaline diuresis, maintaining the urinary pH at about 8 by appropriate intravenous infusion. In severe cases, haemodialysis may help, but extracorporeal haemoperfusion is probably more effective.

Side Effects: Drowsiness, sedation, unsteadiness, vertigo and inco-ordination may occur. During the first week of administration, performance and alertness may be impaired; patients should be warned not to drive or operate machinery if affected. These effects may be potentiated by alcohol.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Panodorm is available in bottles of 50 tablets.

Further information Barbiturates have a high addiction potential. Long-term use or use of high doses for short periods may lead to tolerance and subsequently to physical and psychological dependence. Symptoms of dependence include confusion, defective judgement and loss of emotional control. Withdrawal symptoms occur after long-term normal use (and particularly after abuse) if barbiturate treatment is stopped abruptly. These include nightmares, irritability and insomnia and, in severe cases, tremors, delirium, convulsions and death. Withdrawal symptoms have been reported in neonates after barbiturate treatment during pregnancy and labour.

Product licence number 0071/5077.

pHiso-MED*

Presentation A white solution which forms suds when added to water. It contains 21.1% w/w Chlorhexidine Gluconate Solution BP (equivalent to 4% w/w chlorhexidine gluconate) and 2% Benzyl Alcohol BP as preservative.

Uses 1. Pre-operative preparation of surgeons' and nurses' hands and the skin of patients.

2. As an antiseptic skin cleanser for routine hand washing and for spots and acne on the face, shoulders and chest.

3. For use in maternity units by nurses and mothers, and for bathing babies, as a measure to prevent cross-infection.

Dosage and administration 1. *Pre-operative hand preparation:* Wet the hands and forearms, apply about 5 ml of solution and wash for one minute. Thoroughly clean finger-nails with a brush or scraper. Rinse, and repeat the wash for two minutes. Rinse thoroughly and dry. 2. *Preparation of patients for elective surgery:* Using a sterile swab, the solution is rubbed over the site and surrounding skin for two minutes, adding a little sterile water to work up a lather. Wipe off and dry thoroughly with fresh sterile swabs. Subsequently, at the time of operation, a 0.5% solution of chlorhexidine in alcohol should be applied to the site with sterile gauze swabs. The site and the surrounding skin should be rubbed vigorously for two minutes and until dry. 3. *As an antiseptic skin cleanser:* Wet the area to be cleaned, apply 5 ml of solution and wash for one minute. Rinse

thoroughly and dry. 4. *For bathing infants in maternity unit:* A 1 in 10 dilution of the solution is applied over the baby's body with a swab or with the palm of the hand. Rinse thoroughly with warm water and dry in the usual way.

Contra-indications, warnings, etc Chlorhexidine should not be allowed to come into contact with the brain, meninges or middle ear. During use, ensure that the solution is kept away from the eyes and ears. Material which has been in contact with the solution may be stained brown by hypochlorite bleaches.

Overdosage: If the solution is swallowed, it should be removed from the stomach by gastric lavage and symptomatic treatment applied as necessary.

Pharmaceutical precautions Protect from heat and light.

Legal category GSL.

Package quantities Containers of 150 ml.

Further information Nil.

Product licence number 0071/0178.

PLAQUENIL*

Presentation Plaquenil Tablets are smoothly polished, orange-coloured, sugar-coated tablets with no markings. Each tablet contains 200 mg Hydroxychloroquine Sulphate BP.

Uses Plaquenil Tablets are recommended for the treatment of rheumatoid arthritis, juvenile rheumatoid arthritis, discoid and systemic lupus erythematosus light-sensitive diseases, and the therapy and prophylaxis of malaria. The de-sludging action of Plaquenil may also be used for the prevention of post-operative deep vein thrombosis.

Dosage and administration

1. *For indications other than malaria and 'desludging'.*

Adults: up to 600 mg daily in divided doses. The minimum effective dose has yet to be determined but as little as 200 mg daily is often effective in systemic lupus erythematosus and rheumatoid arthritis. A reduction to this dose when a positive response has been obtained with a higher dose after 3-6 months may be attempted.

Children: 5-7 mg/kg body weight daily. Treatment should be discontinued if no improvement has occurred after 6 months.

2. **Malaria:** **Adults:** To treat an acute attack it is usual to give 800 mg (4 tablets) initially, followed by 400 mg (2 tablets) in six to eight hours, and then 400 mg on each of two successive days. A single dose of 800 mg has been used to eradicate *Plasmodium falciparum* infection and to terminate an acute attack of *Plasmodium vivax*.

3. **Malaria Prophylaxis:** **Adults:** a dose of 400 mg weekly.

Children: 6.4 mg/kg body weight once a week.

Prophylaxis should begin one week before arrival in a malarious area and continue for four to eight weeks after leaving the area.

4. **De-sludging:** **Adults:** Up to 800 mg daily in divided doses

Contra-indications, warnings, etc Because of the risk of irreversible retinal changes, all patients should

have an initial ophthalmological examination before treatment starts and every 3 months during treatment the event of scotomata, nyctalopia or other retinal changes occurring, Plaquenil should be discontinued immediately. When treating adults for long periods it is unwise to exceed a total dosage of 400 mg/day/year.

Because Plaquenil is known to concentrate in the liver it should be used with caution in patients with liver disease or those taking other drugs known to affect the liver. It should be used with caution or not at all in patients with severe gastro-intestinal, neurological blood disorders or with psoriasis.

Use of Plaquenil in pregnancy should be avoided except in the prophylaxis of malaria when the need must outweigh the possible risk.

The 4-aminoquinolines appear to exacerbate pre-existing porphyria. Plaquenil should be given with caution to patients with a history of quinine sensitivity. Drugs known to cause sensitisation or dermatitis, such as phenylbutazone or gold are probably best avoided during Plaquenil treatment. Plaquenil should be administered with caution in patients with glucose-6-phosphate dehydrogenase deficiency.

Though the risk of bone-marrow depression is low, periodic blood counts are advisable and Plaquenil should be discontinued if abnormalities develop. Corneal opacities sometimes appear which may be symptomless, which may cause disturbances such as haloes, blurring of vision or photophobia. They are reversible if treatment is stopped. Defects in visual accommodation may occur on first taking Plaquenil and patients should be warned regarding driving or operating machinery.

Skin reactions, bleaching of the hair and alopecia may also occur, but they usually clear up readily on cessation of treatment.

Patients with psoriasis appear to be more susceptible to skin reactions than others.

Small children are particularly sensitive to the 4-aminoquinolines, therefore patients should be warned to keep Plaquenil out of reach of children.

Other adverse effects include gastro-intestinal disturbances such as nausea, diarrhoea, anorexia, abdominal cramps or, rarely, vomiting. These symptoms usually stop immediately on reducing the dose or on temporarily stopping the treatment. Less frequently, muscle weakness, vertigo, tinnitus, nerve deafness, headache, nervousness and emotional upsets have been reported. Patients should be carefully supervised in view of reports of peripheral neuropathy and toxic psychosis with other 4-aminoquinoline compounds.

Overdosage: The symptoms of massive overdosage may include headache, visual disturbances, cardiovascular collapse, and convulsions, followed by sudden and early respiratory and cardiac arrest.

Since these effects may appear soon after taking massive dose, treatment should be prompt and symptomatic. The stomach should be immediately evacuated either by emesis or by gastric lavage. If convulsions are present, they should be controlled before the stomach is emptied by:

1. An ultra-short-acting barbiturate if due to cerebral stimulation, or
2. The administration of oxygen, or by artificial respiration is due to anoxia, or
3. By vasopressor therapy if due to shock hypotension.

A patient who survives the acute phase and asymptomatic should be closely observed for at least 5

rs. Fluids may be forced and sufficient ammonium oride may be administered to acidify the urine for a v days to hasten urinary excretion. Alternatively tereaprol can be given by intramuscular injection 1–3 mg/kg body weight four to six times a day for ee days, then every 12 hours for 10 days). Ammonium oride is also useful in patients who show toxic nptoms due to sensitivity to the drug. Recovery under treatment has followed the ingestion 36 Plaquenil Tablets while an estimated dose of 54 lets has proved rapidly fatal.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Plaquenil is supplied in bottles of 0 tablets.

Further information Nil.

Product licence number 0071/5083.

ROMINAL*

Presentation Prominal Tablets 30 mg are white, biconvex tablets, 6.4 mm in diameter, marked P30 on one side and plain on the other. Each tablet contains 30 mg ethylphenobarbitone BP.

Prominal Tablets 60 mg are white, biconvex tablets, 11 mm in diameter, marked P60 on one side and plain on the other. Each tablet contains 60 mg methylphenobarbitone.

Prominal Tablets 200 mg are white, bi-convex tablets, 13.3 mm diameter, marked P200 on one side and plain on the other. Each tablet contains 200 mg methylphenobarbitone.

Uses Prominal Tablets are recommended for the treatment of epilepsy.

Dosage and administration *Adults:* For epilepsy the usual dosages, which must be fixed individually, range from 100 to 600 mg, the average being 200–400 mg. It is recommended that sedative dosages range from 30 to 100 mg daily.

Contra-indications, warnings, etc

Contra-indications: Acute intermittent porphyria and patients who are hypersensitive or who exhibit idiosyncrasy to barbiturates.

Precautions: The possibility of tolerance or dependence developing should be considered. Abrupt cessation of treatment may give rise to withdrawal symptoms. Use with caution in senile or debilitated patients. Large doses should not be given to those with renal or liver damage. Severe pulmonary insufficiency, even normal therapeutic doses may depress respiration. Barbiturates may potentiate the central depressant effect of alcohol and affect the action of a number of other drugs.

Anticonvulsant drugs are as useful to an epileptic during pregnancy as they are at other times and for the individual epileptic mother the chance of an abnormal baby due to drug treatment is small. However, a number of reports have appeared in the literature suggesting the possible implication of the epileptic state, anticonvulsants and folic acid deficiency as causative agents in certain congenital abnormalities. Scientific knowledge does not yet permit an adequate definition to be made of the respective roles of these three factors. It is recom-

mended, therefore, that if anticonvulsants are judged necessary during pregnancy, adequate folic acid supplements should be given and the epilepsy controlled as completely as possible.

Overdosage: Where patients are seen within four hours of taking an overdose, gastric aspiration or lavage may be beneficial in adults, while children who are conscious may be given an emetic, e.g. Syrup of Ipecacuanha.

The prime objective in treating methylphenobarbitone overdose is to maintain vital function (respiration, cardiovascular and renal function, and electrolyte balance) while the majority of the drug is metabolised by hepatic enzymes. At the same time some of the drug is excreted unchanged by the kidneys. Given normal renal function, this latter process may be enhanced by alkaline diuresis, maintaining the urinary pH at about 8 by appropriate intravenous infusion. In severe cases, haemodialysis may help, but extracorporeal haemoperfusion is probably more effective.

Side Effects: Drowsiness, sedation unsteadiness, vertigo and inco-ordination may occur. During the first week of administration, performance and alertness may be impaired; patients should be warned not to drive or operate machinery if affected. These effects may be potentiated by alcohol. Other adverse reactions may include a 'hang-over' effect, paradoxical excitement, confusion, memory defects and skin rashes in patients who may be sensitive to this type of drug.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Prominal Tablets (30 mg, 60 mg and 200 mg) are supplied in bottles of 100.

Further information Nil.

Product licence numbers

Prominal Tablets 30 mg	0071/5084
Prominal Tablets 60 mg	0071/5085
Prominal Tablets 200 mg	0071/5086

PYROGASTRONE*

Presentation White, round, strawberry-flavoured chewable tablets. 22.2 mm in diameter, marked with a symbol on one side and PG on the other. Each tablet contains:

Carbenoxolone Sodium BP	20 mg
Magnesium Trisilicate BP	60 mg
Dried Aluminium Hydroxide Gel BP	240 mg

in a base containing 210 mg Sodium Bicarbonate BP and 600 mg Alginate Acid BP.

Uses For the treatment of oesophageal inflammation, erosions and ulcers due to hiatus hernia or other conditions causing gastric reflux and for the relief of heartburn, flatulence and other symptoms associated with reflux oesophagitis.

Dosage and administration For oral administration only.

Adults: 1 tablet to be chewed three times daily immediately after meals and 2 tablets to be chewed at bedtime.

Treatment should be continued for at least six weeks, but up to 12 weeks treatment may be necessary to ensure maximum healing effect.

Contra-indications, warnings, etc Pyrogastrone

should not be prescribed for patients suffering from severe cardiac, renal or hepatic failure. Nor should it be prescribed for patients on digitalis glycosides unless serum electrolyte levels are monitored at weekly intervals to detect promptly the development of hypokalaemia.

Special care should be exercised with patients predisposed to sodium and water retention, potassium loss and hypertension (e.g. the elderly and those with cardiac, renal and hepatic disease) since the carbenoxolone content of Pyrogastron can induce similar changes. Potassium supplements should be considered for those at risk from developing hypokalaemia.

Regular monitoring of weight and blood pressure which should indicate the development of such effects is advisable for all patients. A thiazide diuretic should be administered if oedema or hypertension occurs (spironolactone or amiloride should not be used because they hinder the therapeutic action of carbenoxolone). Potassium loss should be corrected by the administration of oral supplements.

No teratogenic effects have been reported with carbenoxolone sodium, but careful consideration should be given before prescribing Pyrogastron for women who may become pregnant.

Overdosage: If the tablets have been recently ingested, the stomach should be emptied by gastric lavage. Serum electrolytes should be monitored and any deficiency in potassium should be corrected, using the intravenous route if necessary or slow-release or effervescent tablets of potassium chloride. Water retention and sodium balance should be corrected by means of a diuretic. (Spironolactone or amiloride would appear to be a logical choice).

Pharmaceutical precautions Store in a dry place.

Legal category POM.

Package quantities Boxes containing 25 foil strips of 4 tablets.

Further information The alginate antacid base of Pyrogastron tablets forms a clinging viscous foam which has buffering capacity. This relieves symptoms, either by coating the oesophageal wall, by impeding oesophageal reflux, or the foam may reflux instead of the acid gastric contents. The incorporation of carbenoxolone into the formulation has been shown to exert an additional healing effect on oesophageal ulcers possibly by improving mucus synthesis and/or by increasing the life-span of oesophageal epithelium.

Although Pyrogastron quickly relieves symptoms, treatment should be continued for at least six weeks, but up to 12 weeks' treatment may be necessary to ensure a maximum healing effect.

Made under licence from Biorex Laboratories. Brit. Pat. No. 1390683.

Product licence number 0071/0138.

RESONIUM* A

Presentation Resonium A is ground and flavoured sodium polystyrene sulphonate. It is a buff-coloured powder with a pleasant vanilla odour and sweet taste.

Uses Resonium A is an ion-exchange resin which is recommended for the treatment of hyperkalaemia associated with anuria or severe oliguria. It is also used to treat hyperkalaemia in patients requiring dialysis and in

patients on regular haemodialysis or on prolonged peritoneal dialysis.

Dosage and administration Resonium A is for oral or rectal administration only. The dosage recommendations detailed in this section are a guide only; the precise requirements should be decided on the basis of regular serum electrolyte determinations.

Adults:

1. **Oral:** Usual dose 15 g three or four times a day. The resin is given by mouth in a little water, or it may be made into a paste with some sweetened vehicle.

2. **Rectal:** In cases where vomiting may make oral administration difficult, the resin may be given rectally as a suspension of 30 g resin in 100 ml 2% methylcellulose (medium viscosity) and 100 ml water, as a daily retentive enema. In the initial stages administration by this route as well as orally may help to achieve a more rapid lowering of the serum potassium level.

The enema should if possible be retained for at least nine hours. If both routes are used initially it is probably unnecessary to continue rectal administration once the oral resin has reached the rectum.

Children: 1 g/kg body weight daily in divided doses for acute hyperkalaemia. Dosage may be reduced to 0.5 g/kg body weight in divided doses for maintenance therapy.

The resin is given orally, preferably with a drink or little jam or honey. When refused by mouth it should be given rectally, using a dose at least as great as that which would have been given orally.

Contra-indications, warnings, etc The possibility of potassium depletion should be considered and adequate biochemical control is essential during treatment. Administration of the resin should be stopped when the serum potassium level falls to 5 mmol/litre.

Overdosage: In the event of overdosage the resin should be removed from the alimentary tract by the use of laxatives or enemas and appropriate measures taken to restore serum potassium levels to normal.

In patients with severe renal damage the sodium ion liberated by Resonium A may lead to sodium overload and congestive heart failure. In such cases Calcium Resonium (calcium polystyrene sulphonate) may be used in place of Resonium A.

Pharmaceutical precautions It is suggested that Resonium A should not be administered in fruit squashes since these have a high potassium content.

Legal category P.

Package quantities Lever-lid tins containing 454 g Resonium A together with a 15 g plastic spoon.

Further information Nil.

Product licence number 0071/5087.

ROCCAL* ANTISEPTIC ROCCAL* CONCENTRATE 10X

Presentation Roccal Antiseptic and Roccal Concentrate 10X are clear blue solutions containing 1% or 10% benzalkonium chloride respectively. The solutions, when shaken, have a characteristic antiseptic odour and are miscible with water in all proportions.

Uses Roccal is recommended for use as an antiseptic in wound cleansing (including cuts, bites and abrasions)

or sterilisation of dressings, breast and nipple shield hygiene, vaginal douching and as a bladder washout. It may also be used as a skin antiseptic and as a general disinfectant.

Dosage and administration Roccal is for topical use only. The following dilutions of Roccal Antiseptic are recommended for the uses indicated.

Use	Concentration of benzalkonium chloride	Dilution of Roccal
Bladder washout	1:5,000 to 1:20,000	1:50 to 1:200
Breast and nipple shield hygiene ect.	1:1,000 to 1:2,000	1:10 to 1:20
Dressings General	1:4,000	1:40
disinfectant	1:1,000 to 1:8,000	1:10 to 1:80
Skin disinfectant	1:1,000 to 1:2,000	1:10 to 1:20
Vaginal douching	1:2,000 to 1:5,000	1:20 to 1:50
Wound cleansing including cuts, bites and abrasions	1:1,000 to 1:5,000	1:10 to 1:50

Roccal Concentrate 10% is intended for the preparation of Roccal Antiseptic only, by diluting 1 in 10 with water.

Contra-indications, warnings, etc Roccal should not be mixed with strong soap solution or with antiseptics containing soap such as solutions of chloroxylenol, lysol, the black and white fluids or with products containing anionic detergents such as pHiso-MED.

Roccal appears to be relatively non-irritant to skin and mucous membranes. Although benzalkonium chloride may be used as a preservative for eye drops Roccal is not recommended for use in the eyes because of the additives it contains. The presence of benzalkonium chloride in a urine sample may give rise to a false-positive result in tests for protein.

Accidental ingestion: The oral toxic dose of benzalkonium chloride is estimated to be between 1 and 3 g. The main signs of poisoning are vomiting, collapse and coma. Roccal acts primarily as a local irritant on the throat, oesophagus and gastro-intestinal tract. Toxic doses lead to restlessness, apprehension, dyspnoea, cyanosis, convulsions, muscle weakness and death due to paralysis of respiratory muscles.

Treatment consists of giving milk, egg whites or even a mild soap solution by mouth, followed by emesis or gastric lavage with a weak soap solution. Respiration should be supported by oxygen or artificial respiration if necessary.

Convulsions should be treated by short-acting barbiturates. Central nervous system stimulants are usually ineffective.

Pharmaceutical precautions The potency of a 10% solution of benzalkonium chloride is unchanged even after 10 years of storage. Roccal may be boiled or autoclaved without loss of bactericidal activity as shown by phenol coefficient determinations. The efficacy of solutions of Roccal is not affected by freezing and subsequent thawing.

Dilutions of Roccal should not be prepared with tap

water due to possible interference by certain cations such as calcium, magnesium, iron and aluminium.

Roccal 1:10 (benzalkonium chloride 1:1,000) is compatible with the following substances:

Acriflavine	Natural rubber
Adrenaline	Oil of sassafras 1.5–2.5%
Alcohol	Oxytetracycline
Amethocaine NCI	Penicillin
Benzocaine	Phenol
Boroglycerin	Phenylephrine HCl
Camphor	Pilocarpine (2% solution or less)
Carbachol	Polyethylene glycol
Chlorbutol 1:5,000	Procaine HCl
Cocaine	Resorcin (cloudy when mixed)
Cresol	Rose water
Eosin	Scopolamine
Ephedrine HCl	Sodium bicarb. and phosphate
Eserine sulphate (not salicylate salt)	Sodium carbonate and sodium nitrate
Formaldehyde 1%	Sulphadiazine sodium
Fuchsin	Sulphanilamide
Glycerin 5–15%	Trisodium phosphate
Homatropine 5%	Urea
Hydrazine hydrate 0.1–0.5%	Urethane
Lime water	Zinc chloride (up to and including 1%)
Mercurial salts 1%	
Methylene blue	
Methylparaben	

But incompatible with these substances:

Aluminium	Citric acid
Benzylephedrine	Ethylparaben
Boric acid 5%	Fluorescein sodium
Caramel	Hydrogen peroxide
Iodine	Sodium citrate and tartrate
Kaolin	Sodium lauryl sulphate
Lanolin	Sulphapyridine
Mild silver proteinate	Sulphathiazole
Physostigmine	Sulphathiazole sodium
Pilocarpine nitrate (3% or more)	Synthetic rubber (some)
Pine oil	Tartaric acid
Potassium iodine	Yellow oxide of mercury
Potassium permanganate	Zinc oxide
Saponin 0.1–0.5%	Zinc peroxide
Silicates	Zinc sulphate
Silver salts	

Legal category GSL.

Package quantities Roccal Antiseptic is supplied in glass bottles containing 250 ml or 500 ml, or in translucent plastic bottles containing 2.25 litres.

Roccal Concentrate 10X is supplied in translucent plastic bottles containing 2.25 litres or amber glass bottles containing 4.54 litres.

Further information Nil.

Product licence numbers

Roccal Antiseptic 0071/5088

Roccal Concentrate 0071/5089

SEOMINAL*

Presentation Seominal Tablets are pale yellow, bi-convex tablets, 10.3 mm in diameter, marked III on one side and scored on the other. Each tablet contains 10 mg Phenobarbitone BP, 325 mg Theobromine BP and 0.2 mg Reserpine BP.

Uses Seominal Tablets are recommended for the treatment of mild to moderate essential hypertension.

Dosage and administration *Adults:* The average initial dosage of Seominal is 1 tablet twice daily, or for the more severe cases, three times daily, but the possibility of excessive sedation must be borne in mind. This dosage is continued until improvement has been maintained for some time.

Thereafter the daily dosage may be reduced to 1 tablet. Some patients may even discontinue with the drug for a time.

It must be emphasised that, because of the slow onset of hypotensive action, no improvement in blood pressure readings may be observed for a month or so, although a tranquillising effect may be apparent within a few days. Thereafter Seominal should be continued for some weeks in full dosages.

Contra-indications, warnings, etc

Contra-indications: Seominal should not be used for patients with anxiety or depression or in those with gastric ulceration, cardiac arrhythmia, myocardial infarction or renal failure. It should not be given with MAO inhibitors. It may cause severe hypotension in patients who have recently suffered strokes.

It is also contra-indicated in acute intermittent porphyria and in those who are hypersensitive or exhibit an idiosyncrasy to barbiturates.

Precautions: Some patients exhibit idiosyncrasy to barbiturates, and such individuals' response to these compounds is likely to be restlessness and excitement even in the absence of pain. Skin reactions are the most common type of allergic manifestation. Barbiturates should be used with caution in debilitated or senile patients. Large doses should not be given to patients with renal impairment or with diseases of the liver. In severe pulmonary insufficiency, even normal doses of barbiturates may depress the respiration.

The possibility of tolerance or dependence developing should be considered. Abrupt cessation of treatment in these circumstances may give rise to withdrawal symptoms. Barbiturates may potentiate the central depressant effect of alcohol and affect the action of a number of other drugs, by hepatic enzyme induction including coumarin type anticoagulants, septemic steroids (including oral contraceptives), phenytoin, griseofulvin, rifampicin, phenothiazines and tricyclic antidepressants.

Overdosage: There have been no reports of overdosage with Seominal. Symptoms of acute toxicity would probably be those caused by the individual ingredients. Theobromine could cause gastro-intestinal disturbances, haemorrhage, insomnia, tremor and convulsions. An overdosage of reserpine may produce diarrhoea, dizziness, fatigue, headache, nasal stuffiness, flushing, hypotension and bradycardia or tachycardia, Parkinsonism, convulsions, etc. Diphenhydramine may be used for the Parkinsonism and noradrenaline or phenylephrine for the hypotension.

Where patients are seen within four hours of taking an overdose, gastric aspiration or lavage may be beneficial in adults, while children who are conscious may be given an emetic, e.g. Syrup of Ipecacuanha.

The prime objective in treating phenobarbitone overdosage is to maintain vital functions (respiration, cardiovascular and renal function, and electrolyte balance) while the majority of the drug is metabolised by hepatic enzymes. At the same time some of the drug is excreted unchanged by the kidneys. Given normal renal function,

this latter process may be enhanced by alkaline diuresis maintaining the urinary pH at about 8 by appropriate intravenous infusion. In severe cases, haemodialysis may help, but extracorporeal haemoperfusion is probably more effective.

Diuresis will not hasten the excretion of theobromine or reserpine. Measures may be required to correct the hypotensive effect of reserpine, supportive measures including the head-down position, the intravenous infusion of plasma expanders and the administration of a vasopressor agent such as noradrenaline or dopamine may be indicated.

Side-effects: Minor reactions include excessive sedation, headache, dizziness, nasal stuffiness, dry mouth, nausea, diarrhoea or cutaneous eruptions. Lowering the dose or halting medication for a short time generally results in their disappearance. Mental depression is the most serious side-effect associated with reserpine. If depressive symptoms develop during treatment with Seominal the drug must be stopped, and if the depression does not resolve within a few days psychiatric advice should be sought.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Seominal is available in bottles of 100 or 500 tablets.

Further information Nil.

Product licence number 0071/5090.

SOLPADEINE*

Presentation Solpadeine Tablets are flat, white, bevelled edged tablets which effervesce vigorously when placed in water. Each tablet is 25.4 mm in diameter and contains 500 mg Paracetamol BP, 8 mg Codeine Phosphate BP and 30 mg Caffeine BP.

Uses Solpadeine Tablets are recommended for the relief of pain in the treatment of rheumatic pain, sciatica and lumbago as well as in sprains and strains, headaches, sinusitis and influenza.

Dosage and administration *Adults:* 2 tablets dissolved in at least half a tumbler of water, taken three or four times a day if necessary.

Children: Children 7–12 years old may be given $\frac{1}{2}$ –1 tablet dissolved in water. Children should not be given doses of Solpadeine more frequently than every 4 hours and not more than 4 doses should be given on any 24-hour period.

Not suitable for children under 7 years of age.

Contra-indications, warnings, etc Solpadeine contains 425 mg sodium in each tablet. It should therefore be prescribed with caution in long-term treatment of patients with hypertension, cardiac or renal insufficiency, oedema of pregnancy or wherever a restricted salt intake is indicated.

There is epidemiological evidence of the safety of paracetamol in human pregnancy. Codeine has been used for many years without apparent ill consequences and animal studies have not shown any hazard.

Overdosage: Ingestion of an excessive number of Solpadeine Tablets is unlikely because of the size of the tablets and their effervescent nature.

Naloxone can be used to combat the depression due to codeine overdosage. An overdosage of paracetamol

can cause hepatic necrosis. Patients appear well for the first three days, then succumb with liver damage. The hepatic changes produced by overdosage of paracetamol appear to result from the accumulation of a highly reactive intermediate metabolite in the hepatocytes. N-acetyl-cysteine intravenously, or l-methionine orally, protects the liver if administered within 10 hours of ingesting an overdose.

Pharmaceutical precautions Solpadeine Tablets should be protected from light and moisture.

Legal category P.

Package quantities Solpadeine Tablets are packed in laminate strips and supplied in boxes of 12, 24 and 60 tablets.

Further information Nil.

Product licence number 0071/5091.

SULFAMYLYL* CREAM

Presentation Sulfamylon Cream is a smooth, white to pale yellow, water-miscible cream with a slight acetous odour and containing 8.5% w/w mafenide as the acetate.

Uses Sulfamylon Cream is recommended for the prophylaxis and treatment of infection, particularly that due to *Pseudomonas* species in second and third degree burns.

Dosage and administration Sulfamylon Cream is for topical use only.

Adults: Sulfamylon Cream should be applied to a thickness of 1–2 mm (a layer sufficient to prevent seeing the burn surface), once or twice daily with a sterile gloved hand. Any covering lost owing to a change of body linen or a shift of position should be replaced by further applications. In the first 24 hours of the post-burn period the wound is moist and exudative and may require more frequent applications. Dressings are not usually required, but if necessary a thin layer of gauze may be used.

The length of treatment will depend on the rate of separation of the eschar and the appearance of the granulating surface necessary for skin grafting. Duration of treatment may vary from five days to three to four weeks.

Children: The product should be applied according to the recommendations for adults.

Contra-indications, warnings, etc Sulfamylon Cream should not be used if the patient has a known sensitivity to mafenide or any other sulphonamide. It is not known if there is cross-sensitivity to other sulphonamides. It should be used with care in patients with known pulmonary dysfunction. If persistent acidosis occurs, treatment should be suspended for 24–48 hours, when continuous fluid therapy will usually restore acid-base balance.

Fungal colonisation in and below the eschar may occur concomitantly with reduction of bacterial growth in the burn wound. However, fungal dissemination through the infected burn wound is rare.

As is the case with all preparations, the need for treatment during pregnancy should be carefully weighed against any possible risk to the foetus. Occasionally application of the cream may be accompanied by pain or a burning sensation severe enough to require an analgesic or sedation. Allergic manifestations, such as

maculopapular rash, oedema, erythema and eosinophilia, also occur in a small portion of patients.

Pharmaceutical precautions Store in cool, not refrigerated conditions, and protect from light. The cream has an estimated shelf-life of 12 months. The normal precautions involved in aseptic dressing should be observed to prevent contamination. It is recommended that each patient should have an individual jar of cream and any cream remaining after 24 hours should be discarded.

Legal category POM.

Package quantities Black plastic jars each containing 500 g.

Further information Nil.

Product licence number 0071/5093.

SULFOMYL*

Presentation Sulfomyl is a clear, colourless solution in a dropper-bottle presentation. The solution contains 5% w/v mafenide propionate and has an odour of chlorbutanol.

Uses Sulfomyl is recommended for the treatment of superficial eye infections.

Dosage and administration *Adults: First-aid for minor eye injuries:* 3 or 4 drops are instilled into the injured eye.

Established infection: 3 or 4 drops are instilled into the eye three or four times a day.

Children: The adult dosage recommendations may be followed for children.

Contra-indications, warnings, etc Although no instances of allergy or irritation have been reported with Sulfomyl Eye Drops, they should not be used in patients known to be sensitive to other sulphonamides.

Pharmaceutical precautions Nil.

Legal category P.

Package quantities Polythene drop bottles each containing 10 ml.

Further information Nil.

Product licence number 0071/5094.

TRANCOPAL

Presentation Trancopal tablets are flat, yellow tablets with bevelled edges 9.5 mm in diameter, marked with a symbol on one side and plain on the reverse. Each tablet contains 200 mg chlormezanone.

Uses Trancopal tablets are recommended for the short-term treatment of insomnia. They are also recommended for the symptomatic treatment of anxiety states where muscle tension is prominent and as an adjunct to the treatment of acute musculo-skeletal disorders associated with painful muscle spasm.

Dosage and administration For oral administration only.

Adults: Sleep disturbances: usually 400 mg at night.

States of anxiety and skeletal muscle tension: usually 200 mg repeated up to 3 or 4 times daily or a single dose of 400 mg at night.

Elderly: Half the normal adult dose or less may be sufficient for a therapeutic response in the elderly.

Children: Not recommended.

Contra-indications, warnings, etc Trancopal tablets are contra-indicated in patients sensitive to chlormezanone and in those taking monoamine oxidase inhibitors. There is insufficient evidence of safety of chlormezanone in human pregnancy but it has been in use for many years without apparent ill consequences; animal studies have not shown hazard. However, do not use during pregnancy, especially the first trimester, unless there are compelling reasons.

Trancopal at high doses may modify the patient's reactions (performance at skilled tasks, alertness, etc.) to a varying extent, depending on individual susceptibility. Therefore, patients should be advised not to drive or operate machinery during treatment, if affected. If Trancopal is administered with CNS depressants, it is possible that their sedative effect may be intensified. As with other drugs acting on the central nervous system, patients should avoid alcohol while receiving Trancopal since the response cannot be predicted.

Trancopal should be given with caution to patients with hepatic or renal insufficiency.

Overdosage: The signs and symptoms of overdosage with chlormezanone resemble those seen with other central depressant drugs, for example, somnolence, prostration, muscular incoordination and memory disturbances. In severe cases, there may be hypotension, respiratory depression and loss of consciousness.

Symptomatic treatment should follow gastric lavage.

Side effects: Drowsiness and dizziness have been the commonest side effects, particularly at higher doses. Other reported side effects include nausea, lightheadedness, headache, lethargy, skin rashes and dryness of the mouth. Cholestatic jaundice has occurred.

The dependence potential of chlormezanone is no known.

Pharmaceutical precautions Nil.

Legal category POM.

Package quantities Trancopal tablets are available in bottles of 60.

Further information Nil.

Product licence number 0071/5098.

**Trade Mark*

Wyeth Laboratories

Huntercombe Lane South
Taplow
Maidenhead, Berks



ALUDROX*

Presentation Aludrox Gel consists of Aluminium Hydroxide Mixture BP containing the equivalent of 3.5–4.4% w/w Al_2O_3 presented as a white gel with the odour and flavour of peppermint.

Aludrox Tablets are white, flat, bevelled-edge tablets, 16 mm in diameter, marked ALUDROX on one face and WYETH on the other face. Each tablet contains 375 mg aluminium hydroxide (present in 750 mg aluminium hydroxide-sucrose stable mixture).

Uses Aludrox Tablets and Gel are antacid preparations indicated for the relief of hyperacidity, particularly that associated with peptic ulceration and dyspepsia. They may also be prescribed in the treatment of hyperphosphataemia.

Dosage and administration Route of administration: Oral.

Dosage – Adults: For antacid use:

Tablets: 2 tablets half an hour after meals and on retiring. The tablets should be chewed before swallowing.

Gel: Two 5 ml doses four times daily between meals and on retiring.

In hyperphosphataemia: Larger doses may be given according to the requirements of the patient.

Children: Not recommended in infancy. Otherwise proportional to adult dosage for 70 kg adult.

Contra-indications, warnings, etc

Contra-indications: The aluminium ion combines with phosphate to form an insoluble complex which is not absorbed, and when high doses are given together with a low phosphorus diet phosphate depletion occurs. This regime is used in the treatment of phosphate calculi and hyperphosphataemia associated with chronic renal failure, although phosphate depletion does not occur in patients on a normal diet. Aludrox is contra-indicated in patients with hypophosphataemia.

Precautions:

1. Aluminium hydroxide may form a complex with tetracyclines and reduce absorption when given concomitantly.
2. Aluminium hydroxide may reduce absorption of digoxin.

Side-effects: Few side effects are to be expected. In some patients constipation may develop, but this is easily overcome by the administration of a suitable laxative preparation or by the joint administration of magnesium hydroxide.

Pharmaceutical precautions Store in a cool place. Where necessary dispense Aludrox Gel into suitable well-closed glass or polythene bottles.

Legal category GSL.

Package quantities Aludrox Tablets: Boxes of 60.

Aludrox gel: Polythene bottles of 200 ml, 500 ml, and 2 litres.

Further information There is no evidence to suggest that Aludrox Gel (or tablets) should not be given to breast-feeding mothers.

Product licence numbers

Aludrox Gel 0011/5000

Aludrox Tablets 0011/5001

APISATE*

Presentation Apisate tablets are two-layer tablets of 11.0 mm diameter. Both layers are yellow, the lighter coloured face is marked WYETH, the other face is plain. Each tablet contains:

Diethylpropion hydrochloride (in a sustained action formulation)	75 mg
Thiamine Hydrochloride BP	5 mg
Riboflavine BP	4 mg
Pyridoxine Hydrochloride BP	2 mg
Nicotinamide BP	30 mg

Uses Apisate, containing diethylpropion hydrochloride, in a sustained action formulation, with a supplement of B-complex vitamins, is designed to give anorectic activity throughout the waking hours.

Apisate is suitable for treatment of patients with moderate to severe obesity for whom dietary supervision is also provided.

Dosage and administration Route of administration: Oral.

Dosage – Adults: Dosage depends on eating habits. Most patients require only one tablet a day, taken early morning or mid-afternoon. Some patients however, may require 2 tablets; one at each of these two times.

Children: Not recommended for children under 12 years of age.

Current medical opinion supports intermittent use of appetite suppressants. Apisate may be given 4–8 weeks followed by a similar period without medication.

Contra-indications, warnings, etc

Contra-indications:

1. Use in emotionally unstable individuals, including psychotics, who are known to be susceptible to alcohol or drug abuse.
2. Use in patients concomitantly treated with MAOIs or within two weeks of such treatment.
3. Use of diethylpropion is also contra-indicated in patients with advanced arteriosclerosis, hyperthyroidism, severe hypertension, glaucoma or idiosyncrasy to sympathomimetic amines.
4. Concurrent use with other appetite suppressant drugs.

Precautions: 1. Prolonged use of diethylpropion may induce dependence with a withdrawal syndrome on cessation of therapy. Several cases of toxic psychoses have been reported after excessive use of diethylpropion and a very small number have been reported in which the recommended dosage appears not to have been exceeded. The psychosis was temporary and cleared up when the drug was discontinued. Patients should be advised not to exceed the stated dose.

2. Efficacy in use for more than 6 months, and safety in long term use have not been established. Longer term use may carry an increased risk of dependence.

Since its introduction in 1958, diethylpropion has been used by at least 33,000,000 patients. Against this background of extensive clinical use, reports of abuse have been very rare. Most of the subjects who abused diethylpropion had previously misused other drugs, e.g. amphetamine or phenmetrazine, and many were described as having unstable personalities.

3. Diethylpropion should be used with caution in patients with hypertension, angina pectoris, cardiac arrhythmias and peptic ulceration. Caution should also be observed in patients with epilepsy, anxiety or tension states or severe depression.

4. This product should be regarded as an adjunct in weight reduction, the primary management of which depends on dietary control. Administration of Apisate should not be continued if weight loss does not occur.

5. Diethylpropion may interact with sympathomimetic agents. Care should be taken when treating hypertensive patients receiving hypotensive drugs. Animal experiments suggest that anti-obesity agents can block or reverse the actions of such agents when taken together. Diethylpropion should not be given concurrently with psychotropic drugs, including sedatives.

6. Apisate should not be administered during pregnancy or lactation unless in the judgement of the physician such administration is clinically justifiable. Special care should be taken in the first three months of pregnancy.

7. Patients should be warned against driving or operating machinery until it is established that they are not over-stimulated while taking Apisate.

Side-effects: Diethylpropion has negligible effect on blood pressure, pulse rate or cardiac activity. Side-effects are infrequent and rarely severe enough to require discontinuation of treatment. They include sleeplessness, restlessness, increased nervousness, euphoria, agitation, palpitations, depression, psychosis, hallucinations, dependence, nausea, vomiting, dry mouth, headache, tachycardia, constipation and allergic rashes. Gynaecomastia has been reported rarely.

Overdosage: A few unsuccessful suicide attempts by deliberate overdosage of diethylpropion hydrochloride have been reported in adults. Dosage ranged from 450 to 2,250 mg. Transient sequelae included semi-coma or coma, lethargy, increased irritability and nausea.

A number of cases of accidental overdosage have been reported in children aged 6 months to 3½ years. Known doses taken were from 50 to 1,100 mg. The most frequent effects were motor hyperactivity, excitability, tachycardia, rapid respiration, pupillary dilatation, and flushing.

Treatment of overdosage is initially by gastric lavage and close observation. The foregoing reports show that individual reactions may differ and further treatment will be symptomatic.

Recovery occurred in all patients with overdosage

except one, in whom treatment with a large intravenous dose of sodium amobarbital was implicated.

Pharmaceutical precautions Store in a cool dry place, keep tightly closed. Where necessary dispense into suitable, well-closed glass bottles.

Legal category POM.

Package quantities Bottles of 100.

Further information Diethylpropion, including illegally manufactured tablets have been the subject of social abuse for euphoriant effect.

Product licence number 0011/5004.

ATIVAN* TABLETS

Presentation Ativan tablets are capsule shaped containing 1 mg or 2.5 mg lorazepam, approximately 4 × 8 mm with WYETH on one side and a break bar on the other. The 2.5 mg tablets are yellow and the 1 mg tablets are blue. Both are supplied in a blister pack.

Uses Ativan is indicated for the following: mild, moderate and severe anxiety states, phobic or obsessional states, moderate to severe tension states, anxiety in psychosomatic, organic or psychotic illness, insomnia associated with anxiety, premedication before operative dentistry and as a sedative for the anxious dental patient, premedication before general surgery.

Dosage and administration Route of administration: Oral.

Dosage: Adults: Mild anxiety – 1–4 mg daily in divided doses.

Moderate/severe anxiety – up to 8 mg daily in divided doses.

Severe anxiety, phobic or obsessional/compulsive state – up to 10 mg daily.

Insomnia – 1–4 mg before retiring.

Premedication – 2–3 mg the night before operation, 2–4 mg one or two hours before operation.

Elderly: The elderly may respond to lower doses and half the normal adult dose or less may be sufficient.

Children: Not recommended for children.

Dentistry: 1–2.5 mg, 1½–2 hours before dental treatment. For operative dentistry dosage as for premedication.

Contra-indications, warnings, etc

Contra-indication: Ativan should not be given to patients with a previous history of sensitivity to benzodiazepines.

Precautions and warnings: 1. Concomitant administration with central nervous system depressants, including alcohol, general anaesthetics, narcotic analgesics, monoamine oxidase inhibitors and antidepressants will result in an accentuation of their effects.

2. Prolonged or excessive use of benzodiazepines may occasionally result in the development of some psychological dependence with withdrawal symptoms on sudden discontinuation. This is more likely in patients with a history of alcoholism, drug abuse or in patients with marked personality disorders.

Treatment in all patients should be withdrawn gradually. Careful monitoring of all patients is essential.

3. As with other drugs acting on the central nervous system, patients should be cautioned against driving or operating machinery until it is established that they do not become dizzy or drowsy while taking lorazepam.

4. Ativan tablets should not be administered during pregnancy or lactation unless in judgement of the physician such administration is clinically justifiable. Special care should be taken in the first three months of pregnancy.

5. This product should be used with caution in patients with impairment of renal or hepatic function.

6. Elderly patients or those suffering from cerebral vascular changes such as arteriosclerosis are likely to respond to smaller doses.

7. Ativan should be used with caution during labour. Respiratory depression, poor sucking and hypothermia in the neonate have occasionally been reported especially in patients who are at high risk.

8. Ativan does not depress respiration in most patients but the drug should be used with caution in patients with acute or chronic pulmonary insufficiency.

9. The use of benzodiazepines may release suicidal tendencies in depressed patients. Other rarely reported behavioural effects of the benzodiazepines include paradoxical aggressive outbursts, excitement and confusion.

Overdosage: As with other benzodiazepines, overdosage should not present a threat to life. General supportive measures should be used. Treatment is symptomatic and gastric lavage may be of use if performed shortly after ingestion. If the patient is conscious, an emetic such as ipecacuanha may be given. The patient is likely to sleep and a clear airway should be maintained.

Side-effects: Ativan is well tolerated and imbalance or ataxia is an indication of excessive dosage. Daytime drowsiness may be seen initially and is to be anticipated in the effective treatment of anxiety. It will normally diminish rapidly and may be minimised in the early days of treatment by giving the larger proportion of the day's dose before retiring.

Occasional confusion, hangover, headache on waking, dizziness, blurred vision and nausea have also been reported.

Pharmaceutical precautions Store in a cool dry place.

Legal category POM.

Package quantities 1 mg and 2.5 mg tablets are supplied in boxes of 100 (5 × 20).

Further information Ativan is a short acting benzodiazepine. It is rapidly absorbed from the gastro-intestinal tract and is metabolised by a simple one-step process to a pharmacologically inactive glucuronide. The elimination half-life of Ativan is about 12 hours so that steady state plasma levels are quickly reached and there is minimal risk of excessive accumulation, giving a wide margin of safety.

Product licence numbers

Tablets 1 mg 0011/0034

Tablets 2.5 mg 0011/0036

ATIVAN* INJECTION ▼

Presentation Ativan injection is a clear, colourless solution containing lorazepam at a concentration of 4 mg/ml supplied in 1 ml quantities in clear glass ampoules.

Uses Ativan injection is indicated for:

• Pre-operative medication or premedication for uncom-

fortable or prolonged investigations, e.g. bronchoscopy, arteriography, endoscopy.

The treatment of acute anxiety states, acute excitement or acute mania. The control of status epilepticus.

Dosage and administration *Route of administration:*

Ativan injection can be given intravenously or intramuscularly. However, the intravenous route is to be preferred. Care should be taken to avoid injection into small veins and intra-arterial injection.

Absorption from the injection site is considerably slower if the intramuscular route is used and as rapid an effect may be obtained by oral administration of Ativan tablets.

Preparation of the injection: Ativan injection is slightly viscous when cool. To facilitate injection it may be diluted 1:1 with normal Saline or Water for Injections BP immediately before administration. If given intramuscularly it should always be diluted.

Ativan injection is presented as a 1 ml solution in a 2 ml ampoule to facilitate dilution.

Ativan injection should not be mixed with other drugs in the same syringe.

Dosage:

1. **Premedication:** 0.05 mg/kg (3.5 mg for an average 70 kg man). By the intravenous route the injection should be given 30–45 minutes before surgery when sedation will be evident after 5–10 minutes and maximal loss of recall will occur after 30–45 minutes. By the intramuscular route the injection should be given 1–1½ hours before surgery when sedation will be evident after 30–45 minutes and maximal loss of recall will occur after 60–90 minutes.

2. **Anxiety:** 0.025–0.03 mg/kg (1.75–2.1 mg for an average 70 kg man). Repeat 6 hourly. Ativan injection is not recommended for children under 12.

3. **Status epilepticus:** Adults: 4 mg intravenously. Children: 2 mg intravenously.

Contra-indications, warnings, etc

Contra-indications:

1. Ativan injection should not be given to patients with a previous history of sensitivity to the benzodiazepines.

2. Ativan injection is not recommended for out-patient use unless the patient is accompanied.

Precautions and warnings:

1. Patients should remain under observation for at least eight hours and preferably overnight.

2. Patients should not drive or operate machinery within 24 hours of administration of Ativan injection and should be advised not to take alcohol.

3. The effects of centrally acting cerebral depressant drugs may be potentiated.

4. This product should be used with caution in patients with impairment of renal or hepatic function.

5. The injection should be given slowly except in the control of status epilepticus where rapid injection is required.

6. Elderly patients may require a lower dosage.

7. Ativan injection should not be administered during pregnancy or lactation unless in the judgement of the physician such administration is clinically justifiable. Special care should be taken in the first three months of pregnancy.

Overdosage: As with other benzodiazepines, overdosage should not present a threat to life. General supportive measures should be used and the treatment of overdos-

age is symptomatic. The patient is likely to sleep and a clear airway should be maintained.

Side-effects: Ativan injection is well tolerated and imbalance or ataxia are signs of excessive dosage. Drowsiness may be an initial effect and is to be anticipated in the effective treatment of anxiety. It will normally diminish as treatment continues. Occasional confusion, hangover, headache on waking, drowsiness or dizziness, blurred vision and nausea have also been reported.

Pharmaceutical precautions Store in a refrigerator up to 8°C. Protect from light.

Legal category POM.

Package quantities 10 × 1 ml ampoules per pack.

Further information As with other benzodiazepines, Ativan crosses the placental barrier and foetal concentration will be the same as that in the mother. Ativan will be present in the milk of nursing mothers, but as with other benzodiazepines this is not significant if the mother is receiving Ativan injection within the recommended doses.

Ativan is metabolised by a simple one-step process to a pharmacologically inactive glucuronide. There is minimal risk of accumulation after repeated doses, giving a wide margin of safety. Ativan injection is compatible with a wide range of other drugs and has minimal effect on blood pressure and respiration. Tolerance at the injection site is good.

Product licence number 0011/0051.

BARATOL* ▼

Presentation Baratol tablets are round, convex, film coated tablets containing indoramin hydrochloride equivalent to 25 or 50 mg indoramin base. The 25 mg tablets are blue, 8.00 mm in diameter and marked WYETH on one face and '25' on the other. The 50 mg tablets are green, 9.5 mm in diameter, marked WYETH on one face and '50' on the other face which is also scored.

Uses *Actions:* Baratol is an alpha adrenoceptor blocking agent which acts selectively and competitively on post-synaptic alpha-1 receptors, causing a decrease in peripheral resistance.

Indications: Baratol tablets are indicated for the treatment of all grades of essential hypertension.

Dosage and administration

Initial dose: 25 mg twice daily for all patients.

Dose titration: The dosage of Baratol should be titrated as necessary to control blood pressure to a maximum of 200 mg daily in two or three divided doses. The daily dosage may be increased by the progressive addition of 25 mg or 50 mg, made at intervals of two weeks. When unequal doses are used, the largest dose should be given at night in order to avoid daytime sedation.

Combination with other anti-hypertensive agents: Baratol is effective in lowering blood pressure in all grades of hypertension, either used alone or when combined with other anti-hypertensive agents. The anti-hypertensive effect of Baratol is enhanced by concomitant administration of a thiazide diuretic or a beta-adrenoceptor blocking drug. Control of most cases of mild and moderate hypertension should be achieved by using Baratol alone or by adding Baratol to the regimen of a

patient already under treatment with a thiazide diuretic. In severe hypertension, a combination of Baratol, a thiazide diuretic and a beta-adrenoceptor blocking drug is effective in many such patients.

When Baratol is used in combination with other anti-hypertensive agents, the dose of Baratol should be titrated in the same way as when it is used alone.

Contra-indications, warnings, etc

Contra-indications: Baratol tablets should not be prescribed for:

1. Patients with established heart failure.
2. Patients already under treatment with MAOIs.

Precautions:

1. Drowsiness is sometimes seen in the initial stages of treatment with Baratol or when dosage is increased too rapidly. Patients should be warned not to drive or operate machinery until it is established that they do not become drowsy while taking Baratol.

2. Incipient cardiac failure should be controlled with diuretics and digitalis before treatment with Baratol.

3. Caution should be observed in prescribing Baratol for patients with hepatic or renal insufficiency or Parkinson's disease.

4. Animal experiments indicate no teratogenic effects but Baratol tablets should not be prescribed for pregnant women unless considered essential by the physician.

5. There is no data available on the excretion of Baratol in human milk but the drug should not be administered during lactation unless in the judgement of the physician such administration is clinically justifiable.

Side-effects: Sedation occurs in some patients but is rarely intolerable and is usually overcome by a modest reduction in dosage. Less commonly, dry mouth, nasal congestion, weight gain, dizziness, failure of ejaculation and depression have also been noted.

Treatment of overdose: There is no information available at present of the effects of acute overdose in humans with Baratol. The results of animal work suggest that toxic effects may include sedation, hypotension and hypothermia. In some species of animals fits have occurred at high doses.

In these circumstances suggested therapy is along the following lines:

1. Recent ingestion of large numbers of tablets would require lavage or a dose of ipecacuanha to remove any of the product still in the stomach of the conscious patient.

2. Temperature should be monitored and hypothermia treated appropriately.

3. Treatment of sedation should be by observation and the use of stimulants avoided.

4. Fits have not been seen in humans, but should they occur, the use of barbiturates should be avoided because of the potentiation of the sedative effect of Baratol.

Legal category POM.

Pharmaceutical precautions Store below 25°C and protect from light.

Package quantities Bottles of 100.

Further information Baratol is an alpha adrenoceptor blocking agent which acts selectively and competitively on post-synaptic alpha-1 receptors. It can be used in a wide range of patients. Baratol is one of a new class of alpha-blockers and offers considerable improvement over earlier non-selective alpha-blockers. It is especially suited for patients for whom beta-adrenoceptor blockade is contra-indicated, for example, in patients with a history of obstructive airways disease.

Reflex tachycardia is not associated with treatment with Barotal, probably because of a myocardial membrane-stabilising effect which prevents reflex acceleration of cardiac activity which was associated with the earlier non-selective alpha-blockers.

Postural hypotension is not a problem. Barotal has no effect on resistance vessels and shows no selectivity for veins in animals and humans and therefore venous pooling is not produced.

No mutually antagonistic interactions have been noted when patients are treated concomitantly with Barotal and a tricyclic antidepressant.

Barotal has been used concomitantly with cardiac glycosides and other anti-hypertensive drugs with no interaction. Rebound hypertension has not been observed after withdrawal of Barotal.

Selective alpha-1-blockade has been shown to be useful in the treatment of congestive heart failure. As yet, there is insufficient data to determine whether Barotal can also be indicated in this disorder. However, in hypertensive patients with cardiac insufficiency the selective alpha-blocking properties of Barotal may be beneficial.

Product licence numbers

5 mg tablets 0011/0071

0 mg tablets 0011/0058

DAVENOL

Presentation Davenol linctus is a clear, orange viscous liquid with not more than a slight turbidity, an odour of gingerine and a sweet taste. Each 5 ml dose contains:

holcodine BP	4 mg
phedrine Hydrochloride BP	7 mg
carbinoxamine maleate	2 mg

Uses Davenol is indicated in the treatment of all types of cough.

Dosage and administration Route of administration: Oral.

Dosage: Adults: One or two 5 ml doses three or four times daily.

Children: Up to one 5 ml dose three or four times daily according to age.

Contra-indications, warnings, etc Precautions:

1. Davenol may cause drowsiness although this is unlikely at the recommended dose. Patients should be cautioned not to drive or operate machinery until it is established that they are not affected in this way.

2. Davenol linctus should not be administered during pregnancy or lactation unless in the judgement of the physician such administration is clinically justifiable. Special care should be taken in the first three months of pregnancy.

3. In common with all products containing sympathomimetic agents, Davenol should be used with caution in patients being treated for asthma.

Treatment of overdose: Not reported. Treatment should be symptomatic.

Pharmaceutical precautions Where necessary disperse Davenol Linctus into suitable, well-closed glass bottles. When required Davenol Linctus may be diluted with Syrup BP. It should not be diluted with water.

Legal category P.

Package quantities Polythene Bottles of 100 ml and 500 ml.

Further information Nil.

Product licence number 0011/5016.

EQUAGESIC

Presentation Equagesic Tablets are three layer, flat bevel-edged tablets, 12.0 mm in diameter. A white layer is sandwiched between a yellow layer and a pink layer. The yellow face is marked WYETH and the pink face is plain. Each tablet contains:

Ethoheptazine citrate	75 mg
Meprobamate BP	150 mg
Aspirin BP	250 mg

Uses Equagesic is an analgesic with muscle-relaxant properties indicated for short-term symptomatic treatment of pain occurring in musculo-skeletal disorders and tension headache.

Dosage and administration Route of administration: Oral.

Dosage - Adults: 2 tablets three or four times daily as needed for the relief of pain.

Elderly: The elderly may respond to lower doses and half the normal adult dose or less may be sufficient.

Children: Not recommended for children.

Contra-indications, warnings, etc

Contra-indications:

1. Equagesic should not be used in patients known to be hypersensitive to the active ingredients or to compounds related to meprobamate such as carisoprodol or carbromal.

2. Meprobamate should not be used in patients with a known propensity for dependence on drugs including alcohol and in patients susceptible to attacks of acute intermittent porphyria.

3. Aspirin should not be used in patients with active peptic ulceration, haemophilia or in renal disease.

Precautions and warnings: Equagesic tablets should not be administered during pregnancy or lactation unless in the judgement of the physician such administration is clinically justifiable. Special care should be taken in the first three months of pregnancy.

2. This product may cause drowsiness. Patients receiving this medication should not drive or operate machinery unless the drug has been shown not to interfere with physical or mental ability.

3. Meprobamate may increase the effects of concurrently administered central nervous system depressants including alcohol.

4. The concurrent use of CNS depressant drugs should be avoided in hepatic insufficiency.

5. Meprobamate may induce seizures in epileptic patients. Convulsions have been seen after abrupt withdrawal of high doses of meprobamate after long term use.

6. Some degree of dependence may occasionally occur with meprobamate in certain cases if dosage recommendations are exceeded with withdrawal symptoms on sudden discontinuation. This is more likely in individuals with emotionally unstable personalities if the drug is taken over long periods, or in others liable to alcohol or other drug dependence. Treatment in these cases should be withdrawn gradually.

Equagesic is recommended for use for short periods only and therefore the risk of dependence occurring with this product is very small.

Aspirin: 7. (a) Aspirin may prolong labour and contribute to maternal and neonatal bleeding and is best avoided at term. It may precipitate bronchospasm and may induce attacks of asthma in susceptible subjects. Aspirin should

only be used with great caution in patients with a history of peptic ulceration.

(b) Concomitant administration with certain other medications such as coumarin anticoagulants, corticosteroids or oral hypoglycaemics may require adjustment of dosage of the various drugs. The action of uricosuric agents may be inhibited.

Overdosage: Meprobamate. Acute poisoning with meprobamate produces coma, shock, vasomotor and respiratory collapse. Very few suicide attempts have proved successful and documented fatal doses have ranged from 12 gm to 47.6 gm. Recovery has occurred after ingestion of similar large amounts (20–40 gm). Gastric lavage is only effective within a short period of drug ingestion as meprobamate is rapidly absorbed from the gastrointestinal tract. Blood concentrations may be reduced by a regime of forced alkaline diuresis or haemodialysis. The respiration may require assistance.

Individual response in overdosage with meprobamate is variable but in some cases the symptoms may be severe. It is therefore, advisable that caution should be observed in prescribing drugs, which contain meprobamate, to patients with depression or to others who may be liable to suicidal ideation or intent.

Aspirin: Overdosage with aspirin will result in the appearance of the signs and symptoms of salicylism. Treatment of aspirin poisoning is largely symptomatic and directed towards correction of the acid-base balance and electrolyte balance of the plasma.

Side-effects: Drowsiness, dizziness and nausea may be experienced with Equagesic but these symptoms usually disappear as treatment continues.

Hypersensitivity reactions may occur rarely both to meprobamate and to aspirin. With meprobamate these reactions include skin rashes and may arise after one to four doses. They may be generalised or local and include urticaria, itchy maculopapular rashes or erythema. Severe systemic reactions with shaking chills and fever, nausea and vomiting, hypotension and collapse have occurred very occasionally and may resemble an anaphylactic shock reaction. There have been a few reports of acute nonthrombocytopenic purpura.

Hypersensitivity reactions to aspirin may manifest themselves as asthma, skin reactions and shock. Aspirin may induce gastro-intestinal haemorrhage, which is occasionally severe but in most cases blood loss is not significant.

Pharmaceutical precautions Store in a cool dry place. Keep tightly closed. Where necessary dispense Equagesic Tablets into suitable well-closed glass bottles.

Legal category POM.

Package quantities Bottles of 100.

Further information Safety and efficacy have not been established beyond short-term use.

Product licence number 0011/5009.

MICROVAL* ▼

Presentation Microval tablets are round white lustrous coated, convex tablets 5.0 mm in diameter. Each tablet contains 30 mcg levonorgestrel.

Uses Oral contraception. Microval is particularly indicated for the older woman changing from combined oral

contraceptives and for women for whom oestrogen treatment is considered unsuitable.

Dosage and administration The tablets are started on the first day of menstruation and taken daily without interruption for as long as contraception is desired. The should be taken at the same time each day, preferably after the evening meal or at bedtime so that the interval between tablets is always about 24 hours. Protection may be reduced when the interval increases beyond 24 hours.

During the first cycle additional contraceptive precautions should be taken for the first 14 days.

If a tablet is not taken at the usual time it should be taken as soon as possible and the next tablet taken at the usual time. If the interval between tablets is more than 27 hours protection may be impaired. The patient should take one tablet as soon as she remembers and thereafter one tablet daily as before but should use additional contraceptive measures until the tablets have been taken regularly for 14 days. If a tablet is missed, the patient should take 1 tablet daily as before but should use additional contraceptive measures until the tablets have been taken regularly for 14 days.

If vomiting occurs shortly after a tablet has been taken contraceptive protection can be maintained by taking another tablet, provided that it is taken within three hours of the normal time. The last tablet in the pack may be used for this purpose. If repeated vomiting or diarrhoea endanger absorption additional contraceptive precautions should be used for 14 days after the symptoms have disappeared.

Irregular spotting or bleeding may occur with a proportion of women initially but menstrual regularity is usually re-established after the first few cycles. Those patients whose menstrual patterns do not become reasonably regular after three to four cycles or who have prolonged bleeding or amenorrhoea lasting for two months should be instructed to return for advice.

Women who change from a combined oral contraceptive to Microval should stop taking the previous product leave seven clear days and take the first Microval tablet on the eighth day, then continue to take 1 tablet daily. Additional contraceptive precautions should be taken until the fourteenth tablet has been taken.

Microval does not diminish the yield of breast milk and can be used from the seventh post-partum day.

Contra-indications, warnings, etc

Contra-indications: Microval should not be given –

1. To patients with established hepatic disease or to those in whom there is evidence of persistently abnormal liver function such as the Dubin-Johnson and Rotor syndromes, or to those who have idiopathic recurrent jaundice of pregnancy.

2. To patients with a history of infectious hepatitis until the liver function tests have returned to normal values.

3. To patients with abnormal vaginal bleeding of unknown aetiology.

4. To patients with suspected pregnancy.

5. Although the risk of thromboembolism has not been associated with progestogen-only contraceptives it is at present required that a history of thromboembolic disorders should be regarded as a contra-indication.

Precautions:

1. Oral contraceptive medication should be discontinued if there is a gradual or sudden, partial or complete

loss of vision, proptosis or diplopia, papilloedema or any evidence of retinal or vascular lesions.

2. Caution should be observed in prescribing oral contraceptives for any patients with a history of migraine, or if migraine is being treated with vasoconstrictor drugs. If migraine worsens or migraine or severe headache develops for the first time during treatment, medication should be discontinued immediately.

3. A small fraction of the progestogen has been identified in the milk of mothers receiving the drug. The long-range effects to the nursing infant is currently unknown.

4. Examination of the pelvic organs, breasts and blood pressure should precede prescription of Microval and should be repeated regularly.

5. Ectopic pregnancies appear to occur more frequently on progestogen-only oral contraceptives.

Side-effects: Microval is well tolerated but certain endocrine effects which are also characteristic of ovulatory cycles may occur. Those noted are headache, light weight gain, nausea, breast tenderness and spotting between periods. The incidence of such effects with Microval is low and tends to decrease as treatment continues.

Drug interactions: Caution should be observed in prescribing oral contraceptives for patients taking other drugs since various interactions have been reported. Pregnancies have been reported in women taking oral contraceptives concurrently with rifampicin and other anti-biotics, anti-epileptic drugs, barbiturates and other edative drugs.

Steroids affect drug metabolism and the therapeutic or toxic effects of other drugs may be modified. Interactions have been reported between oral contraceptives and tricyclic antidepressants, anticoagulants and corticosteroids.

Overdosage: No reports of serious ill-effects from overdosage with oral contraceptives have been reported. In general, therefore, treatment of overdosage is not necessary. If overdosage is, however, discovered within two or three hours and is so large that treatment seems desirable, gastric lavage or a suitable dose of ipecacuanha can be used. There are no specific antidotes and further treatment should be symptomatic.

Pharmaceutical precautions Store at or below room temperature.

Legal category POM.

Package quantities Microval tablets are supplied in blister packs of 35 tablets.

Further information Estimates from clinical trials show that, if the tablets are taken correctly, out of 100 women taking them for one year, on average one woman may become pregnant during that year. Microval although not quite as effective as combined oral contraceptives, provides an extremely high degree of protection and is very much more effective than withdrawal, rhythm, rhythm method or chemicals and comparable to the I.U.C.D. and diaphragm.

Levonorgestral is a totally synthetic progestogen which possesses no inherent oestrogenicity. It has anti-oestrogenic properties and has minimal effects on metabolic functions.

Product licence number 0011/0040.

MUCAINE*

Presentation Mucaine Suspension is a white suspension with the odour and flavour of peppermint. Each 5 ml contains:

Oxethazaine	10 mg
Magnesium Hydroxide BPC	100 mg
Aluminium Hydroxide Mixture BP	4.75 ml

Uses Mucaine is an antacid mixture containing a topical anaesthetic and is indicated for oesophagitis whatever its cause, including peptic oesophagitis with or without hiatus hernia, radiation oesophagitis and the heartburn of late pregnancy.

The relief obtained in the symptomatic treatment of oesophagitis is due to the surface anaesthetic, oxethazaine, aided by the physical and antacid properties of the vehicle. Oxethazaine is stable at the levels of acidity or alkalinity found in the upper gastrointestinal tract and has relatively prolonged action.

Dosage and administration Route of administration: Oral.

Dosage - Adults: One to two 5 ml doses should be taken three or four times daily, 15 minutes before meals, and at bedtime, or as required. The dose should not be washed down with a drink.

Children: Not recommended for children.

Contra-indications, warnings, etc

Contra-indications: The aluminium ion combines with phosphate to form an insoluble complex which is not absorbed. When high doses are given together with a low phosphorus diet, phosphate depletion occurs, although phosphate depletion does not occur in patients on a normal diet. Mucaine is contra-indicated in patients with hypophosphataemia.

Side-effects: Mucaine is well tolerated and the side-effects which have been reported are almost invariably mild and transient in nature, consisting principally of dryness of the mouth, soreness of the tongue or nausea.

Precautions:

1. Magnesium and aluminium hydroxides may form complexes with tetracyclines and reduce the absorption when given concomitantly.

2. Aluminium hydroxide may reduce absorption of digoxin.

3. Mucaine suspension should not be given during the first three months of pregnancy or lactation unless in the judgement of the physician such administration is clinically justifiable.

Action in case of overdosage: Not reported. Treatment should be symptomatic.

Pharmaceutical precautions Store in a cool place. Where necessary dispense Mucaine Suspension into suitable well-closed glass or polythene bottles. When required Mucaine Suspension may be diluted with Syrup BP.

Legal category POM.

Package quantities Polythene bottles of 500 ml.

Further information It is important to stress that Mucaine should not be washed down with a drink because maximal relief depends on good contact between the inflamed mucosal surface and the suspension as it passes down the oesophagus.

Product licence number 0011/5014.

NORMISON®

Presentation Normison capsules are opaque yellow, oval, soft gelatin capsules containing 10 mg or 20 mg temazepam. The 10 mg capsules are No. 4 capsules printed with WYETH in black lettering. The 20 mg capsules are No. 7.5 oval soft gelatin capsules printed WYETH on one side and 20 on the other in red lettering.

Uses Normison is indicated for the treatment of insomnia, and for premedication before minor surgery or other procedures especially when hospital admission is not essential.

Dosage and administration Route of administration: Oral.

Adults: Insomnia: Dosage: 10–30 mg half an hour before retiring. The dose may be increased to 40 or 60 mg in patients who do not respond to the lower dose because of severe or persistent insomnia.

Premedication:

Dosage: 20–40 mg, 30–60 minutes before surgical or other procedures.

Children: Normison has not been evaluated for the treatment of children.

Contra-indications, warnings, etc

Contra-indications: Normison should not be given to patients with a previous history of sensitivity to benzodiazepines.

Precautions:

1. Concomitant administration with central nervous system depressants, including alcohol, general anaesthetics, narcotic analgesics, monoamine oxidase inhibitors and antidepressants will result in an accentuation of their effects.

2. Prolonged or excessive use of benzodiazepines may occasionally result in the development of some psychological dependence with withdrawal symptoms on sudden discontinuation. Treatment in these cases should be withdrawn gradually. Careful usage seldom results in the development of dependence.

3. When used as a hypnotic, daytime drowsiness is unlikely to be a problem with Normison since the short half-life usually ensures that the effects disappear by the morning. As with other drugs acting on the central nervous system, however, patients should be cautioned against driving or operating machinery until it is established that they do not become dizzy or drowsy while taking Normison.

4. Normison capsules should not be administered during pregnancy or lactation unless in the judgement of the physician such administration is clinically justifiable. Special care should be taken in the first three months of pregnancy.

5. Elderly patients or those suffering from cerebral vascular changes such as arteriosclerosis are likely to respond to smaller doses.

6. After medication with Normison before surgical or other procedures, patients should be accompanied home.

Side-effects: Because of its short half-life, the effects of temazepam are usually restricted to the night of ingestion. Drowsiness or dizziness on waking is rare. Morning headaches, transient rashes and mild gastro-intestinal disturbances have occasionally been reported.

Overdosage: As with other benzodiazepines, overdoses should not present a threat to life. General supportive measures should be used. Treatment is

symptomatic and gastric lavage may be of use performed shortly after ingestion. If the patient conscious, an emetic such as ipecacuanha may be given. The patient is likely to sleep and a clear airway should be maintained.

Pharmaceutical precautions Store in a cool, dry place. When necessary dispense Normison capsules in suitable well-closed glass bottles.

Legal category POM.

Package quantities 10 mg: bottles of 100, 500 and 1,000.

20 mg: bottles of 100 and 500.

Further information Normison is a short acting benzodiazepine. It is rapidly absorbed from the liquid filled soft gelatin capsules and peak plasma levels are usually reached in 20 to 40 minutes. Normison has plasma half life of less than six hours, Normison is metabolised by a simple one-step process to a pharmacologically inert glucuronide. There are no major active metabolites and virtually no risk of accumulation. Clinical studies have shown minimal effects on REM sleep patterns and on psychomotor performance on the day after treatment with Normison.

Product licence numbers

10 mg capsules 0011/0060

20 mg capsules 0011/0063

OVRAN®**OVRAN 30®****OVRANETTE®**

Presentation Ovrin tablets are round, white, convex tablets, 6.5 mm in diameter, both faces marked WYETH. Each tablet contains 250 mcg levonorgestrel (d-norgestrel) and 50 mcg Ethinylloestradiol BP.

Ovrin 30 tablets are round, white, convex tablets 6.5 mm in diameter, one face marked WYETH and the other plain. Each tablet contains 250 mcg levonorgestrel (d-norgestrel) and 30 mcg Ethinylloestradiol BP.

Ovrinette tablets are round, white, convex tablets 6.5 mm in diameter, one face marked WYETH and the other face marked '30'. Each tablet contains 150 mcg levonorgestrel (d-norgestrel) and 30 mcg Ethinylloestradiol BP.

Uses Oral contraception. Treatment of endometriosis, spasmodic dysmenorrhoea, pre-menstrual tension, oligomenorrhoea. Treatment of abnormal uterine bleeding such as menorrhagia, metropathia haemorrhagica. Emergency treatment of acute uterine bleeding.

Dosage and administration **Contraception:** For the first course of medication the tablets are started on the fifth day of the cycle, counting the first day of menstruation as day one. One tablet is taken at the same time each day for 21 days followed by seven days without medication. On the eighth day the tablets are started again. Additional contraceptive precautions should be taken until the fourteenth tablet of the first cycle has been taken. In subsequent cycles the protection cover every day of the cycle, provided that the tablets are taken correctly. During the seven clear days, withdrawal bleeding should occur. If a cycle with amenorrhoea occurs the patient should seek medical advice.

Women who change from another oral contraceptive to Ovrin, Ovrin 30 or Ovrinette should stop taking the

previous product, at the end of the pack leave seven clear days and take the first Ovran, Ovran 30 or Ovranette tablet on the eighth day, then continue to take 1 tablet daily for 21 days. Additional contraceptive precautions should be taken until the fourteenth tablet of the first cycle has been taken.

Occasionally spotting or bleeding may occur in some women initially, but menstrual regularity is usually re-established after the first few cycles. If medication is discontinued because of severe breakthrough bleeding new course should be started on the fifth day from the start of bleeding. Additional contraceptive precautions should be taken until the fourteenth tablet of the new course has been taken.

If a tablet is forgotten the woman should take two on the following day at the usual time. If more than one tablet is missed, tablet taking should be resumed when remembered with the tablet appropriate for that day and additional precautions should be taken until the next withdrawal bleed. Withdrawal bleeding may occur as a result of missed tablets, but the patient should continue to take the tablets as directed.

Treatment with Ovran, Ovran 30 or Ovranette should be withdrawn six weeks before elective surgery or treatment of varicose veins by injection of sclerosant.

After childbirth oral contraception is usually started as soon as spontaneous menstruation has been resumed. No other method of contraception should be used in the interval between delivery and the first course, unless it started within seven days of delivery.

Oral contraception may be started on the fifth day after an abortion or miscarriage.

If vomiting or diarrhoea impair absorption additional contraceptive precautions should be taken until the next withdrawal bleed.

Other indications: Ovran and Ovranette can be used for the indications listed below, but Ovran usually provides the more convenient dosage unit.

Endometriosis: Treatment should be continuous with 1 Ovran tablet daily. If spotting or breakthrough bleeding occurs it may be necessary to give 2 tablets daily or orally 3 tablets daily.

Spasmodic dysmenorrhoea, premenstrual tensions, ligamentorrhoea: Dosage as for oral contraception.

Postponement of menstruation: If postponement of a withdrawal bleed is considered desirable, the women should continue taking the tablets for the period during which delay is required. A seven-day gap should then be left before starting a new pack. If spotting or breakthrough bleeding occurs dosage should be increased to 2 tablets daily.

Functional uterine bleeding: When the diagnosis has been established dosage is similar to the dosage for oral contraception, but in the first one or two cycles it may be necessary to give 2 Ovran tablets (or in exceptional cases, 3) daily in order to control the regularity of the cycle.

Emergency treatment of the acute uterine bleeding: 2 Ovran tablets are given immediately. If bleeding continues medication is continued at a dose of 4 tablets daily. This can usually be reduced to 2 tablets within two to four days. Treatment should continue for 10 days and after this time it can either be discontinued to be followed after seven days by a complete course of 1 tablet daily for 21 days (see 'Functional uterine bleeding') or it can be continued for one to three months to inhibit the menses (see 'Postponement of menstruation'). In the

latter case it should be possible to reduce the dosage to 1 tablet daily.

Contra-indications, warnings, etc

Contra-indications: Ovran, Ovran 30 and Ovranette, like other progestogen-oestrogen combinations, should not be given:

1. To patients with established hepatic disease or to those in whom there is evidence of persistently abnormal liver function such as the Dubin-Johnson and Rotor syndromes, or to those who have idiopathic recurrent jaundice of pregnancy.
2. To patients with a history or suspicion of carcinoma of the reproductive organs or breasts.
3. To patients with a history or evidence suggestive of thromboembolic or cerebrovascular disease or phlebitis.
4. To patients with cardiovascular disease.
5. To patients with a history of infectious hepatitis until the liver function tests have returned to normal values.
6. To patients with abnormal, vaginal bleeding of unknown aetiology.
7. To patients with known or suspected oestrogen-dependent neoplasia.
8. To patients with suspected pregnancy.
9. To patients with sickle cell anaemia.
10. To patients with deterioration of otosclerosis during pregnancy.
11. To patients with a history of herpes gestationis.

Precautions:

1. Under the influence of oestrogen-progestogen preparations, pre-existing uterine fibromyomata may increase in size.
2. Oestrogen-progestogen preparations may cause some degree of fluid retention. Conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation.
3. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree.
4. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. Diabetic patients should be carefully observed while receiving therapy.
5. Susceptible women may experience an increase in blood pressure following administration of contraceptive steroids. Caution should therefore be exercised in prescribing oral contraceptives for women with a history of hypertension.
6. Oral contraceptive medication should be discontinued if there is a gradual or sudden, partial or complete loss of vision, proptosis or diplopia, papilloedema or any evidence of retinal or vascular lesions.
7. Caution should be observed in prescribing oral contraceptives for any patient with a history of migraine, or if migraine is being treated with vasoconstrictor drugs. If migraine worsens or migraine or severe headache develops for the first time during treatment, medication should be discontinued immediately.
8. A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant is currently unknown.
9. Hepatic lesions (adenomas, hepatomas, hamartomas, regenerating nodules, etc.), occasionally fatal, have been reported in women taking oral contraceptives. Such lesions may present as an abdominal mass or with

the signs and symptoms of an acute abdomen. These lesions should be considered if the patient has abdominal pain or evidence of intra-abdominal bleeding. Such lesions have been reported in short-term as well as long-term users of oral contraceptives.

10. In breakthrough bleeding or irregular vaginal bleeding, non-functional causes should be borne in mind.

11. The risk of arterial thrombosis associated with combined oral contraceptives increases with age, and this risk is aggravated by cigarette smoking. The use of combined oral contraceptives by women in the older age group, especially those who are cigarette smokers, should therefore be discouraged and alternative methods advised.

12. Examination of the pelvic organs, breasts and blood pressure should precede prescription of an oral contraceptive and should be repeated regularly.

13. Certain conditions require careful observation during treatment with oral contraceptives. These are: a history of depression, varicose veins, diabetes, hypertension, epilepsy, otosclerosis, multiple sclerosis, porphyria, tetany, disturbed liver function, gall-stones, renal diseases, chloasma, uterine fibroids, asthma, the wearing of contact lenses or any condition prone to worsen during pregnancy.

Side-effects: Oral contraceptives produce certain endocrine effects characteristic of ovarian oestrogens and progesterone. The hormones secreted during an ovulatory cycle may produce similar effects including headache, slight weight gain, nausea, breast tenderness, changed libido, depressive moods, and spotting between periods. The overall incidence of such effects with Ovran, Ovran 30 and Ovranette is low and tends to decrease as treatment cycles continue. Cycle control is good and spotting and breakthrough bleeding occur only rarely. Extensive studies on considerable numbers of women taking oral contraceptives indicate some increased risks over non-pregnant women who are not taking oral contraceptives. These include thromboembolism, impaired glucose tolerance and even more rarely, liver dysfunction, hypertension and raised serum lipids.

Drug interactions: Caution should be observed in prescribing oral contraceptives for patients taking other drugs since various interactions have been reported. Pregnancies have been reported in women taking oral contraceptives concurrently with rifampicin and other antibiotics, anti-epileptic drugs, barbiturates and other sedative drugs.

Steroids affect drug metabolism and the therapeutic or toxic effects of other drugs may be modified. Interactions have been reported between oral contraceptives and tricyclic anti-depressants, anticoagulants and corticosteroids.

Overdosage: No reports of serious ill-effects from overdosage with combined oral contraceptives have been reported. In general, therefore, treatment of overdosage is not necessary. If overdosage is, however, discovered within two or three hours and is so large that treatment seems desirable, gastric lavage or a suitable dose of ipecacuanha can be used. There are no specific antidotes and further treatment should be symptomatic.

Pharmaceutical precautions Store at, or below, room temperature.

Legal category POM.

Package quantities Ovran, Ovran 30, and Ovranette are supplied in memo packs of 21 tablets.

Further information Levonorgestrel is a totally synthetic progestogen which possesses no inherent oestrogenicity. It has anti-oestrogenic properties and has minimal effects on metabolic functions.

Pearls Index: Ovran, 0.19. Ovran 30, 0.13. Ovranette 0.35.

Product licence numbers

Ovran	0011/0015
Ovran 30	0011/0050
Ovranette	0011/0041

PENIDURAL* (ORAL)

Presentation Penidural Oral Suspension is a smooth pink suspension with a sweet cherry flavour. Each 5 ml dose contains: 229 mg Benzathine Penicillin BP (equivalent to 300,000 units Penicillin G).

Penidural Oral Drops is a smooth pink suspension with a sweet cherry flavour. Each 1 ml contains 115 mg Benzathine Penicillin BP (equivalent to 150,000 units Penicillin G).

Uses Penidural Oral presentations are indicated for the treatment of mild to moderately severe penicillin-sensitive infections and prophylaxis of penicillin-sensitive secondary infections especially in children.

Dosage and administration Route of administration Oral.

Dosage: Benzathine penicillin is a repository penicillin which gives effective blood levels for a long period, six to eight-hourly dosage being adequate in most patients.
Penidural oral suspension: Adults: Two 5 ml doses three to four times daily.

Children: One 5 ml dose three to four times daily.

Penidural oral drops: Adults: Not recommended.

Children: 1 dropful (0.1 mega units) four to six times daily according to age.

Contra-indications, warnings, etc

Contra-indications: Benzathine penicillin is contra-indicated in patients with a previous history of penicillin hypersensitivity and in small babies whose mothers have such a history.

Precautions and warnings: 1. Prolonged use of an anti-infective may result in the development of super infection due to organisms resistant to that anti-infective.

2. Penidural oral suspension should not be administered during pregnancy or lactation unless in the judgement of the physician such administration is clinically justifiable. Special care should be taken in the first three months of pregnancy.

Side-effects: Penicillin may cause an acute anaphylactic reaction which can be fatal. This reaction appears to occur more frequently in patients with bronchial asthma or other allergic disorders. Reactions have been reported after the use of all forms of penicillin by all routes of administration but are less likely after oral penicillin because of slower absorption.

Penidural is otherwise virtually free from side-effect: apart from occasional loose stools or borborygmi.

Pharmaceutical precautions *Penidural Oral Suspension:* Store in a cool place. Where necessary dispense Penidural Oral Suspension into suitable well-closed

glass bottles. When required Penidural Oral Suspension may be diluted with Syrup BP.

Penidural Oral Drops: Store in a cool place.

Legal category POM.

Package quantities Penidural Oral Suspension: Bottles of 100 ml.

Penidural Oral Drops: Bottles of 10 ml.

Further information Nil.

Product licence numbers

uspension 0011/5019

rops 0011/5018

ERENID-D*

ERENID*-FORTE

Presentation Serenid-D Tablets are presented as tablets containing 10 mg or 15 mg oxazepam.

Serenid-D 10 mg tablets are white flat bevel edged tablets 6.5 mm in diameter, marked WYETH on one face and 10 on the other.

Serenid-D 15 mg tablets are white, flat, bevel edged tablets, 8.0 mm in diameter, marked 15 on one face and WYETH on the other.

Serenid Forte is presented as red/green No. 4 hard gelatin capsules printed with the word WYETH, containing 30 mg oxazepam.

Uses Serenid-D and Serenid Forte are indicated in the control and management of all degrees of anxiety, tension, irritability and related symptoms. Anxiety associated with depression. Phobic states. Other neurotic reactions, e.g. obsessive-compulsive reactions where the underlying factor is intense anxiety. Anxiety in psychotic patients, in whom it may allow reduced dosage of neuroleptic drugs. Anxiety associated with organic disorders. Alcoholism, in combination with other agents in the management of the acute stages.

Dosage and administration Route of administration: oral.

Dosage – Serenid Forte:

Adults: Severe anxiety – 1–2 capsules three times daily. Less severe anxiety – 1 capsule three times daily and at night. Patients with severe sleep disturbance can be given 2 capsules at night.

Children: Serenid Forte has not been evaluated for the treatment of children.

Dosage – Serenid-D:

Adults: Mild to moderate anxiety – one or two 15 mg tablets three (or four) times daily.

Geriatric patients or those who are particularly sensitive to the effects of benzodiazepines – 10–20 mg three or four times daily.

Children: Serenid-D has not been evaluated for the treatment of children.

Contra-indications, warnings, etc

Contra-indications: Oxazepam should not be given to patients with a previous history of sensitivity to benzodiazepines.

Precautions and warnings:

1. Concomitant administration with central nervous system depressants, including alcohol, general anaesthetics, narcotic analgesics, monoamine oxidase inhibitors

and antidepressants will result in an accentuation of their effects.

2. Prolonged or excessive use of benzodiazepines may occasionally result in the development of some psychological dependence with withdrawal symptoms on sudden discontinuation. Treatment in these cases should be withdrawn gradually. Careful usage seldom results in the development of dependence.

3. As with other drugs acting on the central nervous system, patients should be cautioned against driving or operating machinery until it is established that they do not become dizzy or drowsy while taking oxazepam.

4. Serenid-D and Serenid Forte should not be administered during pregnancy or lactation unless in the judgement of the physician such administration is clinically justifiable. Special care should be taken in the first three months of pregnancy.

5. The use of anxiolytic drugs may uncover covert suicidal tendencies, in patients with a psychological depressive component of the illness.

6. Serenid-D and Serenid Forte should not be used in labour unless considered essential. High single doses or repeated low doses of other benzodiazepines have been reported to produce hypotonia, poor sucking and hypotension in the neonate and irregularities in the foetal heart.

Side-effects: Transient mild drowsiness is commonly seen in the first few days of therapy. If it becomes troublesome dosage should be reduced. In a few cases dizziness, vertigo, headache and, rarely, syncope have occurred either alone or with drowsiness. Mild excitatory effects with stimulation of affect have sometimes been reported in psychiatric patients; these reactions may be secondary to relief of anxiety and usually appear in the first two weeks of therapy.

Other side effects include rare cases of minor diffuse skin rashes (morbilliform, urticarial and maculopapular), nausea, lethargy, oedema, slurred speech, tremor and altered libido. Such effects have been infrequent and are generally controlled with reduction of dosage.

Overdosage: A few cases of attempted suicide with oxazepam have been reported, but none has been successful with oxazepam alone. Records show that up to 540 mg have been taken without long-term ill-effects.

As with other benzodiazepines, overdosages should not present a threat to life. General supportive measures should be used. Treatment is symptomatic and gastric lavage may be of use if performed shortly after ingestion. If the patient is conscious, an emetic such as ipecacuanha may be given. The patient is likely to sleep and a clear airway should be maintained.

Pharmaceutical precautions Store in a cool, dry place.

Legal category POM.

Package quantities *Serenid-D 10 mg and 15 mg. Tablets:* Packs of 100.

Serenid Forte Capsules: Bottles of 100.

Further information Serenid-D and Serenid Forte is particularly suitable for elderly patients because of its short half-life and lack of accumulation.

Serenid-D and Serenid Forte is a short-acting benzodiazepine. It is metabolised by a simple one-step process to a pharmacologically inert glucuronide. There are no major metabolites. The elimination half-life is 6–8 hours and there is minimal risk of excessive accumulation.

Product licence numbers

Serenid-D 10 mg 0011/5022

Serenid-D 15 mg 0011/5023

Serenid Forte 0011/5024

SPARINE* (ORAL)

Presentation Sparine is presented as tablets containing 25 mg, 50 mg or 100 mg Promazine Hydrochloride BP per tablet and as an oral suspension. Each 5 ml suspension contains promazine embonate equivalent to 50 mg Promazine Hydrochloride BP.

Sparine Tablets 25 mg: Yellow, sugar-coated tablets, 7.5 mm in diameter.

Sparine Tablets 50 mg: Orange, sugar-coated tablets, 10 mm in diameter.

Sparine Tablets 100 mg: Red, sugar-coated tablets, 11 mm in diameter.

Sparine Suspension: Yellow suspension with an odour and taste of pineapple.

Uses Sparine is indicated for: Control of agitation, e.g. in the elderly, in ambulant and outpatient psychotics, agitated mental defectives, etc. Alleviation of nausea and vomiting. Potentiation of analgesics, e.g. in terminal carcinoma.

Dosage and administration Route of administration: Oral.

Dosage - Adults: Sparine Tablets - 25-100 mg three or four times daily. In frail subjects 25 mg initially.

Sparine Suspension - One 5 ml dose three times daily: increase if necessary.

Children: Sparine Tablets and Suspension - dose proportional to dose for 70 kg adult.

Contra-indications, warnings, etc

Contra-indications: Use in patients hypersensitive to the active ingredient.

Precautions and warnings:

1. Phenothiazines should only be used with great caution in patients with a history of jaundice or with existent liver dysfunction or blood dyscrasias, coronary insufficiency or cardiac disease.

2. The concomitant administration of this product with other medication such as central nervous system depressants (including alcohol and anaesthetics) or antihypertensives or anticholinergics will result in accentuation of their effects, while potentiation of action will also occur with monoamine oxidase inhibitors, antidepressants and analgesics.

3. Sparine Tablets and Suspension should not be administered during pregnancy or lactation unless in the judgement of the physician such administration is clinically justifiable. Special care should be taken in the first three months of pregnancy.

4. Patients receiving phenothiazines over a prolonged period require regular and careful surveillance with particular attention to potential for inducing eye changes, effects on haemopoiesis, liver dysfunction, myocardial conduction effects, particularly if other concurrently administered drugs also have potential effects on these systems.

5. Phenothiazines may induce drowsiness. Persons taking these drugs should not drive or operate machinery unless the drug has been shown not to interfere with physical or mental ability.

6. Use of phenothiazines at high (relative or absolute)

doses may induce extrapyramidal side-effects, dyskinesia, akathisia, dystonia. These are likely to be particularly severe in children.

7. Prolonged administration of phenothiazines may result in persistent or tardive dyskinesias particularly in the elderly.

8. Care should be exercised if Sparine is used for the treatment of patients with cerebral arteriosclerosis, coronary heart disease or other conditions in which a fall in blood pressure might be undesirable.

9. Sparine Suspension is formulated with aluminium hydroxide which may complex tetracyclines if given concomitantly.

Treatment of overdosage: Ingestion of large amounts of promazine is followed by deep sleep, with or without pronounced fall in blood pressure and without particular change in respiration rate, other than the slow attendant upon sedation. Occasionally an initial period of excitement may precede coma, followed by grand mal seizures.

In the absence of any specific antidote, treatment should be based on ordinary therapeutic principles with special emphasis on the following measures: (a) gastric lavage; (b) treat convulsions if present; (c) correction of acute hypotension if necessary; (d) counteraction of the effects of an excess of promazine hydrochloride on the central nervous system; (e) control and natural recovery of excessive hypothermia.

Side-effects: Sparine is a member of the phenothiazine group of drugs and the side-effects associated with the group have been noted, e.g. drowsiness, transient postural hypotension, allergic skin conditions and agranulocytosis. The incidence of these effects is considerably lower than with other drugs of this group.

Pharmaceutical precautions Store Sparine Suspension in a cool place and protect from light. When required Sparine Suspension may be diluted with Syrup BP.

Legal category POM.

Package quantities *Sparine Tablets 25 mg and 50 mg:* Bottles of 250.

Sparine Tablets 100 mg: Bottles of 50 and 250.

Sparine Suspension: Bottles of 150 ml and 1 litre.

Further information Nil.**Product licence numbers**

Sparine Tablets 25 mg 0011/5050

Sparine Tablets 50 mg 0011/5056

Sparine Tablets: 100 mg 0011/5057

Sparine Suspension: 0011/5045

SPARINE* (PARENTERAL)

Presentation Sparine injection is a clear, colourless aqueous solution containing 50 mg Promazine Hydrochloride BP per millilitre.

Uses Sparine injection is indicated for: senile agitation and confusion, pre-delivery sedation, severe pain, nausea and vomiting, hiccup, secondary anxiety, pain and sickness in the elderly, acute or severe agitation or mania, chronic psychoses and psychoneuroses, premedication before ECT, acute alcoholism, treatment of drug withdrawal symptoms, hyperemesis gravidarum, severe vomiting during or after labour, sedation prior to operative or diagnostic procedures under local or regional anaesthesia, radiation sickness, examination and management

of cases of head injury, tetanus, chorea, priapism, toxic psychosis.

Dosage and administration Route of administration: Parenteral.

Dosage: Adults: 50 mg Sparine intramuscularly. Repeat if necessary after six to eight hours. In frail subjects, 25 mg. In obstetrics, 50 mg Sparine with 50 mg pethidine in the same syringe. The daily dose should not exceed 1 g.

If Sparine is injected intravenously it must be diluted with an equal volume of saline.

Children: 25 mg Sparine intramuscularly. Repeat if necessary after six to eight hours. Otherwise proportional to dose for 70 kg adult.

Contra-indications, warnings, etc

Contra-indications:

1. Use in patients in coma.
2. Use in patients hypersensitive to the active ingredient.

Precautions and warnings:

1. Phenothiazines should only be used with great caution in patients with a history of jaundice or with existent liver dysfunction, or blood dyscrasias, coronary insufficiency or cardiac disease.

2. The concomitant administration of this product with other medication such as central nervous system depressants (including alcohol and anaesthetics) or antihypertensives or anticholinergics will result in accentuation of their effects, while potentiation of action will also occur with monoamine oxidase inhibitors, antidepressants and analgesics.

3. Sparine injection should not be administered during pregnancy or lactation unless in the judgement of the physician such administration is clinically justifiable. Special care should be taken in the first three months of pregnancy.

4. Patients receiving phenothiazines over a prolonged period require regular and careful surveillance with particular attention to potential for inducing eye changes, effects on haemopoiesis, liver dysfunction, myocardial conduction effects, particularly if other concurrently administered drugs also have potential effects on these systems.

5. Phenothiazines may induce drowsiness. Persons taking these drugs should not drive or operate machinery unless the drug has been shown not to interfere with physical or mental ability.

6. Use of phenothiazines at high (relative or absolute) doses may induce extrapyramidal side-effects, dyskinesia, akathisia, dystonia. These are likely to be particularly severe in children.

7. Prolonged administration of phenothiazines may result in persistent or tardive dyskinesias particularly in the elderly.

8. Administration by the intravenous route may induce local vascular spasm or thrombophlebitis. The preparation must be diluted before use. Arteriolar spasm and gangrene have been reported following accidental intra-arterial injection of high concentrations.

9. Care should be exercised if Sparine is used for the treatment of patients with cerebral arteriosclerosis, coronary heart disease or other conditions in which a fall in blood pressure might be undesirable.

Treatment of overdose: Ingestion of large amounts of promazine is followed by deep sleep, with or without a pronounced fall in blood pressure and without particular

change in respiration rate, other than the slowing attendant upon sedation. Occasionally an initial period of excitement may precede coma, followed by grand mal seizures.

In the absence of any specific antidote, treatment should be based on ordinary therapeutic principles with special emphasis on the following measures: (a) gastric lavage; (b) treat convulsions if present; (c) correction of acute hypotension if necessary; (d) counteraction of the effects of an excess of promazine hydrochloride on the central nervous system; (e) control and natural recovery of hypothermia.

Side-effects: Sparine is a member of the phenothiazine group of drugs and the side-effects associated with that group have been noted, e.g. drowsiness, transient postural hypotension, allergic skin conditions and agranulocytosis. The incidence of these effects is considerably lower than with other drugs of this group.

Pharmaceutical precautions Sparine Injection should not be mixed with other injections with the exception of Pethidine Injection BP.

Legal category POM.

Package quantities Boxes of 10 by 1 ml or 2 ml ampoules.

Further information Nil.

Product licence number 0011/5043.

TRINORDIOL* ▼

Presentation The memo pack holds six light brown tablets, containing 50mcg levonorgestrel and 30 mcg Ethinyloestradiol BP, five white tablets containing 75 mcg levonorgestrel and 40 mcg Ethinyloestradiol BP and ten ochre tablets containing 125 mcg levonorgestrel and 30 mcg Ethinyloestradiol BP.

All tablets are round 5.6 mm in diameter with a lustrous sugar coating.

Uses Oral contraception.

Dosage and administration *Contraception:* For the first course of medication the tablets are started on the first day of the cycle, counting the first day of menstruation as day one. One tablet is taken at the same time each day for 21 days followed by seven days without medication. On the eighth day the tablets are started again. The protection covers every day of the cycle, provided that the tablets are taken correctly. During the seven clear days withdrawal bleeding should occur. If a cycle with amenorrhoea occurs the patient should seek medical advice.

Women who change from another oral contraceptive to Trinordiol should stop taking the previous product at the end of the pack and take the first tablet of Trinordiol on the day after taking the last tablet of their old pack, then continue to take 1 tablet daily for 21 days. If it is preferred to leave a seven-day gap before starting Trinordiol, then additional contraceptive precautions should be taken for the first 14 days of the first cycle.

Occasionally spotting or bleeding may occur in some women initially, but menstrual regularity is usually re-established after the first few cycles. If medication is discontinued because of severe breakthrough bleeding a new course should be started on the fifth day from the start of bleeding. Additional contraceptive precautions should be taken until the fourteenth tablet of the new course has been taken.

If a tablet is forgotten the woman should take two on the following day at the usual time. If more than one tablet is missed, tablet taking should be resumed when remembered with the tablet appropriate for that day and additional precautions should be taken until the next withdrawal bleed. Withdrawal bleeding may occur as a result of missed tablets, but the patient should continue to take the tablets as directed. Treatment with Trinordiol should be withdrawn six weeks before elective surgery or treatment of varicose veins by injection of sclerosant.

After childbirth oral contraception is usually started as soon as spontaneous menstruation has been resumed. Another method of contraception should be used in the interval between delivery and the first course, unless it is started within seven days of delivery.

Oral contraception may be started on the fifth day after an abortion or miscarriage.

If vomiting or diarrhoea impair absorption, additional contraceptive precautions should be taken until the next withdrawal bleed.

Contra-indications, warnings, etc

Contra-indications: Trinordiol like other progestogen-oestrogen combinations, should not be given:

1. To patients with established hepatic disease or to those in whom there is evidence of persistently abnormal liver functions such as Dubin-Johnson and Roter syndromes, or to those who have idiopathic recurrent jaundice of pregnancy.
2. To patients with a history or suspicion of carcinoma of the reproductive organs or breasts.
3. To patients with a history or evidence suggestive of thromboembolic or cerebrovascular disease or phlebitis.
4. To patients with cardiovascular disease.
5. To patients with a history of infectious hepatitis until the liver function tests have returned to normal values.
6. To patients with abnormal vaginal bleeding of unknown aetiology.
7. To patients with known or suspected oestrogen-dependent neoplasia.
8. To patients with suspected pregnancy.
9. To patients with sickle cell anaemia.
10. To patients with deterioration of otosclerosis during pregnancy.
11. To patients with a history of herpes gestationis.

Precautions:

1. Under the influence of oestrogen-progestogen preparations, pre-existing uterine fibromyomata may increase in size.
2. Oestrogen-progestogen preparations may cause some degree of fluid retention. Conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation.
3. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree.
4. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. Diabetic patients should be carefully observed while receiving therapy.
5. Susceptible women may experience an increase in blood pressure following administration of contraceptive steroids. Caution should therefore be exercised in prescribing oral contraceptives for women with a history of hypertension.

6. Oral contraceptive medication should be discontinued if there is a gradual or sudden, partial or complete loss of vision, proptosis or diplopia, papilloedema or any evidence of retinal or vascular lesions.

7. Caution should be observed in prescribing oral contraceptives for any patient with a history of migraine, or if migraine is being treated with vasoconstrictor drugs. If migraine worsens or migraine or severe headache develops for the first time during treatment, medication should be discontinued immediately.

8. A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant is currently unknown.

9. Hepatic lesions (adenomas, hepatomas, hamartomas, regenerating nodules, etc), occasionally fatal, have been reported in women taking oral contraceptives. Such lesions may present as an abdominal mass or with the signs and symptoms of an acute abdomen. These lesions should be considered if the patient has abdominal pain or evidence of intra-abdominal bleeding. Such lesions have been reported in short-term as well as long-term users of oral contraceptives.

10. In breakthrough bleeding or irregular vaginal bleeding, non-functional causes should be borne in mind.

11. The risk of arterial thrombosis associated with combined oral contraceptives increases with age, and this risk is aggravated by cigarette smoking. The use of combined oral contraceptives by women in the older age group, especially those who are cigarette smokers, should therefore be discouraged and alternative methods advised.

12. Examination of the pelvic organs, breasts and blood pressure should precede prescription of an oral contraceptive and should be repeated regularly.

13. Certain conditions require careful observation during treatment with oral contraceptives. These are: history of depression, varicose veins, diabetes, hypertension, epilepsy, otosclerosis, multiple sclerosis, porphyria, tetany, disturbed liver function, gall-stones, renal disease, chloasma, uterine fibroids, asthma, the wearing of contact lenses or any condition prone to worsen during pregnancy.

Side-effects: Oral contraceptives produce certain endocrine effects characteristic of ovarian oestrogens and progesterone. The hormones secreted during an ovulatory cycle may produce similar effects including headache, slight weight gain, nausea, breast tenderness, changed libido, depressive moods and spotting between periods. The overall incidence of such effects with Trinordiol is low and tends to decrease as treatment cycles continue. Cycle control is good and spotting and breakthrough bleeding occur only rarely. Extensive studies on considerable numbers of women taking oral contraceptives indicate some increased risks over non-pregnant women who are not taking oral contraceptives. These include thromboembolism, impaired glucose tolerance and even more rarely, liver dysfunction, hypertension and raised serum lipids.

Drug interactions: Caution should be observed in prescribing oral contraceptives for patients taking other drugs since various interactions have been reported. Pregnancies have been reported in women taking oral contraceptives concurrently with rifampicin and other antibiotics, anti-epileptic drugs, barbiturates and other sedative drugs.

Steroids affect drug metabolism and the therapeutic or

toxic effects of other drugs may be modified. Interactions have been reported between oral contraceptives and tricyclic antidepressants, anticoagulants and corticosteroids.

Overdosage: No reports of serious ill-effects from overdosage with combined oral contraceptives have been reported. In general, therefore, treatment of overdosage is not necessary. If overdosage is, however, discovered within two or three hours and is so large that treatment seems desirable, gastric lavage or a suitable dose of ipecacuanha can be used. There are no specific antidotes and further treatment should be symptomatic.

Pharmaceutical precautions Store at, or below, room temperature.

Legal category POM.

Package quantities Trinordiol is supplied in packs of 21 tablets.

Further information Levonorgestrel is a totally synthetic progestogen which possesses no inherent oestrogenicity. It has anti-oestrogenic properties and has minimal effects on metabolic functions.

Research has shown that it is unnecessary to give the same doses of hormones throughout the cycle. The three-phase dosage mimics the secretion of hormones in a natural cycle and allows the total intake of steroids to be reduced while maintaining contraceptive efficacy and good cycle control.

Product licence number 0011/0066.

***Trade Mark**

Zyma (United Kingdom) Limited

Westhead

10 West Street

Alderley Edge

Cheshire SK9 7XP



FENOSTIL*

Presentation *Fenostil-Retard Tablets*: Round, biconvex, greyish-white in colour, stamped on one face with the Zyma logo and on the reverse with the initials KA: diameter 9 mm, thickness 4.4 mm. Each tablet contains 2.5 mg dimethindene maleate in an inert slow release matrix.

Uses Antihistamine.

Indicated for allergic conditions including hay fever, allergic rhinitis, urticaria, allergic dermatoses and pruritus.

Dosage and administration For oral administration.

Adults: 1 tablet, swallowed whole, morning and evening.

Children: No formulation of a dose suitable for children is available.

Contra-indications, warnings, etc There are no known contra-indications.

Warnings: May cause drowsiness: if affected do not drive or operate machinery. Avoid alcoholic drink.

In keeping with current medical practice, use during pregnancy should be avoided unless considered essential by a physician.

Treatment of overdose: There is no specific antidote to Fenostil. Immediate treatment consists of forced emesis followed by gastric lavage with luke-warm water and instillation of approximately 10 g activated charcoal and 20–30 g sodium sulphate dissolved in water. Should convulsions or hypertonicity occur these may be treated with diazepam or phenobarbitone injection. Severe respiratory depression may necessitate mechanical respiration.

Pharmaceutical precautions Store in a cool, dry place protected from light.

Legal category P.

Package quantities Containers of 100.

Further information Pharmacological studies show Fenostil to have a specific, potent, antihistaminic activity with low toxicity, long duration of action and one of the highest reported therapeutic ratios for an antihistaminic substance.

Product licence number 0030/5000.

ISMELIN* EYE DROPS

Presentation A clear colourless odourless solution containing guanethidine sulphate 5% w/v., with benzalkonium chloride BP as a preservative.

Uses Mode of Action.

The precise mechanism of action of Ismelin in reducing intra-ocular tension has not yet been fully determined,

but a working hypothesis could be envisaged in which the therapeutic benefits are mediated by a local effect on the release of catecholamines, particularly those involved in the transmission of sympathetic impulses from terminal nerve fibres to target organs. This would be in line with the generally accepted concept of Ismelin activity in anti-hypertensive therapy. In relation to the eye one would have to postulate that to a greater or lesser extent the following ocular conditions are related to sympathetic overactivity: exophthalmos, lid retraction and lid lag in thyrotoxicosis, and secretion of aqueous humor in glaucoma.

Indications:

The reduction of intra-ocular pressure in glaucoma of the open angle type.

The treatment of exophthalmos and lid retraction caused by endocrine imbalance.

Dosage and administration Ismelin eye drops are intended for local administration to the eye.

Dosage: Exophthalmos and lid retraction: Initially one drop twice daily for at least one week, reducing thereafter to one drop daily. The dosage should be reduced as soon as possible to the minimum required to maintain the initial response – one drop on alternate days may be adequate.

Open angle glaucoma: Initially one drop twice daily for at least a week. Dosage should then be adjusted according to the patient's needs, which may be one drop once or twice daily, or if necessary two drops once or twice daily, but rarely in excess of this.

Contra-indications, warnings, etc *Contra-indications*: Use in narrow angle glaucoma or in patients with a shallow anterior chamber. Hypersensitivity to any of the components of the formulation. Ismelin Eye Drops should not be used during or within 14 days of treatment with a monoamine oxidase inhibitor.

Precautions: Soft contact lenses (hydrophilic lenses) should not be worn during treatment with Ismelin Eye Drops.

Side-effects: Conjunctival vasodilation is regarded as a pharmacological side effect of Ismelin, but does not generally prove troublesome at the recommended dosage. Hyperaemia with discomfort is usually a sign of overdose. Some degree of ptosis, valuable in the management of exophthalmos, may represent an adverse effect in glaucoma but will usually respond to a reduction in dosage or frequency of administration. The slight myosis which occurs in most cases during Ismelin treatment causes little or no inconvenience and accommodation is not usually affected. At prolonged high dosage a tendency to superficial punctate keratitis has been reported, responding either to a reduction in dosage or interruption of treatment.

No systemic effects have been reported with Ismelin eye drops, even at maximum dosage.

Pharmaceutical precautions Store in a cool place.

Do not exceed the stated dose.

The drops should not be used later than one month after first breaking the seal.

Legal category POM.

Package quantities Ismelin eye drops 5 ml.

Further information The results of therapy with Ismelin eye drops have been in many cases dramatic, particularly in terms of cosmetic improvement of the unsightly eye manifestations such as lid retraction, lid lag and exophthalmos, which occur in a high proportion of patients with thyrotoxicosis.

There is minimal local irritation when the eye drops are used carefully according to the recommended dosage. Also considerable subjective relief of symptoms has been afforded even when the reduction in physical signs has been minimal.

Product licence number 0030/5901.

OTRIVINE-ANTISTIN* STERILE EYE DROPS

Presentation A clear colourless odourless solution containing xylometazoline hydrochloride 0.05% w/v and antazoline sulphate 0.5% w/v, with benzalkonium chloride BP as a preservative.

Uses Otrivine-Antistin is a combination of a long acting vaso-constrictor and an antihistamine. The eye drops are suitable for use in the relief of conjunctivitis associated with seasonal and perennial allergies, such as hay fever, and in all non-infective conditions of the conjunctiva, such as irritation caused by smoke or dust, or following the removal of foreign bodies.

Dosage and administration This preparation is intended for local administration to the eye.

Dosage: 1 or 2 drops instilled 2-3 times per day into the conjunctival sac will be found to be effective. Mydriatics and miotics may be administered simultaneously with Otrivine-Antistin Eye Drops when necessary.

Contra-indications, warnings, etc *Contra-indications:* Hypersensitivity to any of the components of the formulation. Presence of narrow angle glaucoma. Otrivine-Antistin Eye Drops should not be used during or within 14 days of treatment with a monoamine oxidase inhibitor.

Precautions: Use with caution in the presence of hypertension, cardiac irregularities, hyperthyroidism or hyperglycaemia (diabetes). Rebound congestion may follow prolonged frequent use. Soft contact lenses (hydrophilic lenses) should not be worn during treatment with Otrivine-Antistin Eye Drops. Inflammation arising from infection should receive appropriate antibacterial therapy.

Side effects: Both Otrivine and Antistin are well tolerated in the eye and for the majority of patients will be non-irritant, but in a few cases, however, slight transient local stinging may occur. Other side effects which may occur include headache, insomnia, drowsiness and in sensitive patients, tachycardia.

Pharmaceutical precautions Store in a cool place.

The drops should not be used later than one month after first breaking the seal.

Legal category P.

Package quantities Otrivine-Antistin Sterile Eye Drops 10 ml.

Further information Nil.

Product licence number 0030/5900.

PAROVEN*

Presentation Greyish-yellow, opaque, hard gelatin capsule (size No. 2) imprinted 'Paroven Zyma'. Each capsule contains 250 mg 0-(β -hydroxyethyl)-rutosides.

Uses Paroven improves capillary function by reducing abnormal leakage, probably by maintaining the integrity of endothelial cell junctions. Improved tissue perfusion increases the O₂ content of venous blood.

For long-term relief of the symptoms of capillary impairment (fragility and permeability) associated with venous insufficiency, especially of the lower limb, for example painful heavy tired legs, night cramps, paraesthesia, restless legs, ankle oedema, varicose states with or without ulceration, post-phlebitic syndrome. Haemorrhoids.

Dosage and administration For oral administration.

Adults: Initially 3-4 capsules per day. This dosage may be reduced as improvement occurs. The capsules are best taken at mealtimes.

Children: No known indication; therefore not recommended for children.

Contra-indications, warnings, etc There are no known contra-indications.

Side-effects: Minor complaints such as slight gastrointestinal upsets, flushes and headaches have been reported, although in most trials authors remarked on freedom from side-effects.

Precautions: Teratogenic studies in animals have revealed no adverse effects. However, in keeping with current medical practice, the use of Paroven during the first trimester of pregnancy should be avoided.

Pharmaceutical precautions No special storage requirements.

Legal category P.

Package quantities Containers of 100 capsules.

Further information Nil.

Product licence number 0030/5002.

TANDERIL* EYE OINTMENT

Presentation A white to yellowish-white soft ointment, containing 10% Oxyphebutazone BP as active ingredient and phenyl ethyl alcohol 0.5% as a preservative in a special paraffin base.

Uses Anti-inflammatory: Disease of the anterior segment of the eye and conjunctival sac: Blepharitis, conjunctivitis, kerato-conjunctivitis, episcleritis, keratitis and disease of the anterior uveal tract.

Inflammation following trauma:

Traumatic injury, penetrating and non-penetrating.

Post Operative:

Following cataract, squint or other surgical procedures.

Note: Herpes Simplex:

While Tanderil eye ointment is not recommended for the treatment of a simple dendritic ulcer it may prove particularly valuable in treating other stages of the disease which may develop, e.g. metaherpetic ulcer, disciform keratitis or anterior uveitis. In view of the serious nature of this disease, it is recommended that these patients be under close medical supervision and if necessary additional therapy be instituted.

Dosage and administration Apply to the affected eye two to five times a day.

Contra-indications, warnings, etc *Contra-indications:* Previous local or systemic sensitivity to pyrazole compounds such as phenylbutazone and oxyphenbutazone.

Side-effects: Intolerance to the eye ointment may develop after continued use, the signs being: oedema of the eyelid, epiphora (minimal), redness of the palpebral and bulbar conjunctiva.

Precautions: In the treatment of purulent inflammatory eye conditions, appropriate anti-infective therapy should be given concurrently with Tanderil eye ointment.

Although there is no evidence that Tanderil eye ointment increases intra-ocular pressure, it should be used with caution in cases of glaucoma secondary to injury or infection.

While application of Tanderil eye ointment results in adequate concentrations of Tanderil in the anterior part of the globe, to ensure maximum therapeutic effectiveness in the treatment of conditions involving the posterior uveal tract, retina or choroid, it is recommended that Tanderil be given systemically either alone or in combination with local application of the ointment.

Pharmaceutical precautions Store in a cool place.

Use within one month of opening the tube.

Dilutants to this formulation are not recommended.

Legal category POM.

Package quantities Ophthalmic tubes of 5 g.

Further information Experimental studies confirm that following local application of the ointment to the eye, Tanderil penetrates the corneoscleral barrier and is present in therapeutic concentrations in the aqueous humor, iris and ciliary body.

In therapeutic concentrations Tanderil does not affect lens metabolism, intra-ocular pressure in the normal eye or in latent glaucoma, nor does it impede tissue healing or promote cataract formation.

Furthermore, in contrast to the anti-inflammatory corticosteroids, Tanderil does not enhance viral replication or the invasiveness of bacterial pathogens.

Product licence number 0030/0017.

TANDERIL* CHLORAMPHENICOL EYE OINTMENT

Presentation A white to yellowish white soft ointment containing 10% Oxyphenbutazone BP and 1% Chloramphenicol BP as active ingredients and phenyl ethyl alcohol 0.5% as a preservative.

Uses Anti-inflammatory and antibacterial.

Disease of the anterior segment of the eye and conjunctival sac: blepharitis, conjunctivitis, episcleritis, keratitis and disease of the anterior uveal tract.

Inflammation of the eye following trauma and prophylaxis of secondary bacterial infection.

Post Operative:

Following squint, cataract or other surgical procedures

Note: Herpes Simplex:

The ointment is not contraindicated in the treatment of simple dendritic ulcer, but in view of the serious nature of this disease it is recommended that these patients be under close medical supervision and the necessary additional therapy be instituted.

Dosage and administration Apply to the inner surfaces of the lower lid of the affected eye two to five times daily.

Contra-indications, warnings, etc *Contra-indications:* Previous local or systemic sensitivity to pyrazole compounds such as phenylbutazone and oxyphenbutazone. Sensitivity to chloramphenicol.

Side-effects: Intolerance to the eye ointment may develop after continued use, the signs being: oedema of the eyelid, epiphora (minimal), redness of the palpebra and bulbar conjunctiva.

Pharmaceutical precautions Store in a cool place.

Use within one month of opening the tube.

Legal category POM.

Package quantities Ophthalmic tubes of 5 g.

Product licence number 0030/0018.

VIBROCIL*

Presentation *Nasal Spray and Nasal Drops:* A clear colourless solution with slight odour of lavender. Each 100 ml of solution contains:

Dimethindene maleate	0.025 g
Phenylephrine base	0.250 g
Neomycin sulphate	0.350 g

Nasal Gel: A colourless gel with slight odour of lavender. Each 100 g of Nasal Gel contains:

Dimethindene maleate	0.025 g
Phenylephrine base	0.250 g
Neomycin sulphate	0.350 g

Uses For common colds, acute and chronic rhinitis, allergic and vasomotor rhinitis, pollenosis (hay fever), acute and chronic sinusitis in children and adults.

Vibrocil does not interfere with the activity of the cilia.

Dosage and administration For topical application to the nasal mucosa.

Spray: Adults: 3 sprays in each nostril three to four times a day. For children the use of Drops or Gel is recommended.

Drops: Infants and children under six years: 1-2 drops in each nostril three to four times a day.

Children over six and adults: 3-4 drops in each nostril three to four times a day.

Gel: Apply a small quantity as high up the nostril as possible.

Adults: Use three to four times a day.

Children: Two to three times a day.

Contra-indications, warnings, etc Hypersensitivity to neomycin. Concurrent use in patients who are receiving monoamine oxidase inhibitors or have received them in the previous 14 days.

Precautions: The following precautions concerning the constituents should be noted:

Prolonged use of neomycin may result in the development of super-infection due to organisms, including fungi, resistant to neomycin. Neomycin may be toxic if absorbed from extensive open surfaces when symptoms of nephrotoxicity and ototoxicity could occur, particularly in patients with impaired renal function. Phenylephrine should be used with caution in patients with hypertension, cardiovascular disease or thyrotoxicosis; prolonged or excessive use may induce tachyphylaxis and rebound congestion.

Dimethindene maleate has potent antihistamine activity with low toxicity and a high therapeutic ratio but the possibility of drowsiness, as with other antihistamines in hypersensitive patients should be observed. If affected, the patient should not drive or operate machinery. Avoid alcoholic drink.

Side-effects: Vibrocil is very well tolerated and does not interfere with the activity of the nasal cilia.

Pharmaceutical precautions Store in a cool dry place protected from light.

Legal category POM.

Package quantities *Spray:* 10 ml nebulisers – plastic.

Drops: 15 ml amber dropper bottles with plastic screw cap.

Gel: 12 g in aluminium printed tubes with lacquered interior.

Further information Nil.

Product licence numbers

Gel 0030/5008

Spray 0030/5009

Drops 0030/5010

ZYMAFLUOR*

Presentation *Zymafluor 1.0 mg:* Round, bi-convex tablets with bevelled edge, greyish-yellow in colour, diameter 5 mm, thickness 2.1 mm. Each tablet contains 2.21 mg sodium fluoride equivalent to 1 mg available fluorine.

Zymafluor 0.25 mg: Round, bi-convex, white tablets, slightly sweet to the taste with odour of peppermint, diameter 4.0 mm, thickness 2.6 mm. Each tablet contains 0.55 mg sodium fluoride equivalent to 0.25 mg available fluorine.

Uses Prophylaxis of dental caries. Fluorine enhances the resistance of teeth to carious decay. The protective action of fluorine is due especially to its accumulation in the outer layers of the dental enamel. This process should begin before eruption of the teeth and continue for a long time afterwards.

Before eruption. Zymafluor when swallowed is carried

to the developing teeth by the blood stream and thus permits effective pre-eruptive fluoridation. After their eruption the teeth take up fluorine both by internal channels and especially by way of direct contact with the fluorine contained in the saliva. Zymafluor Tablets should thus not be swallowed whole: it is extremely important that they be allowed to dissolve slowly in the mouth.

Dosage and administration For oral administration. Not to be taken except on the advice of a dentist, doctor or pharmacist. Zymafluor should be given regularly, without interruption, from birth until about 16 years.

Intake of Zymafluor during pregnancy and feeding will protect the mother's teeth and lay down optimum conditions for a resistant set of milk teeth in her infant.

As soon as the age of the child permits, Zymafluor Tablets should no longer be swallowed, but sucked slowly in the mouth, between the cheek and gum, sometimes on the left and sometimes on the right side. They are best taken in the evening before bedtime. For smaller infants 1 tablet should be crushed and dissolved in a little boiled and cooled water and added to one bottle or solid meal a day, or administered alone.

Zymafluor 0.25 mg: If not otherwise prescribed by the doctor or dentist.

From birth to two years of age: 1 tablet daily.

From two to four years: 2 tablets daily.

From four to five years: 3 tablets daily.

After the age of 5 years Zymafluor is best administered in the form of 1 mg tablets.

Zymafluor 1.0 mg: From the age of 5 years, adults and pregnant women: 1 tablet daily or as prescribed by the doctor or dentist.

Contra-indications, warnings, etc There are no known contra-indications.

Precautions: It is unnecessary to take these tablets in areas where there is fluoridation of the drinking water supplies.

Pharmaceutical precautions Store in a cool dry place.

Legal category P.

Package quantities *0.25 mg strength:* Packs of 400.
1.0 mg strength: Packs of 100.

Further information Nil.

Product licence numbers

0.25 mg strength 0030/5011

1.0 mg strength 0030/5012

*Trade Mark

The reporting of adverse reactions

One of the functions of the Committee on Safety of Medicines is to collect and study reports of adverse reactions to medicines. All doctors and dentists in the United Kingdom are encouraged to report toxicity or side-effects that they observe or suspect.

Certain products which are marked ▼ are recent introductions, and doctors are therefore particularly requested to report details of all suspected adverse reactions to the Committee on Safety of Medicines, preferably on the yellow card issued by the Committee. They are asked to continue to report serious or unusual reactions to all other products.

Even incomplete reports can be helpful and practitioners should not be deterred from reporting because some details are not known.

Special postage-paid forms ('yellow cards') are provided for reports. Supplies of these can be obtained from the Committee at Market Towers, 1 Nine Elms Lane, London SW8 5NQ, telephone 01-720 2188.

The above statement and the symbols marking certain products have been included in the Compendium at the request of the Medicines Division of the Department of Health and Social Security.

The individual companies concerned would find it helpful to be informed by practitioners of any adverse reactions to their products which are reported.

Physiological Values for some Body Fluids

This information concerning physiological values for certain body fluids is reproduced, by permission, from the *Pharmaceutical Handbook*, Nineteenth Edition, The Pharmaceutical Press, London, 1980.

The values given in the following pages have been taken from many sources and represent approximate normal ranges or typical normal values. In practice 'normal' values can vary considerably from laboratory to laboratory depending on the reagents and analytical methods used. Therefore when evaluating the results of laboratory tests the normal values from the laboratory which performed the test should be consulted.

Many factors affect the reliability of laboratory tests. The specimen must be withdrawn and stored in the correct manner, an appropriate preservative being used if necessary. Certain values fluctuate in every person according to diurnal, nocturnal, or seasonal influences. Other factors, such as exercise, posture, stress, or emotional disturbances, and the age and sex of the patient may also influence the results of laboratory tests.

Many drugs and foods can interfere with laboratory tests. This interference may be physical, chemical, or pharmacological. Dyes may interfere with colorimetric or spectrometric determinations. For example, ingestion of carrots, riboflavin, or foods containing yellow pigment prior to withdrawal of a sample will elevate estimates of total bilirubin in plasma. Many chemicals can cause test results to appear abnormally high or low. High values for catecholamines in urine may be obtained if the patient is taking drugs such as methyl dopa. The pharmacological effects of drugs may interfere with laboratory test results. Antihistamines interfere with tests for allergies and mask hypersensitivities.

In the following tables these abbreviations are used: B = Blood; P = Plasma; S = Serum.

BLOOD

Physical Values

Circulation time	3 to 8 seconds (arm to lung)
Freezing-point	-0.52°
Osmolality, plasma	280 to 295 mmol per kg
pH, arterial	7.35 to 7.45
Pressure, arterial	
Systolic	< 140 mmHg
Diastolic	< 90 mm Hg
Specific gravity	1.05 to 1.06
Volume, blood	50 to 80 ml per kg body-weight
Volume, plasma	31 to 55 ml per kg body-weight

Haematological Values

Blood count, complete	
Haematocrit (Packed cell volume)	Male: 40 to 54% Female: 35 to 47%
Haemoglobin	Male: 13 to 18 g per 100 ml Female: 12 to 16 g per 100 ml
Red cell count	Male: 4.5 to 6.5 million per mm ³ or 4.5 to 6.5 × 10 ¹² per litre Female: 3.9 to 5.6 million per mm ³ or 3.9 to 5.6 × 10 ¹² per litre 4000 to 11 000 per mm ³
White cell count	
Coagulation tests	
Bleeding time	
Duke's method	< 7 minutes
Ivy method	< 7 minutes
Clotting time, Lee White method	5 to 11 minutes
Partial thromboplastin time, activated	35 to 60 seconds
Prothrombin time, Quick one stage	12 to 20 seconds
Erythrocyte sedimentation rate (ESR), Westergren method	Male: 3 to 5 mm in 1 hour Female: 4 to 7 mm in 1 hour
Haemoglobin A ₂	1.5 to 3.5%
Haemoglobin F	< 2%
Haptoglobin	0.3 to 2.0 g per litre
Platelet count	150 000 to 400 000 per mm ³ or per µl
Red cell diameter	6.7 to 7.7 µm average 7.2 µm
Red cell thickness	1.7 to 2.5 µm
Red cell volume	23 to 35 ml per kg body-weight
Reticulocyte count	0.5 to 2.0% of red cells
White cell count, differential	
Neutrophils, segmented	2500 to 7500 per mm ³ or per µl
Lymphocytes	1500 to 3500 per mm ³ or per µl
Monocytes	200 to 800 per mm ³ or per µl
Eosinophils	40 to 440 per mm ³ or per µl
Basophils	15 to 100 per mm ³ or per µl

BLOOD—continued**Blood Gases and Acid-Base Values**

Base excess	± 2.3 mmol per litre
Bicarbonate	
Plasma	21 to 30 mmol per litre
Standard	22 to 28 mmol per litre
Buffer base	45 to 50 mmol per litre
Carbon dioxide	
Arterial $p\text{CO}_2$	36 to 44 mmHg
Total CO_2	23 to 33 mmol per litre
Oxygen	
Arterial $p\text{O}_2$	90 to 110 mmHg

Chemical Values

		<i>Metric</i>	<i>SI</i>
Alpha-amino acid nitrogen	P	30 to 55 mg per litre	2.1 to 4 mmol per litre
Ammonium nitrogen (enzymatic method)	B	400 to 800 µg per litre	29 to 57 µmol per litre
Amylase	S	0.8 to 1.8 Somogyi units per ml 3 to 10 Wohlgemuth units per ml 86 to 268 iu per litre	— — —
Angiotensin II	B	12 to 36 ng per litre	11.6 to 34.9 pmol per litre
Ascorbic acid	B	5 to 20 mg per litre	28 to 114 µmol per litre
Bicarbonate	P	—	21 to 28 mmol per litre
Bilirubin,			
total	S	1 to 15 mg per litre	1.7 to 25 µmol per litre
total newborn	S	10 to 120 mg per litre	17 to 205 µmol per litre
Caeruloplasmin,			
adult	S	300 to 600 mg per litre	—
child	S	130 to 300 mg per litre	—
Calcium,			
total	S	85 to 105 mg per litre	2.1 to 2.6 mmol per litre
ionised	S	40 to 50 mg per litre	1 to 1.25 mmol per litre
Catecholamines,			
at rest			
Adrenaline	P	55 ng per litre	0.3 nmol per litre
Nor-adrenaline	P	254 ng per litre	1.5 nmol per litre
Chloride	S	3.368 to 3.723 g per litre (as chloride)	95 to 105 mmol per litre
	or		
	P		
Copper	S	0.7 to 1.5 mg per litre	11 to 24 µmol per litre
	or		
	P		
Cortisol 9 am	P	50 to 260 µg per litre	138 to 717 nmol per litre
5 pm	P	20 to 180 µg per litre	55 to 497 nmol per litre
Creatinine	S	6 to 15 mg per litre	53 to 133 µmol per litre
	or		
	P		
Cyanocobalamin	S	100 to 800 ng per litre	74 to 590 pmol per litre
Fibrinogen	P	2 to 4 g per litre	—
Folate	S	3 to 25 µg per litre	—
Gastrin	S,	5 to 290 ng per litre	—
	or		
	P		
Glucagon	P	0.4 to 1.4 µg per litre	115 to 402 pmol per litre
Glucose, fasting	S	0.7 to 1.1 g per litre	3.9 to 6.1 mmol per litre
	or		
	P		
Growth hormone	S	< 10 µg per litre	—
Immunoglobulins	S		
IgA		0.5 to 4 g per litre	—
IgD		5 to 50 mg per litre	—
IgE		0.1 to 1.3 mg per litre	—
IgG		8 to 16 g per litre	—
IgM		0.4 to 2.9 g per litre	—
Insulin	S	4 to 30 milliunits per litre	—
Iodine, protein-bound (PBI)	S	35 to 80 µg per litre	276 to 630 nmol per litre
Iron, total	S	0.5 to 1.8 mg per litre	9 to 32 µmol per litre
Iron-binding capacity	S	2.5 to 4.5 mg per litre	45 to 81 µmol per litre

PHYSIOLOGICAL VALUES

BLOOD—continued

	<i>Metric</i>	<i>SI</i>
stones (acetoacetate and acetone)	B <30 mg per litre	—
lactic acid,		
arterial	B 30 to 70 mg per litre	0.3 to 0.8 mmol per litre
venous	B 50 to 200 mg per litre	0.56 to 2.2 mmol per litre
urea	B <800 µg per litre	<3.9 µmol per litre
lipids,		
total	S 4 to 10 g per litre	—
cholesterol	S 1.1 to 3.0 g per litre	2.8 to 7.8 mmol per litre
triglycerides	S 0.4 to 1.5 g per litre	—
magnesium	S 18 to 30 mg per litre	0.7 to 1.2 mmol per litre
phenylalanine	S <40 mg per litre	<242 µmol per litre
phosphatase,		
acid, total	S 0.5 to 4 King-Armstrong units per 100 ml	—
alkaline, total	S 4 to 13 King-Armstrong units per 100 ml	—
phosphorus, inorganic adults	S	
	or 25 to 45 mg per litre	0.8 to 1.5 mmol per litre
potassium	P 137 to 196 mg per litre	3.5 to 5 mmol per litre
olactin	S 2 to 15 µg per litre	—
roteins,		
total serum	S 60 to 84 g per litre	—
albumin	S 30 to 52 g per litre	—
globulin	S 23 to 37 g per litre	—
uric acid	B 3 to 10 mg per litre	34 to 114 µmol per litre
uridium	P 3.1 to 3.4 g per litre	135 to 148 mmol per litre
phosphate, inorganic	S 9 to 60 mg per litre	94 to 625 µmol per litre
transaminases		
SGOT	S 0 to 30 iu per litre	—
SGPT	S 0 to 24 iu per litre	—
thyroid hormone tests		
Thyroid stimulating hormones (TSH)	S 0.5 to 3.5 milliunits per litre	—
T ₃ (Radio-immuno-assay)	S 0.7 to 1.9 µg per litre	—
T ₄ (radio-immuno-assay)	S 40 to 120 µg per litre	—
T ₄ Free	S 10 to 40 ng per litre	—
urea nitrogen (BUN)	B 80 to 250 mg per litre	5.7 to 17.9 mmol per litre
	or	
	S	
urea	B 171 to 535 mg per litre	2.9 to 8.9 mmol per litre
uric acid	S 15 to 70 mg per litre	89 to 417 µmol per litre
vitamin A	S 150 to 900 µg per litre	0.5 to 3.1 µmol per litre
vitamin C	S 0.5 to 1.5 mg per litre	8 to 23 µmol per litre

CEREBROSPINAL FLUID

Physical Values

Freezing-point	−0.540° to −0.603°
Osmolality	306 mmol per kg
pH	7.33 to 7.37
Pressure	60 to 180 mm of water
Specific gravity	1.0062 to 1.0082
Volume, adults	100 to 160 ml

Chemical Values

Calcium	1 to 1.5 mmol per litre
Chloride	120 to 130 mmol per litre
Glucose	2.5 to 4.5 mmol per litre
Lactate dehydrogenase	0.2 to 4 iu per ml
Protein	
Lumbar	150 to 500 mg per litre
Cisternal	100 to 300 mg per litre
Ventricular	0 to 150 mg per litre
Albumin/Globulin ratio	2:1
Infants < 1 year	1:1
Albumin	100 to 300 mg per litre
Globulin	60 to 160 mg per litre
Urea	2 to 7 mmol per litre

URINE

Physical Values

Glomerular filtration rate	100 to 150 ml per minute
Osmolality	100 to 1000 mmol per kg
pH	4.5 to 8.0
Specific gravity	1.010 to 1.025
Volume, normal adult	800 to 2000 ml per 24 hours

Chemical Values

	<i>Metric</i>	<i>SI</i>
α Amino acid nitrogen	50 to 300 mg per 24 h	3.6 to 21.4 mmol per 24 h
δ Aminolaevulinic acid	0.1 to 7.5 mg per 24 h	0.8 to 57 μ mol per 24 h
Calcium	100 to 300 mg per 24 h	2.5 to 7.5 mmol per 24 h
Catecholamines		
Adrenaline	< 20 μ g per 24 h	< 109 nmol per 24 h
Nor-adrenaline	< 100 μ g per 24 h	< 591 nmol per 24 h
Chloride	3.545 to 8.863 g per 24 h	100 to 250 mmol per 24 h
Creatine, adults	0 to 100 mg per 24 h	0 to 763 μ mol per 24 h
Creatinine	1 to 2 g per 24 h	8 to 18 mmol per 24 h
Formiminoglutamic acid (FIGLU)	0 to 3 mg per 24 h	0 to 17 μ mol per 24 h
After 15 g of L-Histidine	4 mg per 8 h	23 μ mol per 8 h
Homovanillic acid (HVA)	0 to 15 mg per 24 h	0 to 82 μ mol per 24 h
Hydroxyindole acetic acid (HIAA)	3 to 14 mg per 24 h	16 to 73 μ mol per 24 h
Lead	< 100 μ g per 24 h	< 483 nmol per 24 h
Magnesium	49 to 243 mg per 24 h	2 to 10 mmol per 24 h
Oxalate	15 to 40 mg per 24 h	167 to 444 μ mol per 24 h
Phosphate, inorganic	0.5 to 1.5 g per 24 h	16 to 48 μ mol per 24 h
Potassium	1.4 to 3.5 g per 24 h	35 to 90 mmol per 24 h
Protein	< 100 mg per 24 h	—
Urea	10 to 30 g per 24 h	167 to 500 mmol per 24 h
Uric acid, normal diet	0.2 to 0.5 g per 24 h	1.2 to 3 mmol per 24 h
high purine diet	up to 2 g per 24 h	up to 12 mmol per 24 h
Vanillylmandelic acid (VMA)	up to 9 mg per 24 h	up to 45 μ mol per 24 h

Clearance Values*Serum and Urine*

Aminohippuric acid (PAH) clearance	600 to 750 ml per min
Creatinine clearance (endogenous)	95 to 135 ml per min
Inulin clearance	100 to 150 ml per min
Urea clearance	
average standard	41 to 65 ml per min
average maximum	64 to 99 ml per min

'Desirable' Weights for Men and Women

'Desirable' weights for men and women according to height and frame. Ages 25 and over. USA.

Source: Metropolitan Life Insurance Co. (1960)

MEN. Weight in pounds (in indoor clothing).

<i>Height (in shoes)</i>	<i>Small frame</i>	<i>Medium frame</i>	<i>Large frame</i>
5 ft. 2 in.	112 – 120	118 – 129	126 – 141
5 ft. 3 in.	115 – 123	121 – 133	129 – 144
5 ft. 4 in.	118 – 126	124 – 136	132 – 148
5 ft. 5 in.	121 – 129	127 – 139	135 – 152
5 ft. 6 in.	124 – 133	130 – 143	138 – 156
5 ft. 7 in.	128 – 137	134 – 147	142 – 161
5 ft. 8 in.	132 – 141	138 – 152	147 – 166
5 ft. 9 in.	136 – 145	142 – 156	151 – 170
5 ft. 10 in.	140 – 150	146 – 160	155 – 174
5 ft. 11 in.	144 – 154	150 – 165	159 – 179
6 ft. 0 in.	148 – 158	154 – 170	164 – 184
6 ft. 1 in.	152 – 162	158 – 175	168 – 189
6 ft. 2 in.	156 – 167	162 – 180	173 – 194
6 ft. 3 in.	160 – 171	167 – 185	178 – 199
6 ft. 4 in.	164 – 175	172 – 190	182 – 204

WOMEN. Weight in pounds (in indoor clothing).

<i>Height (in shoes)</i>	<i>Small frame</i>	<i>Medium frame</i>	<i>Large frame</i>
4 ft. 10 in.	92 – 98	96 – 107	104 – 119
4 ft. 11 in.	94 – 101	98 – 110	106 – 122
5 ft. 0 in.	96 – 104	101 – 113	109 – 125
5 ft. 1 in.	99 – 107	104 – 116	112 – 128
5 ft. 2 in.	102 – 110	107 – 119	115 – 131
5 ft. 3 in.	105 – 113	110 – 122	118 – 134
5 ft. 4 in.	108 – 116	113 – 126	121 – 138
5 ft. 5 in.	111 – 119	116 – 130	125 – 142
5 ft. 6 in.	114 – 123	120 – 135	129 – 146
5 ft. 7 in.	118 – 127	124 – 139	133 – 150
5 ft. 8 in.	122 – 131	128 – 143	137 – 154
5 ft. 9 in.	126 – 135	132 – 147	141 – 158
5 ft. 10 in.	130 – 140	136 – 151	145 – 163
5 ft. 11 in.	134 – 144	141 – 155	149 – 168
6 ft. 0 in.	138 – 148	144 – 159	153 – 174

The above information is reproduced, by permission, from Obesity and Disease, Office of Health Economics, London, 1969.

Obstetric Table

Calculated from the first day of the last menstrual period.

January October	1 8	2 9	3 10	4 11	5 12	6 13	7 14	8 15	9 16	10 17	11 18	12 19	13 20	14 21	15 22	16 23	17 24	18 25	19 26	20 27	21 28	22 29	23 30	24 31	25 1	26 2	27 3	28 4	29 5	30 6	31 7	January November
February November	1 8	2 9	3 10	4 11	5 12	6 13	7 14	8 15	9 16	10 17	11 18	12 19	13 20	14 21	15 22	16 23	17 24	18 25	19 26	20 27	21 28	22 29	23 30	24 1	25 2	26 3	27 4	28 5				February December
March December	1 6	2 7	3 8	4 9	5 10	6 11	7 12	8 13	9 14	10 15	11 16	12 17	13 18	14 19	15 20	16 21	17 22	18 23	19 24	20 25	21 26	22 27	23 28	24 29	25 30	26 31	27 1	28 2	29 3	30 4	31 5	March January
April January	1 6	2 7	3 8	4 9	5 10	6 11	7 12	8 13	9 14	10 15	11 16	12 17	13 18	14 19	15 20	16 21	17 22	18 23	19 24	20 25	21 26	22 27	23 28	24 29	25 30	26 31	27 1	28 2	29 3	30 4		April February
May February	1 5	2 6	3 7	4 8	5 9	6 10	7 11	8 12	9 13	10 14	11 15	12 16	13 17	14 18	15 19	16 20	17 21	18 22	19 23	20 24	21 25	22 26	23 27	24 28	25 29	26 30	27 1	28 2	29 3	30 4	31 5	May March
June March	1 8	2 9	3 10	4 11	5 12	6 13	7 14	8 15	9 16	10 17	11 18	12 19	13 20	14 21	15 22	16 23	17 24	18 25	19 26	20 27	21 28	22 29	23 30	24 31	25 1	26 2	27 3	28 4	29 5	30 6		June April
July April	1 7	2 8	3 9	4 10	5 11	6 12	7 13	8 14	9 15	10 16	11 17	12 18	13 19	14 20	15 21	16 22	17 23	18 24	19 25	20 26	21 27	22 28	23 29	24 30	25 1	26 2	27 3	28 4	29 5	30 6	31 7	July May
August May	1 8	2 9	3 10	4 11	5 12	6 13	7 14	8 15	9 16	10 17	11 18	12 19	13 20	14 21	15 22	16 23	17 24	18 25	19 26	20 27	21 28	22 29	23 30	24 31	25 1	26 2	27 3	28 4	29 5	30 6	31 7	August June
September June	1 8	2 9	3 10	4 11	5 12	6 13	7 14	8 15	9 16	10 17	11 18	12 19	13 20	14 21	15 22	16 23	17 24	18 25	19 26	20 27	21 28	22 29	23 30	24 1	25 2	26 3	27 4	28 5	29 6	30 7		September July
October July	1 8	2 9	3 10	4 11	5 12	6 13	7 14	8 15	9 16	10 17	11 18	12 19	13 20	14 21	15 22	16 23	17 24	18 25	19 26	20 27	21 28	22 29	23 30	24 31	25 1	26 2	27 3	28 4	29 5	30 6	31 7	October August
November August	1 8	2 9	3 10	4 11	5 12	6 13	7 14	8 15	9 16	10 17	11 18	12 19	13 20	14 21	15 22	16 23	17 24	18 25	19 26	20 27	21 28	22 29	23 30	24 31	25 1	26 2	27 3	28 4	29 5	30 6		November September
December September	1 7	2 8	3 9	4 10	5 11	6 12	7 13	8 14	9 15	10 16	11 17	12 18	13 19	14 20	15 21	16 22	17 23	18 24	19 25	20 26	21 27	22 28	23 29	24 30	25 1	26 2	27 3	28 4	29 5	30 6	31 7	December October

New Products

The following names appear in the index to this issue of the Compendium but did not appear in the 1981-82 edition. It does not necessarily follow that they are recently introduced products.

Abicol 200	Glykola 1186	Opulets Benoxinate 38
Albuminar 77	H-B Vax 837	Opulets Chloramphenicol 38
Alcoderm 40	Healonid 987	Opulets Cyclopentolate 38
Alexan 959	Hexabrix 707	Opulets Fluorescein Sodium 39
Alpha Keri Bath Oil 226	Histoacryl 327	Opulets Sodium Chloride 39
Aluhyde 1183	Human Actrapid 895	Orimeten 294
Antepsin 107	Human Monotard 895	Oruvail 718
Intraderm 241	Hydrenox 207	Ossopan 588
Aspin 71	Hydrocortistab 207	Ovol 1001
Aspoxolox 73	Hyprenan 99	
Attenuvax 835		Pabrinex 944
		Pendramine 753
Benzalip 730	Ichthaband 1181	Percutol 1012
Biliscopin 1138	Inderex 526	Pipril 620
Bi-Novum 925	Isoket 1127	Polytrim 1398
Bronchodil 571		Psorox 414
		Pyralvex 882
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Non-proprietary/Proprietary Names Index

This index of non-proprietary names is provided to enable users of the Compendium to identify the brand names of relevant products when only non-proprietary names are known.

It should be noted that although different products may contain the same active ingredient this does not imply that they are equivalent in regard to bio-availability or therapeutic activity.

Some products contain a number of ingredients and it has not been possible in every instance to identify such products by a reference in this index to each ingredient.

** Products with an asterisk contain a number of active ingredients and may be available in more than one formulation.*

Products without an asterisk contain a single active ingredient; in certain instances such products may also be available with added constituents and these formulations are often designated by the principal brand name with the addition of a suffix or other mark of distinction.

Where a number of presentations of a product bear the same proprietary name, the page number given below is that of the first of the respective entries.

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